ASX, NASDAQ and Media Release
29 February 2024

Opthea Reports Half-Year Financial Results and Business Updates

Enrollment completion of sozinibercept Phase 3 program for wet AMD expected in calendar year (CY) Q2 2024 with top-line data mid-CY 2025

Expanded U.S. leadership team with the appointments of Dr. Frederic Guerard as CEO, Peter Lang as CFO, and Dr. Arshad M. Khanani as Chief Medical Advisor

Cash and cash equivalents of $157.1 million as of December 31, 2023

Melbourne, Australia and Princeton, New Jersey; 29 February 2024 – Opthea Limited (ASX:OPT; NASDAQ:OPT; "Opthea"), a clinical-stage biopharmaceutical company developing novel therapies to treat highly prevalent and progressive retinal diseases, today announced financial results for the six months ended December 31, 2023 and highlighted recent corporate and clinical updates.

"It is a transformative time for Opthea. We substantially advanced the development of sozinibercept, our lead product candidate for the treatment of wet age-related macular degeneration (wet AMD), expanded our U.S. leadership team, strengthened our clinical and regulatory organization, and received US$143 million in funding. We recently announced the completion of enrollment in our first pivotal Phase 3 trial (COAST), in combination with EYLEA® (aflibercept)," said Frederic Guerard, PharmD, Chief Executive Officer of Opthea.

"We believe that sozinibercept has the potential to deliver superior vision gains for millions of people with wet AMD based on our Phase 2b trial results which demonstrated superior and statistically significant improvements in visual acuity for patients treated with sozinibercept in combination with LUCENTIS®(ranibizumab). Sozinibercept therefore has the potential to be the first product in more than 15 years to improve the standard of care in wet AMD and make a tangible difference in the lives of patients," continued Dr. Guerard.

Peter Lang, Chief Financial Officer of Opthea, added, "We are excited about Opthea's progress. Looking ahead, we expect to complete enrollment in our second Phase 3 trial (ShORe), in combination with the standard of care ranibizumab, in the second quarter of CY 2024. In addition, we intend to report the top-line data on the COAST and ShORe trials in mid-CY 2025. We are encouraged by the positive momentum in the sozinibercept program."

Anticipated Milestones

- **Enrollment completion** in the second Phase 3 pivotal ShORe trial evaluating sozinibercept in combination with ranibizumab, expected in Q2 CY 2024.
- **Top-line Phase 3 results** from the COAST and ShORe trials expected by mid-CY 2025.

Corporate Highlights

- In February 2024, **completed enrollment in the COAST Phase 3** pivotal trial evaluating sozinibercept in combination with aflibercept**.**
- In February 2024, **Dr. Arshad M. Khanani, FASRS, a global retina expert joined as Chief Medical Advisor** to support sozinibercept development and launch preparation.
- In February 2024, strengthened the organization with **key clinical and regulatory hires** including Dr. Julie Clark as SVP, Clinical Development, and Dr. Fang Li as SVP, Regulatory Affairs.
- In December 2023, Opthea received **US$85 million** in non-equity funding consisting of the remaining US$35 million from the previously announced Development Funding Agreement (DFA) with Carlyle and its life science franchise, Abingworth, and an additional US$50 million under an amended DFA with a new co-investor.
- In October 2023, **appointed U.S.-based leadership team** with Dr. Frederic Guerard as Chief Executive Officer and Peter Lang, MBA, as Chief Financial Officer, and the transition of Dr. Megan Baldwin to the role of Founder, Chief Innovation Officer.
- In August 2023, Opthea successfully completed a private placement and rights equity offering raising **A$90 million** (**US$58 million)** in Australia.

Financial Results

- US$157.1 million in cash and cash equivalents, as of December 31, 2023.
- Operating Expenses (Research and Development, Patent and Intellectual Property, and Administrative Expenses) totaled US$93.9 million for the six months ended December 31, 2023, up 19% compared to the prior year period, primarily driven by progress in the pivotal Phase 3 clinical program and chemistry, manufacturing, and controls (CMC) activities.
- Net Cash Flows Used in Operating Activities for the six months ended December 31, 2023 ended at ($69.4) million, a slight increase from ($69.3) million for the prior year period.

Upcoming Events

- Leerink Partners Global Biopharma Conference 2024, March 11-13, 2024

See Opthea's 2024 Half Year FY Report, as lodged today on ASX and filed as an exhibit to the Form 6-K furnished with the U.S. Securities and Exchange Commission (the "SEC") on February 29, 2024, for more detailed information, which report can be accessed without charge at www.sec.gov. A copy can also be accessed under the investor section of the www.opthea.com website.

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 standard of care, 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 and improved anatomy, with a reduction in swelling and vascular leakage, with a favorable safety profile.

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 top-line data for Opthea’s Phase 3 clinical trials of sozinibercept, 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, Opthea’s 2024 Half Year Report included as an exhibit to the Form 6-K filed with the SEC on February 29, 2024, 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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