Travere Therapeutics Announces Positive Topline Results from the Ongoing Phase 1/2 COMPOSE Study of Pegtibatinase in Classical Homocystinuria

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Treatment with highest dose pegtibatinase led to a clinically meaningful 55% mean reduction in total homocysteine from baseline and was generally well-tolerated after 12 weeks of treatment

Results provide clinical proof of concept for first potential therapy targeting the underlying enzyme deficiency in classical homocystinuria

Company to host conference call and webcast today at 8:30 a.m. ET

SAN DIEGO, Dec. 15, 2021 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (NASDAQ: TVTX) today announced positive topline results from the ongoing Phase 1/2 COMPOSE Study of pegtibatinase, a novel investigational enzyme replacement therapy being evaluated for the treatment of classical homocystinuria (HCU). In the highest dose cohort to date evaluating 1.5mg/kg of pegtibatinase twice weekly (BIW), treatment with pegtibatinase resulted in rapid and sustained reductions in total homocysteine (tHcy) through 12 weeks of treatment, including a 55.1% mean relative reduction in tHcy from baseline as well as maintenance of tHcy below a clinically meaningful threshold of 100 µmol. To date in the study, pegtibatinase has been generally well-tolerated.

“These promising topline results from the ongoing COMPOSE Study show that pegtibatinase has the potential to improve overall metabolic function and provide clear proof of concept for pegtibatinase as a potential novel therapy for patients living with HCU,” said Bill Rote, Ph.D., senior vice president of research and development at Travere Therapeutics. “With the strength of these data, we are furthering efforts to refine our formulation and explore pegtibatinase dosing, while in parallel engaging with regulators to establish next steps for a pivotal development program designed to ultimately support potential approvals of pegtibatinase for the treatment of HCU.”

“Most patients with HCU are at high risk of developing long term and often devastating complications from HCU because they cannot sustain low levels of toxic homocysteine with currently available treatment options,” said Harvey Levy, M.D., senior physician in medicine/genetics, Division of Genetics and Genomics, Boston Children's Hospital, professor of pediatrics, Harvard Medical School. “The data from the ongoing COMPOSE Study are highly encouraging and provide promise for a potentially novel approach to targeting the underlying enzymatic defect in HCU.”

To date in the COMPOSE Study, a total of 19 patients with HCU have been randomized 3:1 to receive either pegtibatinase or placebo in independent ascending subcutaneous dose cohorts, ranging from 0.33mg/kg once weekly to 1.5mg/kg BIW. The study protocol provided for an unblinded assessment to evaluate safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and clinical effects after twelve weeks of treatment had been completed in the fifth cohort (1.5mg/kg BIW).

Key findings from the topline results:

- To date in the COMPOSE Study, pegtibatinase has been generally well-tolerated.
- There were no discontinuations due to treatment-related adverse events. There was one serious adverse event, moderate acute urticaria (hives), that was categorized by the treating physician to be likely related to pegtibatinase treatment but did not lead to treatment discontinuation and resolved following a single dose interruption.
- Pegtibatinase demonstrated dose-dependent reductions in tHcy during the 12 weeks of treatment.
- At the two highest doses, pegtibatinase appeared to reduce tHcy regardless of starting baseline tHcy levels or background therapy.
- In the highest dose cohort to date of 1.5mg/kg BIW, treatment with pegtibatinase resulted in rapid and sustained reductions in tHcy, resulting in a maintenance of tHcy below a clinically meaningful threshold of 100 µmol from week 2 through week 12 of treatment.
- In the 1.5mg/kg BIW dose cohort, treatment with pegtibatinase resulted in a mean relative reduction from baseline of 55.1% (n=3, mean baseline tHcy = 187.0 µmol), compared to a mean relative reduction from baseline of 4.8% for all patients receiving placebo in the study (n=5, mean baseline tHcy = 131.1 µmol).
- In a dose-dependent manner in the study to date, methionine levels were substantially reduced and cystathionine levels were substantially elevated following treatment with pegtibatinase, suggesting that pegtibatinase acts in a manner similar to the native CBS enzyme.
- The Company plans to present additional detailed study results at an upcoming medical meeting or in a peer-reviewed publication.

Based on these results, the Company is preparing to engage with regulators to establish next steps for a pivotal development program to ultimately support potential approvals of pegtibatinase for the treatment of HCU. In parallel, the Company has initiated one additional cohort in the COMPOSE Study to inform and refine formulation work for future development and commercial purposes and to further evaluate the dose response curve for pegtibatinase. Patients enrolled in the COMPOSE Study are eligible to enter into an open-label extension and receive the 1.5mg/kg dose of pegtibatinase.

Conference Call Information

Travere Therapeutics will host a conference call and webcast today, Wednesday, December 15, 2021, at 8:30 a.m. ET to discuss the topline study results. To participate in the conference call, dial +1 (855) 219-9219 (U.S.) or +1 (315) 625-6891 (International), confirmation code 9690297 shortly before 8:30 a.m. ET. The webcast can be accessed at travere.com, in the Events and Presentations section of the Investors & Media page and will be archived for at least 30 days. A replay of the call will be available from 11:30 a.m. ET, December 15, 2021, to 11:30 a.m. ET, December 22, 2021. The replay number is +1 (855) 859-2056 (U.S.) or +1 (404) 537-3406 (International), confirmation code 9690297.

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 and heart attacks, ophthalmologic and skeletal complications, as well as developmental delay. Current treatment options are limited to protein-restricted diet and supplemental use of vitamin B6 and betaine.

About the COMPOSE Study

The ongoing Phase 1/2 COMPOSE Study is a randomized, multicenter, placebo controlled, double-blind dose escalation trial evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics and clinical effects of pegtibatinase in up to 40 patients with classical homocystinuria. Patients in COMPOSE are randomized 3:1 to receive subcutaneous doses of either pegtibatinase or placebo, and patients are eligible to continue in an open-label extension after the initial blinded twelve-week treatment period.

About Pegtibatinase (TVT-058)

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 Phase 1/2 COMPOSE Study to assess its safety, tolerability, pharmacokinetics, pharmacodynamics and clinical effects in patients with classical HCU. Pegtibatinase has been granted Rare Pediatric Disease and Fast Track designations by the US Food and Drug Administration (FDA), as well as Orphan Drug designation in the US 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 "may", "might", "believes", "thinks", "anticipates", "plans", "expects", "intends" 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 improve overall metabolic function and to be the first potential therapy to target the underlying enzyme deficiency in patients living with HCU; the Company's plans to engage with regulators to establish next steps for a pivotal development program to ultimately support the potential approvals of pegtibatinase for the treatment of HCU; the tolerability profile of pegtibatinase based on the preliminary data from the ongoing Compose Study; promise of the potentially novel approach to targeting the underlying enzymatic defect in HCU; and the ability for the additional cohort in the COMPOSE Study to inform and refine formulation work for future development and commercial purposes and to further evaluate the dose response curve for pegtibatinase. 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 clinical development, regulatory interactions and manufacturing of novel product candidates, as well as risks and uncertainties associated with the Company's business and finances in general, success of its commercial products as well as risks and uncertainties associated with the Company's preclinical and clinical stage pipeline. Specifically, the Company faces risk that the Compose Study will not proceed as planned, risks that pegtibatinase will not be approved for efficacy, safety, regulatory or other reasons, and for each of the Company's programs, risk associated with enrollment of clinical trials for rare diseases and risk that ongoing or planned clinical trials may not succeed or may be delayed for safety, regulatory or other reasons. The Company faces 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; risk 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; 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 faces additional risks associated with the potential impacts the COVID-19 pandemic may have on its business, including, but not limited to (i) the Company's ability to continue its ongoing development activities and clinical trials, (ii) the timing of such clinical trials and the release of data from those trials, (iii) the Company's and its suppliers' ability to successfully manufacture its commercial products and product candidates, and (iv) the market for and sales of its commercial products. 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 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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