Opthea Completes Enrollment in First Pivotal Trial with Sozinibercept

February 14, 2024

COAST trial is evaluating the superiority of sozinibercept combined with EYLEA® (aflibercept) over EYLEA alone in wet AMD

Enrollment of second pivotal trial (ShORe) to complete in calendar Q2 2024

COAST and ShORe top-line results expected by mid-2025

MELBOURNE, Australia, Feb. 14, 2024 (GLOBE NEWSWIRE) -- Opthea Limited (ASX:OPT; NASDAQ:OPT), a clinical-stage biopharmaceutical company developing novel therapies to treat highly prevalent and progressive retinal diseases, today announced that it has completed enrollment of all patients in the COAST Phase 3 pivotal clinical trial investigating sozinibercept (OPT-302, a vascular endothelial growth factor (VEGF)-C/D inhibitor) in combination with aflibercept, an anti-VEGF-A therapy, for the treatment of wet Age-related Macular Degeneration (wet AMD). The sozinibercept clinical program includes two Phase 3 pivotal trials, COAST and ShORe. Enrollment in ShORe is expected to be completed in calendar Q2 2024. Opthea intends to report topline results from these two trials by mid-2025.

"Completion of patient enrollment in our first pivotal trial marks an important milestone in the development of sozinibercept for the treatment of wet AMD. We believe sozinibercept has the potential to provide superior clinical results, based on the strength of our Phase 2b trial, which demonstrated a statistically significant improvement in visual acuity for patients treated with sozinibercept combined with LUCENTIS® (ranibizumab) compared to ranibizumab alone," said Frederic Guerard, PharmD, Chief Executive Officer of Opthea. "We look forward to maintaining this positive momentum and completing enrollment in the ShORe pivotal trial in calendar Q2 2024, with a goal of communicating topline results for both trials by mid-2025."

Dr. Charles C. Wykoff, M.D., PhD, a board-certified Medical and Surgical Retina Specialist, Director of Research at Retina Consultants of Texas™, and Chief Investigator of the Phase 3 COAST trial, commented, "A tremendous thank you to the patients and families participating in our clinical program and also to our investigators and study coordinators. Your dedication and invaluable contributions have played a vital role in the development of this exciting new therapy. Sozinibercept, when used in combination with standard of care anti-VEGF-A treatment, has the potential to be the first therapy to achieve superior visual outcomes over anti-VEGF-A monotherapy and meaningfully improve outcomes for patients with wet AMD."

About Sozinibercept

Sozinibercept (OPT-302) is a soluble form of vascular endothelial growth factor receptor 3 (VEGFR-3) expressed as an immunoglobulin G1 (IgG1) Fc-fusion protein. It binds and neutralizes the activity of VEGF-C and VEGF-D on their endogenous receptors, VEGFR-2 and VEGFR-3. Research indicates that targeted inhibition of VEGF-C and VEGF-D can prevent blood vessel growth and vascular leakage which contribute to the pathophysiology of retinal diseases including wet AMD. Sozinibercept has received Fast Track Designation from the U.S. FDA for the treatment of wet AMD.

Positive results from the Phase 2b study of sozinibercept, administered in combination with LUCENTIS® (ranibizumab) for the treatment of wet AMD, published in *Ophthalmology*, met the pre-specified primary efficacy endpoint of a statistically superior gain in visual acuity at 24 weeks, compared to ranibizumab alone. In addition, secondary outcomes were positive for the combination therapy with sozinibercept, including more participants with gains in vision of 10 or more letters, improved anatomy with reduction in swelling and vascular leakage, with a favorable safety profile.

About COAST and ShORe Phase 3 Clinical Trials

Opthea is conducting two concurrent global pivotal Phase 3 clinical trials for the treatment of wet AMD aiming at demonstrating superiority of its combination therapy versus standard of care: COAST (Combination OPT-302 with Aflibercept Study) and ShORe (Study of OPT-302 in combination with Ranibizumab). If successful, the investigation of sozinibercept in combination with each of these two approved standard of care VEGF-A inhibitors could enable sozinibercept to be administered with either agent, EYLEA® (aflibercept) or LUCENTIS® (ranibizumab).

The two pivotal Phase 3 multi-center, double-masked, sham-controlled trials are designed to assess the efficacy and safety of intravitreal 2.0 mg sozinibercept in combination with anti-VEGF-A treatments. In the COAST trial, sozinibercept is being evaluated in combination with 2.0 mg of EYLEA® (aflibercept). In the ShORe trial, sozinibercept is being evaluating in combination with 0.5 mg of LUCENTIS® (ranibizumab). The primary endpoint for both trials is the mean change in Best Corrected Visual Acuity (BCVA) from baseline to week 52 for sozinibercept combination therapy compared to anti-VEGF-A monotherapy.

In addition, each trial will evaluate the use of sozinibercept treatment dosed every four weeks and every eight weeks after the first three loading doses.

Beyond week 52, patients will continue to be treated for an additional year to evaluate extended safety and tolerability up to a two-year period. To learn more, visit www.opthea.com and ClinicalTrials.gov (COAST trial, ID#: NCT04757636, ShORe trial, ID#: NCT04757610).

About Opthea

Opthea (ASX:OPT; NASDAQ:OPT) is a biopharmaceutical company developing novel therapies 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 sozinibercept, is being evaluated in two pivotal Phase 3 clinical trials (COAST, NCT04757636 and ShORe, NCT04757610) for use in combination with standard-of-care anti-VEGF-A monotherapies to improve overall efficacy and deliver superior vision gains compared to the standard-of-care anti-VEGF-A agents. To learn more, visit www.opthea.com and follow us on X and LinkedIn.

EYLEA® is a registered trademark of Regeneron Pharmaceuticals, Inc.

LUCENTIS® is a registered trademark of Genentech USA, Inc. A member of the Roche Group.

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

This ASX announcement contains certain forward-looking statements, including within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. The words "expect", "believe," "should", "could", "may", "will", "plan" and other similar expressions are intended to identify forward-looking statements. Forward-looking statements in this ASX announcement include statements regarding expectations on the outcomes of Opthea's Phase 3 clinical trials of sozinibercept, the potential for sozinibercept as a combination therapy to be the first therapy to achieve superior visual outcomes over anti-VEGF-A monotherapy and improve vision outcomes for patients with wet AMD, the expected timing for completion of enrollment for ShORe and topline data, the market opportunity for sozinibercept, and the future performance of Opthea. Forward-looking statements, opinions and estimates provided in this ASX announcement are based on assumptions and contingencies which are subject to change without notice, as are statements about market and industry trends, which are based on interpretations of current conditions. Forward-looking statements are provided as a general guide only and should not be relied upon as an indication or guarantee of future performance. They involve known and unknown risks and uncertainties and other factors, many of which are beyond the control of Opthea and its directors and management and may involve significant elements of subjective judgment and assumptions as to future events that may or may not be correct. These statements may be affected by a range of variables which could cause actual results or trends to differ materially, including but not limited to future capital requirements, the development, testing, production, marketing and sale of drug treatments, regulatory risk and potential loss of regulatory approvals, ongoing clinical studies to demonstrate sozinibercept safety, tolerability and therapeutic efficacy, additional analysis of data from Opthea's Phase 3 clinical trials, timing of completion of ShORe clinical trial patient enrollment and clinical research organization and labor costs, intellectual property protections, and other factors that are of a general nature which may affect the future operating and financial performance of the Company including risk factors set forth in Opthea's Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission (the "SEC") on September 28, 2023 and other future filings with the SEC. Actual results, performance or achievement may vary materially from any projections and forward-looking statements and the assumptions on which those statements are based. Subject to any continuing obligations under applicable law or any relevant ASX listing rules, Opthea disclaims any obligation or undertaking to provide any updates or revisions to any forward-looking statements in this ASX announcement to reflect any change in expectations in relation to any forward-looking statements or any change in events, conditions or circumstances on which any such statement is based, except as otherwise required by applicable law.

Authorized for release to ASX by Fred Guerard, CEO

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