Opthea Finalizes Study Designs and Start-up Activities for Phase 3 Pivotal Clinical Trials of OPT-302 in Wet AMD

February 24, 2021

- ***Following consultations with US FDA and EU EMA, two pivotal Phase 3 clinical trial designs are finalized to assess 2 mg OPT-302 administered 4-weekly or 8-weekly in combination with Lucentis® (ShORe study) and Eylea® (COAST study) standard of care***
- ***Internationally recognized retinal disease specialists, Prof Timothy Jackson and Dr Charles Wykoff, named Chief investigators for the ShORe and COAST trials, respectively. In addition, Dr Jason Slakter, founder of the Digital Angiography Reading Center (DARC) in New York, will contribute expertise in ocular imaging.***
- ***Opthea confirms planned initiation of Pivotal Phase 3 trials remains on-track for CY 1Q'21***

MELBOURNE, Australia, Feb. 24, 2021 (GLOBE NEWSWIRE) -- Opthea Limited (ASX:OPT; Nasdaq: OPT), a clinical stage biopharmaceutical company developing a novel therapy to treat highly prevalent and progressive retinal diseases, today announces that it has finalized the protocol study designs and key start-up activities in readiness for the initiation of the Phase 3 ShORe and COAST pivotal clinical trials of OPT-302 in wet age-related macular degeneration (AMD).

Finalization of the Phase 3 trial protocols follows productive consultations with the FDA, EMA and world-renowned Key Opinion Leaders (KOLs) in wet AMD. The trial protocols have also been submitted to relevant regulatory agencies, institutional review boards and human research ethics committees.

Two global experts in the treatment of retinal diseases, Prof Timothy Jackson and Dr Charles Wykoff, will be the Chief investigators for the ShORe *(**S**tudy of **O**PT-302 in combination with **R**anibizumab)* and COAST *(**C**ombination **O**PT-302 with **A**flibercept **St**udy)* trials, respectively.

Professor Jackson, PhD, FRCOphth, is a consultant ophthalmic surgeon at King's College, London, and was also the Chief Investigator on the Opthea Phase 2b wet AMD clinical trial. Dr Wykoff, MD PhD, is the Director of Research, Retina Consultants of Texas and Deputy Chair for Ophthalmology, Blanton Eye Institute, Houston Methodist Hospital, Houston Texas. Another eminent retina specialist, Dr Jason Slakter, founder and Director of the Digital Angiography Reading Center (DARC) in New York, and Clinical Professor of Ophthalmology at NYU School of Medicine, will also provide expertise as a leading authority on ocular imaging for the Phase 3 clinical program.

"The collaborative nature of our study protocol discussions with our KOLs, the FDA and EMA has been very pleasing and the constructive input received ensures that the design of the OPT-302 Phase 3 program has the potential to generate compelling and persuasive clinical data capable of satisfying regulatory requirements," said Dr Megan Baldwin, Chief Executive Officer of Opthea. "With the achievement of other key start-up milestones, including successful scale-up of manufacturing and fill-finish of OPT-302 drug product for use in the trials, we now excitedly look forward to initiating the pivotal Phase 3 studies that are designed to support potential marketing approval of OPT-302 for the treatment of wet AMD."

The global, multi-centre, double-masked, sham-controlled, pivotal Phase 3 clinical trials will each enrol ~990 treatment-naive patients and assess the efficacy and safety of intravitreal 2.0 mg OPT-302 in combination with 0.5 mg ranibizumab (Lucentis®) (ShORe trial) or 2.0 mg aflibercept (Eylea®) (COAST trial), compared to ranibizumab or aflibercept monotherapy, respectively. In addition, extended durability of the OPT-302 treatment effect on clinical outcomes with less frequent every eight-weekly dosing will be compared with OPT-302 administered on an every four-weekly dosing regimen, in combination with each VEGF-A inhibitor. If effective in these Phase 3 studies, OPT-302 could be adopted for administration with either Eylea or Lucentis which had combined sales for retinal diseases of USD$11.9 billion in 2019.

The primary endpoint for both trials is the mean change in Best Corrected Visual Acuity from baseline to week 52 for OPT-302 combination therapy compared to anti-VEGF-A monotherapy. Each patient will continue to be treated for a further year to evaluate extended safety and tolerability over a two-year period.

Opthea remains on track to initiate the trials in the first quarter of calendar year (CY) 2021 and to report top-line data in the second half CY 2023. If the results at the completion of the primary efficacy phase at week 52 of the Phase 3 clinical trials are favourable, the Company intends to submit Biologics License and Marketing Authorisation Applications with the FDA and EMA respectively for marketing approval for OPT-302 for the treatment of wet AMD in the United States, European Union and other global territories.

Additional information on Opthea's technology and clinical trials can be found appended to this announcement and at www.opthea.com.

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About the ShORe Pivotal Phase 3 Clinical Trial

In the Study of OPT-302 in combination with Ranibizumab, or ShORe, Phase 3 trial, ~990 treatment-naive patients with wet AMD will be randomized 1:1:1 to one of three treatment groups. Patients randomized to the standard OPT-302 dosing arm will receive standard of care 0.5 mg ranibizumab every four weeks in combination with 2.0 mg OPT-302 on a every 4-week dosing regimen. In the extended OPT-302 dosing arm, 0.5 mg ranibizumab will be administered every four weeks to week 52, in combination with 2.0 mg OPT-302 administered every four weeks for three loading doses, followed by OPT-302 dosing on an every 8-week dosing regimen to week 52, with a sham injection given at visits where OPT-302 is not administered. Patients randomized to the control arm will receive 0.5 mg ranibizumab in combination with sham intravitreal injections administered every four weeks to week 52.

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/a9349638-ba1f-4094-a755-8093a4bbdbde

About the COAST Pivotal Phase 3 Clinical Trial

In the Combination OPT-302 with Aflibercept STudy, or COAST, Phase 3 trial, ~990 treatment-naive wet AMD patients will be randomized 1:1:1 to one of three treatment groups. Patients randomized to the standard OPT-302 dosing arm will receive 2.0 mg aflibercept administered every four weeks for three loading doses, followed by aflibercept dosing every eight weeks to week 52, in combination with 2.0 mg OPT-302 administered every four weeks to week 52. In the extended OPT-302 dosing arm, 2.0 mg aflibercept in combination with 2.0 mg OPT-302 will be administered every four weeks for three loading doses, followed by dosing every eight weeks to week 52, with a sham injection given at visits where OPT-302 and aflibercept are not administered. Patients randomized to the control arm, will receive 2.0 mg aflibercept administered every four weeks for three loading doses, followed by dosing every eight weeks to week 52, in combination with sham intravitreal injections administered every four weeks to week 52.

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/de959ea2-dff3-4f9b-9754-ca756a624883

The primary and secondary efficacy outcomes for both Phase 3 studies will be determined at the end of the efficacy phase at week 52. Each patient will then continue to be treated for an additional year through week 100 to further evaluate safety and tolerability over a total two-year period.

About Opthea

Opthea (ASX:OPT; Nasdaq: OPT) is a biopharmaceutical company developing a novel therapy to address the unmet need in the treatment of highly prevalent and progressive retinal diseases, including wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME). Opthea's lead product candidate OPT-302 is being developed for use in combination with anti-VEGF-A monotherapies to achieve broader inhibition of the VEGF family, with the goal of improving overall efficacy and demonstrating superior vision gains over that which can be achieved by inhibiting VEGF-A alone.

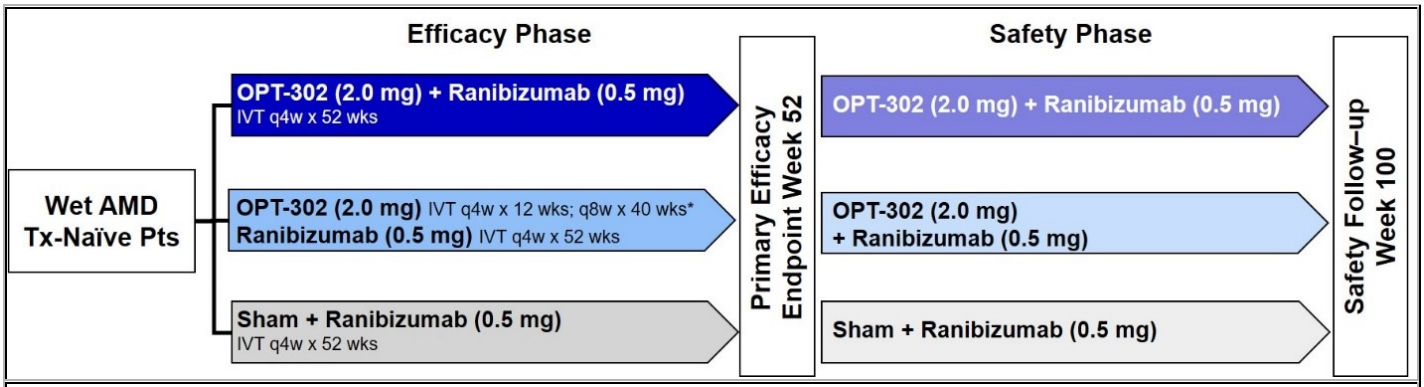
Inherent risks of Investment in Biotechnology Companies

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 commercialization 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 specializing 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

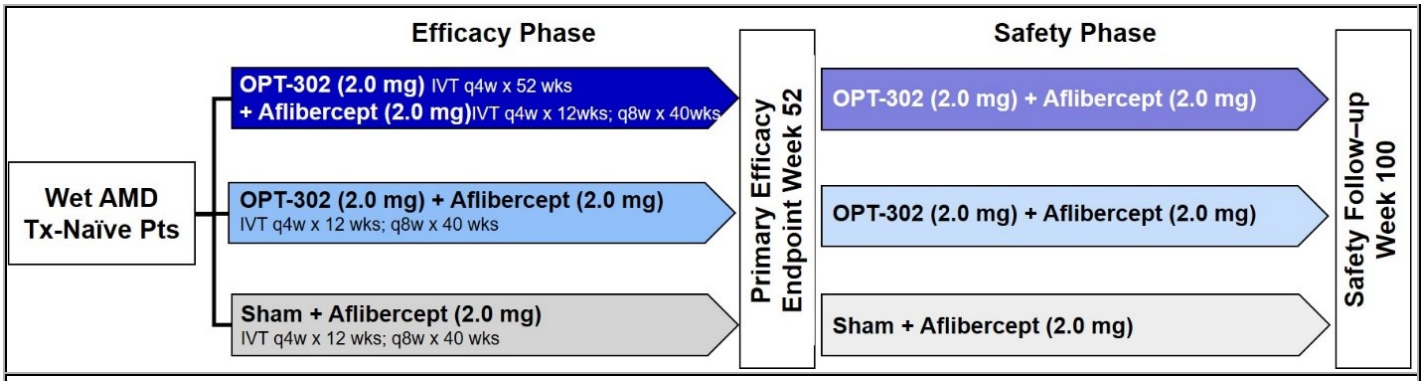
Certain statements in this announcement may contain forward-looking statements, including within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Any statement describing Company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at risk statement, including, but not limited to, the initiation of patient recruitment for Opthea's planned pivotal Phase 3 clinical trials of OPT-302 in wet AMD. Such statements are based on Opthea's current plans, objectives, estimates, expectations and intentions and are subject to certain risks and uncertainties, including risks and uncertainties associated with clinical trials and product development and the impact of general economic, industry or political conditions in Australia, the United States or internationally. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in the final prospectus filed with the SEC on October 19, 2020. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required under applicable law. You should not place undue reliance on these forward-looking statements as predictions of future events, which statements apply only as of the date of this announcement. Actual results could differ materially from those discussed in this ASX announcement.

ShORe Pivotal Phase 3 Clinical Trial



OPT-302 in combination with Ranibizumab

COAST Pivotal Phase 3 Clinical Trial



OPT-302 with Aflibercept