



Third Harmonic Bio Announces Discontinuation of Phase 1b Study of THB001 in Chronic Inducible Urticaria

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-- Company decision follows observation of asymptomatic liver transaminitis in two subjects enrolled in first dose cohort of 200mg BID

-- Evidence of clinical activity observed; full data set to be presented at upcoming scientific conference

-- Multiple chemically distinct, next-generation oral KIT inhibitors in exploratory toxicology studies; on track to nominate development candidate in 2023

CAMBRIDGE, Mass., Dec. 15, 2022 (GLOBE NEWSWIRE) -- Third Harmonic Bio, Inc. (Nasdaq: THRD), a biopharmaceutical company focused on advancing the next wave of medicine for inflammatory diseases, today announced that the company has made the decision to discontinue the ongoing Phase 1b study of its investigational drug candidate, THB001, after observing asymptomatic liver transaminitis in two subjects enrolled in the first dose cohort of 200mg BID.

"We hold patient safety as our top priority in the conduct of our clinical studies, and therefore have decided to terminate the Phase 1b study of THB001," said Natalie Holles, Chief Executive Officer of Third Harmonic Bio. "While this is a deeply disappointing outcome, we are encouraged by the preliminary signs of clinical activity at this starting dose and are optimistic about the potential for a selective oral wild-type KIT inhibitor to become an important treatment modality for mast cell-driven inflammatory diseases. Our early decision to invest in next-generation medicinal chemistry enables us to maintain our leadership position in oral wild-type KIT inhibition with the anticipated nomination of a new development candidate next year."

The Company is initiating nonclinical studies to elucidate the mechanism for the observed transaminitis, which was not predicted by extensive GLP toxicology studies of THB001 nor observed in the Company's Phase 1a study. In parallel with the early clinical development of THB001, the Company has conducted an extensive medicinal chemistry effort to identify chemically distinct next-generation oral wild-type KIT inhibitors and has advanced multiple candidate molecules into exploratory toxicology studies. The Company intends to nominate a development candidate from this program in 2023.

The Phase 1b clinical trial in chronic inducible urticaria was designed to evaluate the safety and tolerability, efficacy and pharmacokinetics of three dose levels of THB001 over 12 weeks of treatment. Five subjects were enrolled in the first dose cohort of 200mg BID. The first subject completed the full 12-week dosing period with no signs or symptoms of liver toxicity. The second and third subjects presented with elevations in alanine transaminase (ALT) and aspartate transaminase (AST) at their week 8 study visits, and dosing was halted for both subjects. All other laboratory and diagnostic measures have indicated no change in liver function in either subject and both subjects remain clinically asymptomatic. No alternate causes for the transaminitis have been identified, and the subjects continue to be closely monitored. Dosing of the fourth and fifth subjects enrolled has been stopped by the Company at weeks 4 and 2 of dosing, respectively, and neither of these subjects has any signs or symptoms of liver toxicity to date. Clinical follow-up of the five enrolled subjects will continue per protocol, but no additional subjects will be enrolled in the trial.

Preliminary analyses show evidence of pharmacodynamic and clinical activity at the 200mg BID dose. The Company plans to present the full data set from the five enrolled subjects at an upcoming scientific conference, and to provide an update on overall corporate strategy and outlook in early 2023.

About Third Harmonic Bio

Third Harmonic Bio is a biopharmaceutical company focused on advancing the next wave of medicine for inflammatory diseases through the development of a novel highly selective, oral small-molecule inhibitor of KIT, a cell surface receptor that serves as the master regulator of mast cell function and survival. Early clinical studies demonstrate that KIT inhibition has the potential to revolutionize the treatment of a broad range of mast-cell-mediated inflammatory diseases, and that a titratable, oral, intracellular small molecule inhibitor may provide the optimal therapeutic profile against this target. For more information, please visit the Third Harmonic Bio website: www.thirdharmonicbio.com.

Forward-Looking Statements

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the timing of additional corporate announcements and presentations, the results and timing of preclinical studies and clinical trials for future development candidates, expectations regarding cash forecasts, and planned clinical and development activities and timelines. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties, including risks and uncertainties related to Third Harmonic's cash forecasts, ability to advance its product candidates, the receipt and timing of potential regulatory submissions, designations, approvals and commercialization of product candidates, our ability to protect our intellectual property, the timing and results of preclinical and clinical trials, changes to laws or regulations, market conditions, geopolitical events, and further impacts of the ongoing COVID-19 pandemic, that could cause actual results to differ materially from what Third Harmonic Bio expects. Further information on potential risk factors that could affect Third Harmonic Bio's business and its financial results are detailed under the heading "Risk Factors" included in Third Harmonic Bio's prospectus dated September 14, 2022 filed with the U.S. Securities and Exchange Commission (SEC) on September 15, 2022, and Third Harmonic Bio's annual and quarterly reports and other filings with the SEC filed from time to time with the SEC. Third Harmonic Bio undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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