OPTHEA

Opthea Announces COAST Phase 3 Trial Topline Results

COAST Phase 3 trial failed to meet primary endpoint of mean change in BCVA from baseline to week 52

Opthea considering impact of negative trial results under its Development Funding Agreement and on the Company as a going concern

Melbourne, Australia, and Princeton, N.J., 24 March, 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 results from its global Phase 3 clinical trial COAST (**C**ombination **O**PT-302 with **A**flibercept **St**udy) in patients with wet AMD.

COAST Topline Results

The global COAST Phase 3 trial evaluated the efficacy and safety of intravitreally administered 2 mg sozinibercept every four or eight weeks in combination with 2 mg aflibercept, as per label, every eight weeks after a loading phase for the treatment of wet AMD. The trial did not meet its primary endpoint of mean change in best corrected visual acuity (BCVA) from baseline to week 52.

In wet AMD patients with minimally classic and occult lesions, participants receiving sozinibercept combination therapy with a dosing regimen of every four weeks (n=296) or every eight weeks (n=297) achieved a mean change in BCVA of 13.2 or 13.2 letters from baseline to week 52, respectively, versus 13.8 letters with aflibercept monotherapy (n=299, p-values of 0.59 and 0.62 respectively). In the overall population, participants receiving sozinibercept combination therapy with a dosing regimen of every four weeks (n=333) or every eight weeks (n=330) achieved a mean change in BCVA of 13.5 and 12.8 letters from baseline to week 52, respectively, versus 13.7 letters with aflibercept monotherapy (n=330, p-values of 0.86 and 0.42 respectively).

There was no numerical difference observed in the key secondary endpoints. Sozinibercept combination therapy was well tolerated.

Following the receipt of these results, Opthea has undertaken a thorough review of the data to ensure both its accuracy and integrity. No anomalies were identified through this process that would cause the Board to adopt an alternative view on the data outlined above.

Impact of COAST Topline Results on Opthea Under the Development Funding Agreement and on Opthea as a Going Concern

Following the negative results in the COAST trial, Opthea has been assessing its rights and obligations under its Development Funding Agreement ("**DFA**") with, among others, the investors under the DFA (the "**DFA Investors**"). In light of these updates, it is possible that under the DFA, Opthea could become required to pay amounts to the DFA Investors that would have a material adverse impact on the solvency of the company. As previously disclosed, certain instances and events may result upon the termination of the DFA, and upon such termination, Opthea will be obligated to pay the DFA Investors up to four multiples of the amounts paid to the Company under

the DFA. Termination can be triggered by a range of events, including, among other things, inability of Opthea to fund development costs, failure by Opthea to continue to use commercially reasonable efforts to develop sozinibercept, Opthea's insolvency, or disagreement with the DFA Investors. Each termination trigger has a corresponding potential repayment amount of US$0, US$229.5 million, US$255.0 million, US$467.5 million or US$680.0 million.

Opthea's Management and Board of Directors have been in active discussions with the DFA Investors, pursuant to and as required under the DFA, to explore possible options for Opthea in respect of its clinical trial program and with a view to identifying whether there is a pathway that represents the best outcome for the company and its shareholders. As such, it is possible that Opthea and the DFA Investors reach a negotiated settlement that is different from the parties' existing rights under the DFA.

It should also be noted that the DFA Investors have security over the assets of Opthea in the form of an "all assets" lien. As a result, Opthea is unable to incur further non-equity funding or dispose of its material assets without the prior consent of the DFA Investors.

A copy of the DFA is included as Exhibit 4.19 to Opthea's Annual Report on Form 20-F filed with the US Securities and Exchange Commission on August 30, 2024.

At this stage, no decision has yet been taken with respect to either trial, including whether to discontinue activities for the COAST trial or accelerate and unmask the ShORe trial. Discussions continue with the DFA Investors to determine the most appropriate course of action.

As of February 28, 2025, Opthea has an unaudited cash and cash equivalents balance of US$113.8M.

In light of these matters, there remains material uncertainty as to Opthea's ability to continue as a going concern.[1] As noted above, discussions with the DFA Investors are ongoing and Opthea cannot be certain as to the outcome of those discussions or when that outcome may become known.

Opthea and its Directors are currently relying on the "safe harbour" provisions in section 588GA of the *Corporations Act 2001* (Cth).

Opthea has requested that trading in its listed securities continue to be suspended on both ASX and Nasdaq until the earlier of Opthea being in a position to provide an announcement to the market by Opthea providing more clarity on these issues or the commencement of trading on Monday, 31 March 2025. The extension to the voluntary suspension is necessary to prevent trading in Opthea's securities on an uninformed basis, pending further clarity on these issues being available and released to the market. Opthea is not aware of any reason why the voluntary suspension should not be extended or of any other information necessary to inform the market regarding the voluntary suspension.

Authorised for release to ASX by The Board of Directors.

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 the possible outcomes for Opthea’s clinical trial program, possible outcomes in connection with the DFA, and Opthea’s ability to continue as a going concern. 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, determinations whether to continue 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.

Investor Inquiries

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

Join our email database to receive program updates:
Email: info@opthea.com Web: www.opthea.com
Source: Opthea Limited

[1] Investors should refer also to the 'going concern' statements contained in Note 2 to Opthea's Condensed Consolidated Financial Statements for the half year ended 31 December 2024 released on 28 February 2025.