Opthea Announces Phase 2b Wet AMD Publication

Baseline angiographic lesion characteristics predictive of clinical response

Published in peer-reviewed journal Ophthalmic Surgery, Lasers and Imaging Retina

Melbourne, Australia and Princeton, NJ, March 3, 2025 -- Opthea Limited (ASX/NASDAQ: OPT "Opthea", the "Company"), a clinical-stage biopharmaceutical company developing novel therapies to treat highly prevalent and progressive retinal diseases, including wet age-related macular degeneration (wet AMD), today announced the publication of sozinibercept Phase 2b data in the peer-reviewed journal *Ophthalmic Surgery, Lasers and Imaging (OSLI) Retina*.

The paper entitled "*Sozinibercept Combination Therapy for Neovascular Age-Related Macular Degeneration: Phase 2b Study Subgroup Analysis by Lesion Type"* reports pre-specified and post-hoc analyses of angiographic predictors of response to sozinibercept combination therapy with ranibizumab in treatment-naïve patients with wet AMD. The analyses are based on choroidal neovascularization (CNV) type lesions (occult, minimally classic, and predominantly classic), and the presence and absence of retinal angiomatous proliferation (RAP) on visual acuity and anatomical outcomes. The data were derived from the randomized, controlled Phase 2b trial in which sozinibercept 2 mg combination therapy led to superior visual gains compared to ranibizumab monotherapy at 24 weeks.

The Phase 2b pre-specified analyses of subgroups showed that in patients with occult and minimally classic lesions excluding RAP, which represented 73% of the Phase 2b total patient population, sozinibercept combination therapy demonstrated a statistically significant additional 5.7 letter mean gain in best corrected visual acuity (BCVA) compared to ranibizumab alone. A greater proportion of patients in this subgroup also gained ≥15 letters and had improved anatomy of better drying of the retina with reduced CNV area at week 24 compared to ranibizumab alone.

"Angiographic lesion characteristics being predictive of patient response are consistent with data reported in real-world trials and have informed the design of Opthea's sozinibercept Phase 3 clinical program," said Frederic Guerard, PharmD, Chief Executive Officer of Opthea. "In fact, the patient demographics and baseline characteristics from COAST and ShORe include a high proportion of enrolled patients with these best responding lesion types. We are looking forward to the anticipated topline data readouts for COAST in early Q2 CY 2025 and for ShORe in mid-CY 2025."

Wet AMD remains the leading cause of vision loss in the elderly, impacting about 3.5 million people in the US and Europe alone. The unmet medical need in wet AMD is significant, with many patients failing to achieve optimal vision outcomes despite treatment with anti-VEGF-A therapies.

About Opthea's Clinical Development Program

The Company's pivotal Phase 3 wet AMD program is comprised of two fully enrolled, concurrent, multicenter, double-masked, randomized clinical trials, COAST (Combination OPT-302 with Aflibercept Study) and ShORe (Study of OPT-302 in combination with Ranibizumab). The trials are designed to assess the safety and superior efficacy of sozinibercept combination therapy versus standard-of-care anti-VEGF-A in wet AMD. The Phase 3 program is designed to support

a broad label and, if successful, enable sozinibercept to be approved for use in combination with any anti-VEGF-A therapy in wet AMD patients. Sozinibercept has received Fast Track Designation from the US FDA for the treatment of wet AMD. To learn more about Opthea's Phase 3 clinical trial program, please visit ClinicalTrials.gov for COAST, NCT04757636, and ShORe, NCT04757610.

In Opthea's prospective, randomized and controlled Phase 2b trial, including 366 treatment-naïve wet AMD patients, sozinibercept was administered in combination with standard-of-care ranibizumab for the treatment of wet AMD. Sozinibercept combination therapy 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 with the combination therapy, including more patients gaining vision of 10 or more EDTRS letters, with improved anatomy, a reduction in swelling and vascular leakage, and a favorable safety profile. These statistically significant results were published in *Ophthalmology* in February 2023.

About Opthea

Opthea (ASX/NASDAQ:OPT) is a biopharmaceutical company developing novel therapies to treat vision-threatening eye diseases, including wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME), which remain leading causes of vision loss worldwide.

Opthea's lead product candidate in Phase 3 development, sozinibercept, is a first-in-class VEGF-C/D 'trap' inhibitor being evaluated in combination with standard-of-care anti-VEGF-A therapies to deliver superior vision to wet AMD patients. Sozinibercept has the potential to become the first therapy in 20 years to enable patients with wet AMD to live fuller and healthier lives.

To learn more, visit our website at www.opthea.com and follow us on X and LinkedIn.

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 US 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 Opthea's ongoing COAST and ShORe clinical trials, including the timing for

anticipated topline data readouts and their potential to support a broad label and, if successful, to enable sozinibercept to be approved for use in combination with any anti-VEGF-A therapy in wet AMD patients; the potential benefits of sozinibercept, including to deliver superior visual outcomes in wet AMD when combined with standard-of-care anti-VEGF-A therapies and to become the first therapy in 20 years to enable patients with wet AMD live fuller and healthier lives; and the estimated patient population of wet AMD. 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's safety, tolerability and therapeutic efficacy, 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 US Securities and Exchange Commission (the "SEC") on August 30, 2024, and other future filings with the SEC. Actual results, performance or achievements 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 Frederic Guerard, PharmD, CEO

Investor Inquiries

PJ Kelleher
LifeSci Advisors, LLC
Email: pkelleher@lifesciadvisors.com
Phone: 617-430-7579

Media Inquiries

Silvana Guerci-Lena
NorthStream Global Partners
Email: silvana@nsgpllc.com

Join our email database to receive program updates:
Tel: +61 (0) 3 9826 0399, Email: info@opthea.com Web: www.opthea.com

Source: Opthea Limited