OPTHEA

Opthea Announces Decision to Discontinue Wet AMD Trials

ShORe Phase 3 topline results accelerated; trial did not meet primary endpoint of mean change in BCVA from baseline to week 52

Opthea and DFA Investors agreed to terminate both COAST and ShORe trials

Opthea continues to consider impact of negative trial results under its Development Funding Agreement (DFA) and on the Company as a going concern

Melbourne, Australia, and Princeton, N.J., 31 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 updates on its Phase 3 clinical program, including the termination of COAST (**C**ombination of **O**PT-302 with **A**flibercept **St**udy) and accelerated topline results from its second Phase 3 trial ShORe (**S**tudy of **O**PT-302 in combination with **R**anibizumab) in patients with wet AMD.

ShORe Topline Results

Following the negative results of the COAST Phase 3 trial announced on 24 March 2025, Opthea determined that the most appropriate course of action for wet AMD patients, shareholders, and other stakeholders was to accelerate the ShORe trial topline data readout, including in consultation with its Development Funding Agreement investors ("**DFA Investors**").

The global ShORe Phase 3 trial evaluated the efficacy and safety of intravitreally administered 2 mg sozinibercept every four or eight weeks in combination with 0.5 mg ranibizumab every four weeks, as per label, versus 0.5 mg ranibizumab monotherapy. 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=301) or every eight weeks (n=301) achieved a mean change in BCVA of 13.3 or 12.9 letters from baseline to week 52, respectively, versus 14.2 letters with ranibizumab monotherapy (n=299, p-values of 0.35 and 0.19 respectively). In the overall population, participants receiving sozinibercept combination therapy with a dosing regimen of every four weeks (n=328) or every eight weeks (n=326) achieved a mean change in BCVA of 13.3 and 12.6 letters from baseline to week 52, respectively, versus 14.3 letters with ranibizumab monotherapy (n=331 p-values of 0.32 and 0.09 respectively).

Sozinibercept combination therapy was well tolerated.

"We are disappointed that COAST and ShORe did not demonstrate the improvements in vision with sozinibercept combination therapy compared to standard of care that we had hoped for," said Frederic Guerard, PharmD, Chief Executive Officer of Opthea. "We are grateful to all patients, clinical investigators and their staff around the world who participated in the sozinibercept Phase 3 clinical program, and for their contributions in investigating new treatments for wet AMD."

“As previously disclosed, the Company has certain obligations under the DFA. In light of the Phase 3 clinical trial results, the Company and the DFA Investors will continue to discuss this matter in good faith, and we will provide updates on this matter in the future,” Dr. Guerard concluded.

Corporate Updates

Following the negative results of the COAST and ShORe trials, Opthea and the DFA Investors agreed to discontinue the development of sozinibercept in wet AMD with immediate effect, and that this decision did not constitute a termination event under the DFA resulting in any amount payable by Opthea.

It remains possible that under the DFA, in certain circumstances upon or following termination of the DFA, Opthea could become required to pay a multiple of the amount funded by the DFA Investors that would have a material adverse impact on the solvency of the Company. As previously disclosed, termination can be triggered by a range of events, including, among other things, Opthea’s insolvency, in which case Opthea will be obligated to pay a multiple of the amounts funded by the DFA Investors.

Opthea continues active discussions with the DFA Investors, pursuant to and as required under the DFA, to explore possible options to deliver the best outcome for the Company and its shareholders.

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.

Opthea estimates it will have unaudited cash and cash equivalents of US$100M at the end of March 2025.

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 is currently relying on the "safe harbour" provisions in section 588GA of the *Corporations Act 2001* (Cth).

Trading in Opthea’s listed securities will be suspended by ASX under ASX Listing Rule 17.3 until Opthea is in a position to provide an announcement to the market providing more clarity on these issues and the impact on Opthea’s financial position.

Authorized for release to ASX by The Board of Directors.

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 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, 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.

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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.