Travere Therapeutics Announces Achievement of Interim Proteinuria Endpoint in the Ongoing Phase 3 DUPLEX Study of Sparsentan in Focal Segmental Glomerulosclerosis

February 2, 2021

Sparsentan achieved statistically significant response on interim proteinuria endpoint compared to irbesartan after 36-weeks of treatment

To date in the study, sparsentan has been generally well-tolerated and has shown a safety profile comparable to irbesartan

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

SAN DIEGO, Feb. 02, 2021 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (NASDAQ: TVTX) today announced that the Company's ongoing pivotal Phase 3 DUPLEX Study of sparsentan in focal segmental glomerulosclerosis (FSGS) achieved its pre-specified interim FSGS partial remission of proteinuria endpoint (FPRE) after 36 weeks of treatment. Sparsentan, an investigational product candidate, demonstrated a statistically significant response on FPRE compared to the active control, irbesartan (p=0.0094*).* Preliminary results from the interim analysis suggest that to date in the study, sparsentan has been generally well-tolerated and has shown a comparable safety profile to irbesartan. Based on the data from the interim analysis, the Company intends to pursue submissions for accelerated approval of sparsentan for FSGS. The Company plans to continue its engagement with regulators in the first half of 2021 to discuss the ongoing study and to establish next steps for filing with the available data set.

"For decades people living with FSGS have faced daily challenges in controlling proteinuria and a fear of progressing to transplant or dialysis because current treatment options are not enough," said Eric Dube, Ph.D., chief executive officer of Travere Therapeutics. "Today, we are very pleased to announce interim proteinuria results from the ongoing DUPLEX Study that demonstrate treatment with sparsentan can lead to significantly greater reductions in proteinuria compared to current standard of care. As we move ahead, our organization will be focused on maintaining high quality in this ongoing study, and on continuing our engagement with regulators to enable submissions for accelerated approval with the available data set."

Consistent with prior guidance, the Company is providing limited data from the interim analyses to maintain trial integrity in the ongoing study. In the DUPLEX Study, a total of 371 patients were randomized 1:1 to receive either sparsentan or irbesartan, the active control. The study protocol provided for an unblinded analysis to evaluate the interim efficacy endpoint – the proportion of patients achieving FPRE, which 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, at Week 36 – following the first approximately 190 patients reaching 36 weeks of treatment. 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).

The confirmatory primary endpoint of the DUPLEX Study to support full regulatory approval is the rate of change in eGFR over 108 weeks of treatment. As of the time of the interim analyses, available long-term eGFR data for the confirmatory endpoint were limited. Consistent with the DUPLEX Study protocol, patients will continue in a blinded manner to assess the treatment effect on eGFR slope over 108 weeks in the confirmatory endpoint analysis.

A preliminary review of the interim safety results indicate sparsentan has been generally well-tolerated and the overall safety profiles in the study to date have been generally comparable between treatment groups.

"These interim results from the largest interventional study in FSGS to date build upon the foundational evidence generated by the Phase 2 DUET Study. We believe these data provide further support for the innovative approach of combining endothelin and angiotensin II receptor antagonism in a single molecule to treat the high unmet need in these rare kidney disorders," said Noah Rosenberg, M.D., chief medical officer of Travere Therapeutics. "I would like to thank the patients and their caregivers, investigators and site staff whose continued commitment is critical to reaching this milestone and to ultimately completing this important study for those living with FSGS."

The DUPLEX Study is fully enrolled and is scheduled to continue as planned on a blinded basis to assess the confirmatory eGFR endpoint after 108 weeks of treatment. Topline results from the confirmatory endpoint are expected in the first half of 2023. The Company is also evaluating sparsentan for the treatment of IgA nephropathy in the ongoing pivotal Phase 3 PROTECT Study, and topline efficacy data from the 36-week interim proteinuria endpoint analysis from that study are anticipated in the third quarter of 2021.

Conference Call Information

Travere Therapeutics will host a conference call and webcast today, February 2, 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 3646349 shortly before 8:30 a.m. ET. The webcast can be accessed at travere.com, in the Events and Presentations section of the Investor Relations page and will be archived for at least 30 days. A replay of the call will be available from 11:30 a.m. ET, February 2, 2021 to 11:30 a.m. ET, February 9, 2021. The replay number is +1 (855) 859-2056 (U.S.) or +1 (404) 537-3406 (International), confirmation code 3646349.

About the DUPLEX Study

The ongoing DUPLEX Study is the largest interventional study to date in FSGS. It is a global, randomized, multicenter, double-blind, parallel-arm, active-controlled Phase 3 clinical trial assessing the efficacy and safety of sparsentan in 371 patients ages 8 to 75 years with primary FSGS. After a two-week washout period, patients are randomized 1:1 to receive either sparsentan or irbesartan, the active control, and subsequently dose titrated to the maximum dose of 800 mg of sparsentan or 300 mg of irbesartan, as tolerated. The DUPLEX Study protocol provides for an unblinded analysis of at least 190 patients to be performed after 36 weeks of treatment to evaluate the interim efficacy endpoint – the proportion of patients achieving a FSGS partial remission of proteinuria endpoint (FPRE), which is defined as urine protein-to-creatinine ratio (UP/C) ≤1.5 g/g and a >40 percent

reduction in Up/C from baseline, at Week 36. The confirmatory endpoint of the study is the change in slope of estimated glomerular filtration rate (eGFR) from baseline after 108 weeks of treatment.

About Focal Segmental Glomerulosclerosis

FSGS is a rare proteinuric kidney disorder that is estimated to affect up to 40,000 patients in the U.S. with similar prevalence in Europe. The disorder is defined by progressive scarring of the kidney and often leads to end-stage kidney disease (ESKD). FSGS is characterized by proteinuria, where protein leaks into the urine due to a breakdown of the normal filtration mechanism in the kidney. Once in the urine, protein is considered to be toxic to other parts of the kidney, especially the tubules, and is believed to contribute to further disease progression. Other common symptoms include swelling in parts of the body, known as edema, as well as low blood albumin levels, abnormal lipid profiles and hypertension.

Reduction in proteinuria appears to be beneficial in the treatment of FSGS and may be associated with a decreased risk of progression to ESKD. Achieving FPRE appears to be associated with long-term preservation of renal function in patients with FSGS. FSGS is currently managed with angiotensin receptor blockers, angiotensin converting enzyme inhibitors, steroids or calcineurin inhibitors.

About Sparsentan

Sparsentan is a novel investigational product candidate, that functions as a high affinity dual-acting antagonist of both the endothelin type A and angiotensin II type 1 receptors, in a single molecule. Pre-clinical data have shown that blockade of both 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 FSGS in the U.S. and Europe. Sparsentan has also been granted Orphan Drug Designation for the treatment of IgAN in the U.S. and has received a positive opinion from the European Medicines Agency Committee for Orphan Medicinal Products on the company's application for Orphan Drug Designation for IgAN in Europe.

Sparsentan is currently being evaluated in the pivotal Phase 3 DUPLEX Study for the treatment of FSGS and the pivotal Phase 3 PROTECT Study for the treatment of IgAN. 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 expectations around the timeline for continuing its engagement with regulators, expectations regarding anticipated accelerated approval regulatory submissions for sparsentan in FSGS based on the available data set from the DUPLEX interim analysis, 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. 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 FSGS under the Subpart H approval pathway, that the FDA will grant accelerated approval of sparsentan for FSGS 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 potential 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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Source: Travere Therapeutics, Inc.