Travere Therapeutics Initiates Pivotal Phase 3 Clinical Trial of Pegtibatinase for the Treatment of Classical Homocystinuria (HCU)

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Potential for pegtibatinase to become first disease-modifying treatment for classical HCU; topline data expected in 2026

SAN DIEGO, Dec. 14, 2023 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (Nasdaq: TVTX) today announced the Company has opened enrollment in the HARMONY Study, a global, randomized pivotal Phase 3 clinical trial of pegtibatinase, a novel investigational enzyme replacement therapy being evaluated for the treatment of classical homocystinuria (HCU). Classical HCU is a rare genetic metabolic disorder caused by a deficiency in the enzyme cystathionine beta synthase (CBS). The study is designed to determine the safety and efficacy of pegtibatinase in reducing plasma total homocysteine (tHcy) levels, a key treatment goal in classical HCU, compared to placebo in participants who are receiving standard of care.

“Classical HCU is a devastating rare disease that often manifests in childhood and can lead to serious complications due to toxic levels of homocysteine. These complications include continuous risk of developing life-threatening thrombotic events, such as heart attack and stroke, skeletal abnormalities, cognitive developmental delays, and intellectual disabilities. Patients and caregivers have limited treatment options, including adherence to highly restrictive diets that often are very challenging to follow and inadequate for maintaining metabolic control of homocysteine levels,” said William Rote, Ph.D., senior vice president of research and development at Travere Therapeutics. “The initiation of the HARMONY Study is an exciting step forward in addressing this significant unmet need and advancing our goal to deliver pegtibatinase as the first disease-modifying treatment option for the classical HCU community.”

The HARMONY Study is a global, randomized, multi-center, double-blind, placebo-controlled Phase 3 clinical trial designed to evaluate the efficacy and safety of pegtibatinase as a novel treatment to reduce tHcy levels. The trial is expected to enroll approximately 70 patients (≥12 to ≤65 years of age at screening) with a diagnosis of classical HCU who continue to have tHcy levels ≥50 µM while maintaining their standard-of-care treatment. Participants will be randomized 1:1 to receive 2.5 mg/kg of pegtibatinase or placebo, administered subcutaneously, for a 24-week blinded treatment duration. The primary endpoint is relative geometric mean change in plasma tHcy levels from baseline compared to weeks 6 through 12, and durability of treatment response through 24 weeks of treatment will be measured as a secondary endpoint. The Company expects topline data from the HARMONY Study to become available in 2026. The Company will also be initiating the ENSEMBLE Study, a Phase 3b, open-label, long-term extension, that will evaluate the ongoing efficacy and long-term safety of pegtibatinase in participants with HCU following their completion of the Phase 1/2 COMPOSE Study or the Phase 3 HARMONY Study. The ENSEMBLE Study will include an optional protein tolerance modification sub-study that will evaluate if eligible patients can increase their natural dietary protein intake while maintaining an acceptable level of metabolic control while receiving pegtibatinase.

The initiation of the Phase 3 HARMONY Study is based on the positive safety and efficacy data from the Phase 1/2 COMPOSE Study. In COMPOSE, pegtibatinase demonstrated dose-dependent reductions in tHcy during 12 weeks of treatment. At the 2.5 mg/kg dose, pegtibatinase provided rapid and sustained reductions in tHcy, with a 67.1% mean relative reduction in tHcy from baseline, as well as maintenance of mean tHcy below the clinically meaningful threshold of 100 µM, over weeks 6 to 12. To date in the COMPOSE Study, pegtibatinase has been generally well-tolerated.

Pegtibatinase has been granted Breakthrough Therapy, Rare Pediatric Disease and Fast Track designations by the U.S. Food and Drug Administration (FDA), as well as Orphan Drug designation in the U.S. and Europe.

About Classical Homocystinuria

Classical homocystinuria (HCU) is a rare genetic metabolic disorder caused by a deficiency in the enzyme cystathionine beta synthase (CBS). CBS is a pivotal enzyme that is essential for the management of methionine and cysteine in the body. Classical HCU leads to toxic levels of homocysteine that can result in life-threatening thrombotic events such as stroke, pulmonary embolism and deep vein thrombosis, ophthalmologic and skeletal complications, as well as developmental delay. Current treatment options are limited to protein-restricted diet and use of vitamin B6 and betaine.

About Pegtibatinase

Pegtibatinase is an investigational PEGylated, recombinant enzyme replacement therapy designed to address the underlying cause of classical homocystinuria (HCU). In preclinical studies, pegtibatinase has demonstrated an ability to reduce total homocysteine levels and improve clinical parameters. Pegtibatinase is currently advancing in the ongoing Phase 1/2 COMPOSE Study to assess its safety, tolerability, pharmacokinetics, pharmacodynamics and clinical effects in patients with classical HCU. In May 2023, the Company announced that data from four patients treated with the highest dose of pegtibatinase showed a clinically meaningful 67.1% mean relative reduction in total homocysteine from baseline and was generally well-tolerated after 12 weeks of treatment. To date, the pegtibatinase program has been granted Breakthrough Therapy designation, Rare Pediatric Disease and Fast Track designations by the FDA, as well as Orphan Drug designation in the U.S. and Europe.

About Travere Therapeutics

At Travere Therapeutics, we are in rare for life. We are a biopharmaceutical company that comes together every day to help patients, families and caregivers of all backgrounds as they navigate life with a rare disease. On this path, we know the need for treatment options is urgent – that is why our global team works with the rare disease community to identify, develop and deliver life-changing therapies. In pursuit of this mission, we continuously seek to understand the diverse perspectives of rare patients and to courageously forge new paths to make a difference in their lives and provide hope – today and tomorrow. For more information, visit travere.com

Forward Looking Statements

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, these statements are often identified by the words “on-track”, “positioned”, “look forward to”, “will,” “would,” “may”, “might”, “believes”, “anticipates”, “plans”, “expects”, “intends,” “potential” or similar expressions. In addition, expressions of our strategies, intentions or plans are also forward-looking statements. Such forward-looking statements include, but are not limited to, references to: the potential for pegtibatinase to become first disease-modifying treatment for classical HCU; expectations regarding the Phase 3 HARMONY Study and sub-studies and the anticipated timing and outcome thereof; and expectations regarding enrollment and data availability and the anticipated timing thereof. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties associated with the regulatory review and approval process, as well as risks and uncertainties associated with the Company’s business and finances in general and its recently announced strategic reorganization, the success of its commercial products and risks and uncertainties associated with the Company’s preclinical and clinical stage pipeline. Specifically, the Company faces risks associated with market acceptance of its commercial products including efficacy, safety, price, reimbursement and benefit over competing therapies, as well as risks associated with the successful development and execution of commercial strategies for such products, including FILSPARI. The risks and uncertainties the Company faces with respect to its preclinical and clinical stage pipeline include risk that the Company’s clinical candidates will not be found to be safe or effective and that current or anticipated future clinical trials will not proceed as planned. Specifically, the Company faces risks related to the timing and potential outcome of its Phase 3 HARMONY Study, the timing and potential outcome of its planned sNDA submission for full approval of sparsentan in IgAN, and the risk that the results from the Phase 3 DUPLEX Study of sparsentan in FSGS will not serve as a basis for a regulatory submission for approval of sparsentan for FSGS. There is no guarantee that regulators will grant full approval of sparsentan for IgAN or FSGS. The Company also faces the risk that its cash runway might not last as long as currently anticipated and the risk that it will be unable to raise additional funding that may be required to complete development of any or all of its product candidates, including as a result of macroeconomic conditions; risks relating to the Company’s dependence on contractors for clinical drug supply and commercial manufacturing; uncertainties relating to patent protection and exclusivity periods and intellectual property rights of third parties; risks associated with regulatory interactions; and risks and uncertainties relating to competitive products, including current and potential future generic competition with certain of the Company's products, and technological changes that may limit demand for the Company’s products. The Company also faces additional risks associated with global and macroeconomic conditions, including health epidemics and pandemics, including risks related to potential disruptions to clinical trials, commercialization activity, supply chain, and manufacturing operations. You are cautioned not to place undue reliance on these forward-looking statements as there are important factors that could cause actual results to differ materially from those in forward-looking statements, many of which are beyond our control. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Investors are referred to the full discussion of risks and uncertainties, including under the heading “Risk Factors”, as included in the Company’s most recent Form 10-K, Form 10-Q and other filings with the Securities and Exchange Commission.

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