Travere Therapeutics Announces FDA Acceptance and Priority Review of New Drug Application for Sparsentan for the Treatment of IgA Nephropathy

May 16, 2022

PDUFA target action date of November 17, 2022

SAN DIEGO, May 16, 2022 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (NASDAQ: TVTX) today announced the U.S. Food and Drug Administration (FDA) has accepted and granted Priority Review of its New Drug Application (NDA) under Subpart H for accelerated approval of sparsentan for the treatment of IgA nephropathy (IgAN). The FDA has indicated that it is not currently planning to hold an advisory committee meeting to discuss the application and has assigned a Prescription Drug User Fee Act (PDUFA) target action date of November 17, 2022.

“For decades people living with IgA nephropathy have had limited treatment options while facing a progression toward end-stage kidney disease. If approved, sparsentan would be the first FDA-approved non-immunosuppressive treatment option for IgA nephropathy, and we aspire to ultimately position sparsentan as a new standard of care,” said Eric Dube, Ph.D., president and chief executive officer of Travere Therapeutics. “Acceptance of the NDA and being granted Priority Review brings us one step closer to potentially delivering sparsentan to the IgA nephropathy community before the end of this year, and we look forward to continuing to work with the FDA throughout the review process.”

The NDA submission for sparsentan is supported by results from the ongoing pivotal Phase 3 PROTECT Study, one of the largest interventional studies to date in IgAN. The PROTECT Study evaluating sparsentan in 404 patients with persistent proteinuria, met its pre-specified interim primary efficacy endpoint measuring change in proteinuria compared to the active control irbesartan. 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 ($p<0.0001$). Preliminary results at the time of the interim assessment suggested that sparsentan had been generally well-tolerated in the study and consistent with its overall observed safety profile.

According to the FDA, a Priority Review designation directs overall attention and resources to the evaluation of applications for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

About IgA Nephropathy

IgA nephropathy (IgAN), also called Berger's disease, is a rare kidney disorder characterized by the buildup of immunoglobulin A (IgA), a protein that helps the body fight infections, in the kidneys. The deposits of IgA cause a breakdown of the normal filtering mechanisms in the kidney, leading to blood in the urine (hematuria), and protein in the urine (proteinuria). Other symptoms of IgAN may include kidney pain, swelling (edema) and high blood pressure.

IgAN is the most common type of primary glomerulonephritis worldwide and a leading cause of end-stage kidney disease (ESKD). IgAN is estimated to affect more than 100,000 people in the U.S. and is one of the leading causes of acute nephritis in Europe and Japan. There are currently no approved non-immunosuppressive treatments indicated for IgAN.

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. In August 2021, the Company announced the PROTECT Study met its pre-specified interim primary efficacy endpoint with statistical significance. 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 ($p<0.0001$). 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. Preliminary results at the time of the interim assessment suggested that sparsentan had been generally well-tolerated to date in the study and consistent with its overall observed safety profile. The PROTECT Study is fully enrolled and is scheduled to continue as planned on a blinded basis to 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.

About Sparsentan

Sparsentan, a Dual Endothelin Angiotensin Receptor Antagonist (DEARA), is a novel investigational product candidate selectively targeting the endothelin A receptor (ET_AR) and the angiotensin II subtype 1 receptor (AT_1R). 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 likelihood of the FDA's potential approval of sparsentan for IgAN by the November 17, 2022 target action date or at all; the expectation around any potential future request by the FDA to hold an advisory committee meeting related to the application; the potential for sparsentan to be the first FDA-approved non-immunosuppressive treatment option for IgA nephropathy and to ultimately become a standard of care; the potential to deliver sparsentan to the IgA nephropathy community before the end of this year; references to the Company's expectations of working with the FDA during the upcoming review process; references to the efficacy, safety and tolerability profile of sparsentan based on the preliminary data from the PROTECT Study interim analysis; 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; references to the estimated number of IgAN patients in the U.S.; 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 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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