Travere Therapeutics Announces Positive Topline Results from Cohort 6 in the Phase 1/2 COMPOSE Study of Pegtibatinase in Classical Homocystinuria

May 31, 2023

Data from the four patients treated with the highest dose of pegtibatinase showed a clinically meaningful 67.1% mean relative reduction in total homocysteine from baseline

Pegtibatinase has been generally well-tolerated to date

The Company is engaging with regulators and expects to initiate a pivotal Phase 3 Study by year-end 2023

Company to host conference call and webcast today at 8.30 a.m. ET

SAN DIEGO, May 31, 2023 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (NASDAQ: TVTX) today announced positive results from cohort 6 in the placebo-controlled Phase 1/2 COMPOSE Study of pegtibatinase, a novel investigational enzyme replacement therapy being evaluated for the treatment of classical homocystinuria (HCU). In this cohort, five patients were randomized in a blinded fashion to receive 2.5 mg/kg of lyophilized pegtibatinase or placebo twice weekly (BIW), with four patients assigned to the treatment group. In this highest dose cohort to date, treatment with pegtibatinase resulted in rapid and sustained reductions in total homocysteine (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 study, pegtibatinase has been generally well-tolerated.

“The results from cohort 6 in the Phase 1/2 COMPOSE Study build upon the dose dependent response observed in cohorts 1-5 and continue to demonstrate pegtibatinase has the potential to improve overall metabolic function in patients living with classical homocystinuria, a rare and devastating disease,” said William Rote, Ph.D., senior vice president of research and development at Travere Therapeutics. “Our goal is to deliver pegtibatinase as the first disease-modifying treatment option for the HCU community and today we are one step closer. We look forward to continuing to engage with regulators to further refine our plans for a potential pivotal Phase 3 study which is expected to initiate by year-end.”

“The current standard of care used to reduce homocysteine levels in individuals living with classical homocystinuria is a highly restrictive diet combined with vitamin B6 and betaine – and this presents significant challenges in maintaining metabolic control of homocysteine levels. As a result, many of these individuals continue to be at a high risk of having toxic levels of homocysteine in their bodies that often results in serious and long-term complications,” said Can Ficicioglu M.D., Ph.D., Clinical Director of the Metabolic Disease Program at Children’s Hospital of Philadelphia. “The impressive reduction of total homocysteine observed with the highest dose of pegtibatinase in the Phase 1/2 COMPOSE Study is very encouraging and offers hope for a potential novel approach to managing this devastating rare disease.”

Key safety findings:

- To date in the study, pegtibatinase has been generally well-tolerated.
- There were no reports of treatment-related serious adverse events, anaphylaxis, or discontinuations in the highest dose cohort treated with the 2.5 mg/kg twice weekly dose of pegtibatinase. To date, no evidence of neutralizing antibody activity has been observed as determined by pharmacokinetic and pharmacodynamic monitoring.
- Two participants receiving 2.5 mg/kg BIW reported moderate injection site reactions (ISRs) associated with urticaria, which resulted in a temporary dose interruption. Both participants restarted treatment at a lower dose after resolution of the ISR and were able to titrate up to the intended dose which was subsequently well-tolerated. There was no persistence or reoccurrence of urticaria with dose titration.

Key efficacy findings:

Summary of Relative Reduction in Geometric Mean of Total Homocysteine from Baseline from Cohorts 1-6 in the Phase 1/2 COMPOSE Study

		Pegtibatinase					
	Placebo	Cohort 1 0.33 mg/kg QW	Cohort 2 0.66 mg/kg QW	Cohort 3 1.0 mg/kg QW	Cohort 4 1.0 mg/kg BIW	Cohort 5 1.5 mg/kg BIW	Cohort 6 2.5 mg/kg BIW
Sample size (n)	6	3	3	3	2	3	4
Baseline Mean	124.8	148.2	134.7	140.7	175.4	186.6	96.8
End Mean*	125.5	142.3	140.4	142.7	131.2	79.9	31.8
Relative Change (%)*	0.6	-4.0	4.2	1.4	-25.2	-57.1	-67.1

*The data referenced in the table above and the analysis conducted in cohort 6 assess the relative reduction in tHcy from baseline in the geometric mean by averaging tHcy over weeks 6, 8, 10, and 12. This measure improves the precision and reliability of assessment of the treatment effect and takes into account that there is some variability in tHcy depending on food intake and diurnal variation.

- In the 2.5 mg/kg BIW dose cohort, treatment with pegtibatinase resulted in a mean relative reduction from baseline of 67.1% (n=4, mean baseline tHcy = 96.8 µM), compared to a 0.6% increase in tHcy levels from baseline for patients receiving placebo in the study (n=6, mean baseline tHcy = 124.8 µM).
- All patients achieved a mean tHcy below the clinically meaningful threshold of 100 µM, over weeks 6 to 12 of treatment. Some patients achieved tHcy below 50 µM, including one patient with a lower tHcy level at baseline achieving normalization of tHcy.
- 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 is engaging with regulators on the design of a potential pivotal Phase 3 study with the expectation of initiating a Phase 3 program by the end of 2023. The Company plans to present additional detailed study results at an upcoming medical meeting or in a peer-reviewed publication.

Conference call information

Travere Therapeutics will host a conference call and webcast today, Wednesday, May 31, 2023, at 8:30 a.m. ET to discuss the topline results from cohort 6 in the Phase 1/2 COMPOSE Study. To participate in the conference call, dial +1 (888) 394-8218 (U.S.) or +1 (323) 994-2093 (International), confirmation code 7036007. The webcast can be accessed on the Investor page of Travere’s website at ir.travere.com/events-presentations. Following the live webcast, an archived version of the call will be available for 30 days on the Company’s website.

About the COMPOSE Study

The 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 treatment period. In December 2021, the Company announced positive topline results through the first five cohorts of the Phase 1/2 COMPOSE Study, showing that treatment with pegtibatinase at a dose of 1.5 mg/kg BIW resulted in rapid and sustained reductions in tHcy through 12 weeks of treatment.

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 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). 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. In preclinical studies, pegtibatinase has demonstrated an ability to reduce total homocysteine levels and improve clinical parameters. 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 US and Europe. The Company is engaging with regulators on the design of a pivotal development program to ultimately support potential approvals of pegtibatinase for the treatment of HCU.

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”, "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 Company’s expectation to initiate a potential pivotal Phase 3 trial of pegtibatinase by year-end 2023; references to the potential for pegtibatinase to improve overall metabolic function in patients living with classical homocystinuria; the Company’s goal to deliver pegtibatinase as the first disease-modifying treatment option for the HCU community; the Company’s plans to continue 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; reference to the Phase 1/2 results offering hope for a potential novel approach to managing HCU; the safety and tolerability profile of pegtibatinase based on the preliminary data from the Phase 1/2 COMPOSE Study; the initial efficacy profile of pegtibatinase based on the preliminary data from the Phase 1/2 COMPOSE Study; the belief that pegtibatinase acts in a manner similar to the native CBS enzyme; and expectations regarding reporting additional detailed study results at an upcoming medical meeting or in a peer-reviewed publication. 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 and regulatory review process, as well as risks and uncertainties associated with the Company’s business and finances in general, 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. 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; 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 or abandoned for safety, regulatory, program assessment or other reasons. There is no guarantee that the Company will be able to align with regulators on the design of, or ultimately proceed with, a pivotal program for pegtibatinase for HCU or that the results of any such Phase 3 trial will be positive and support the future approval of pegtibatinase as a therapy for HCU. 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, including as a result of macroeconomic conditions; 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 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.

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/54878aae-03ca-4ee0-8f7e-bef38837ea4e

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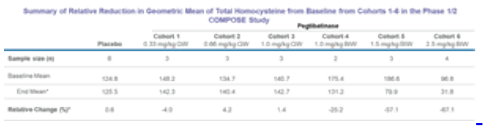

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