Travere Therapeutics Announces Positive Topline Interim Results from the Ongoing Phase 3 PROTECT Study of Sparsentan in IgA Nephropathy

August 16, 2021

Sparsentan treatment group experienced 49.8 percent mean reduction of proteinuria from baseline after 36 weeks, more than threefold the reduction of active comparator; interim primary efficacy endpoint achieved, p<0.0001

To date in the study, sparsentan has been generally well-tolerated and consistent with the previously observed safety profile

Submission of an NDA under Subpart H accelerated approval pathway in the U.S. expected in first half 2022

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

SAN DIEGO, Aug. 16, 2021 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (NASDAQ: TVTX) today announced positive topline interim results from the ongoing pivotal Phase 3 PROTECT Study of sparsentan, an investigational product candidate for the treatment of IgA nephropathy (IgAN). The PROTECT Study met its pre-specified interim primary efficacy endpoint with statistical significance, demonstrating a greater than threefold reduction of proteinuria from baseline after 36 weeks of treatment, compared to the active control irbesartan (p<0.0001). Preliminary results from the interim analysis suggest that to date in the study, sparsentan has been generally well-tolerated and consistent with the observed safety profile to date. Based on the results from the interim analysis, the Company plans to submit an application for accelerated approval in the U.S. in the first half of 2022 and also plans to submit an application for conditional marketing authorization in Europe.

“IgAN is a leading cause of end-stage kidney disease and there is a clear need for novel treatment options to slow the progression of this devastating rare kidney disorder,” said Eric Dube, Ph.D., chief executive officer of Travere Therapeutics. “These data from the PROTECT Study further demonstrate sparsentan’s ability to significantly reduce proteinuria and support its potential to become a new foundational treatment for people living with IgAN, if approved. We will continue our efforts to maintain high quality in this ongoing study, and we look forward to engaging with regulators as we prepare for accelerated approval submissions beginning in the first half of next year.”

Consistent with prior guidance, the Company is providing limited data from the interim analysis to maintain trial integrity in the ongoing study. In the PROTECT Study, a total of 404 patients with persistent proteinuria despite active ACE or ARB treatment, were randomized 1:1 to receive once daily oral doses of either sparsentan or irbesartan, the active control. The study protocol provided for an unblinded interim analysis to evaluate the primary efficacy endpoint – the change in proteinuria (urine protein-to-creatinine ratio) from baseline at Week 36 – approximately 36 weeks following randomization of the first 280 patients. After 36 weeks of treatment, patients receiving sparsentan achieved a mean reduction in proteinuria from baseline of 49.8 percent, compared to a mean reduction in proteinuria from baseline of 15.1 percent for irbesartan-treated patients (p<0.0001).

“Sparsentan has now demonstrated in one of the largest interventional studies to date in IgAN, a statistically robust and clinically meaningful proteinuria reduction relative to a current standard of care,” said Noah Rosenberg, M.D., chief medical officer of Travere Therapeutics. “These data build upon our Phase 2 DUET and Phase 3 DUPLEX studies in FSGS and further strengthen the support for our novel approach with sparsentan as a dual endothelin-angiotensin receptor antagonist being developed for rare kidney disorders. I want to thank all the patients, their families, as well as the investigators and site staff who continue to participate in this ongoing landmark study in IgAN.”

Secondary efficacy endpoints include the rate of change in estimated glomerular filtration rate (eGFR) following the initiation of randomized treatment over 58-week and 110-week periods, as well as the rate of change in eGFR over 52-week and 104-week periods following the first six weeks of randomized treatment. The Company believes that preliminary eGFR data available at the time of the interim analysis are indicative of a potential clinically meaningful treatment effect after two years of treatment. Per study protocol, patients will continue in a blinded manner in the PROTECT Study to fully assess the treatment effect on eGFR slope over 110 weeks in the confirmatory endpoint analysis. Topline results from the confirmatory endpoint analysis are expected in the second half of 2023.

A preliminary review of the interim safety results indicates that to date in the study, both treatment groups were generally well tolerated, and sparsentan appeared consistent with the previously observed safety profile with no new safety signals emerging.

The Company also remains on track to provide a regulatory update on its pivotal Phase 3 DUPLEX Study of sparsentan for the treatment of focal segmental glomerulosclerosis (FSGS) during the third quarter of 2021.

Conference Call Information

Travere Therapeutics will host a conference call and webcast today, Monday, August 16, 2021, at 8:30 a.m. ET to discuss the study results. To participate in the conference call, dial +1 (855) 219-9219 (U.S.) or +1 (315) 625-6891 (International), confirmation code 9558913 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, August 16, 2021, to 11:30 a.m. ET, August 23, 2021. The replay number is +1 (855) 859-2056 (U.S.) or +1 (404) 537-3406 (International), confirmation code 9558913.

About the PROTECT Study

The ongoing PROTECT Study is one of the largest interventional studies to date in IgAN. It is a global, randomized, multicenter, double-blind, parallel-arm, active-controlled clinical trial evaluating the safety and efficacy of 400mg of sparsentan, compared to 300mg of irbesartan, in 404 patients ages 18 years and up with IgAN and persistent proteinuria despite available ACE or ARB therapy. The PROTECT Study protocol provides for an unblinded interim analysis of at least 280 patients to be performed after 36 weeks of treatment to evaluate the primary efficacy endpoint – the change

in proteinuria (urine protein-to-creatinine ratio) at Week 36 from baseline. Secondary efficacy endpoints include the rate of change in eGFR following the initiation of randomized treatment over 58-week and 110-week periods, as well as the rate of change in eGFR over 52-week and 104-week periods following the first six weeks of randomized treatment.

About Sparsentan

Sparsentan, a Dual Endothelin Angiotensin Receptor Antagonist (DEARA), is a novel investigational product candidate. Pre-clinical data have shown that blockade of both endothelin type A and angiotensin II type 1 pathways in forms of rare chronic kidney disease, reduces proteinuria, protects podocytes and prevents glomerulosclerosis and mesangial cell proliferation. Sparsentan has been granted Orphan Drug Designation for the treatment of IgAN and FSGS in the U.S. and Europe.

Sparsentan is currently being evaluated in the pivotal Phase 3 DUPLEX Study for the treatment of focal segmental glomerulosclerosis (FSGS) and the pivotal Phase 3 PROTECT Study for the treatment of IgAN. In February 2021, the Company announced that the ongoing pivotal Phase 3 DUPLEX Study of sparsentan in FSGS achieved its pre-specified interim FSGS partial remission of proteinuria endpoint (FPRE) with statistical significance. FPRE is a clinically meaningful endpoint defined as urine protein-to-creatinine ratio (UP/C) ≤1.5 g/g and a >40 percent reduction in UP/C from baseline. After 36 weeks of treatment, 42.0 percent of patients receiving sparsentan achieved FPRE, compared to 26.0 percent of irbesartan-treated patients (p=0.0094). Preliminary results from the interim analysis suggest that at the time of the interim assessment, sparsentan had been generally well-tolerated and shown a comparable safety profile to irbesartan. In the Phase 2 DUET Study of sparsentan in FSGS, the combined treatment group met its primary efficacy endpoint, demonstrating a greater than two-fold reduction in proteinuria compared to irbesartan, and was generally well tolerated after the eight-week, double-blind treatment period. Irbesartan is part of a class of drugs used to manage FSGS and IgAN in the absence of an approved pharmacologic treatment. If approved for both indications, sparsentan could potentially be the first medicine approved for both FSGS and IgAN.

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 Company's current plan regarding, and expectations around the timeline for, submitting an application for accelerated approval of sparsentan for IgAN; references to the efficacy, safety and tolerability profile of sparsentan based on the preliminary data from the PROTECT Study interim analysis; the potential for sparsentan to become a new foundational treatment for people living with IgAN, if approved; the Company's belief that preliminary eGFR data available at the time of the interim analysis from the PROTECT Study are indicative of a potential clinically meaningful treatment effect after two years of treatment; expectations regarding the future conduct of the ongoing PROTECT study and timing for topline results from the confirmatory endpoint analysis; expectations around the timing for providing a regulatory update on the Company's pivotal Phase 3 DUPLEX Study of sparsentan for the treatment of focal segmental glomerulosclerosis (FSGS); and the potential for sparsentan to become the first medicine approved for both FSGS and IgAN. 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, including the Subpart H accelerated approval pathway in the United States and the conditional marketing authorization (CMA) pathway in the Europe Union, including the risk that the FDA and/or EMA could disagree with the Company's submission of an NDA under Subpart H for accelerated approval, or a Marketing Approval Application ("MAA") under the CMA pathway. Specifically, the Company faces the risk that the Phase 3 DUPLEX Study of sparsentan in FSGS will not demonstrate that sparsentan is safe or effective or serve as a basis for accelerated approval of sparsentan as planned; risk that the Phase 3 PROTECT Study of sparsentan in IgAN will not demonstrate that sparsentan is safe or effective or serve as the basis for accelerated approval of sparsentan as planned; and risk that sparsentan 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. There is no guarantee that the FDA will accept for filing the Company's planned NDA for sparsentan for IgAN under the Subpart H approval pathway, that the FDA will grant accelerated approval of sparsentan for IgAN or that sparsentan will be approved at all. 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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