Travere Therapeutics Provides Regulatory Updates on its Development Programs

August 3, 2022

PDUFA target action date for NDA for sparsentan in IgAN on-track for November 17, 2022

Company to utilize traditional approval process for sparsentan in FSGS following completion of the pivotal Phase 3 DUPLEX Study in 2023

Company and its partner Vifor Pharma applying for conditional marketing authorization of sparsentan for IgAN in Europe; review decision expected in second half of 2023

Pegtibatinase granted Breakthrough Therapy Designation by FDA

Company to host conference call and webcast tomorrow at 8:00 a.m. ET

SAN DIEGO, Aug. 03, 2022 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (NASDAQ: TVTX) today provided regulatory updates for its sparsentan programs in IgA nephropathy (IgAN) and focal segmental glomerulosclerosis (FSGS), as well as its pegtibatinase program for classical homocystinuria (HCU).

Sparsentan NDA for accelerated approval in IgAN on-track for PDUFA target action date of November 17, 2022

The Company recently completed a mid-cycle review meeting with the U.S. Food and Drug Administration (FDA) for its New Drug Application (NDA) currently under priority review for accelerated approval of sparsentan for the treatment of IgAN. The FDA indicated that the NDA review process is proceeding as planned with no advisory committee meeting expected and that it remains on-track for the previously assigned Prescription Drug User Fee Act (PDUFA) target action date of November 17, 2022.

Following FDA feedback on the ongoing pivotal Phase 3 DUPLEX Study, Company planning to pursue traditional approval of sparsentan for FSGS in 2023

The Company also completed its planned Type A meeting with the FDA to discuss a potential submission for accelerated approval of sparsentan for FSGS. In recently received final meeting minutes, the FDA acknowledged the high unmet need for approved therapies as well as the challenges in studying FSGS but indicated that the interim analysis from the ongoing pivotal Phase 3 DUPLEX Study conducted in 2021 together with the recent limited additional estimated glomerular filtration (eGFR) data-cut do not meet their threshold to support an application for accelerated approval in FSGS, which would be the first accelerated approval in FSGS. The FDA indicated that the DUPLEX Study as designed maintains the potential for full approval pending completion of the study and recommends that the Company pursue traditional approval based on two-year eGFR slope. The Company anticipates having topline data from the DUPLEX Study, including full two-year eGFR data, in the first half of 2023 and to be in position to submit an NDA for full approval in the second half of the year.

“Our goal is to enable sparsentan to become a new treatment standard for rare kidney disorders, and we believe we are well-positioned for the first potential approval of sparsentan in IgA nephropathy in November of this year,” said Eric Dube, Ph.D., president and chief executive officer of Travere Therapeutics. “While we are disappointed that we will not be filing for accelerated approval of sparsentan in FSGS, the eGFR data in the DUPLEX Study have continued to progress in a manner consistent with the profile of sparsentan and we remain confident that the study can support an application for full approval in FSGS next year. We look forward to continuing to work with the FDA throughout the ongoing review of our NDA for accelerated approval of sparsentan in IgA nephropathy and as we prepare for an NDA submission for FSGS next year.”

The Company and its partner Vifor Pharma are applying for conditional marketing authorisation of sparsentan for the treatment of IgAN in Europe

The Company and its partner Vifor Pharma are submitting a Conditional Marketing Authorisation (CMA) application for sparsentan for the treatment of IgAN in Europe. A review decision on a potential approval is expected in the second half of 2023. Pending completion of the DUPLEX Study and data supportive of approval, a subsequent CMA variation of sparsentan for the treatment of FSGS is targeted for submission by the end of 2023.

Pegtibatinase granted Breakthrough Therapy Designation for HCU

The FDA recently granted Breakthrough Therapy Designation to pegtibatinase, the Company’s novel investigational enzyme replacement therapy being evaluated for the treatment of HCU.

The Breakthrough Therapy Designation is supported by data from the ongoing Phase 1/2 COMPOSE Study of pegtibatinase in patients with HCU, as well as data from the Company’s ongoing natural history study. In the COMPOSE Study, treatment with 1.5mg/kg, twice weekly doses of 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. As of the data cut-off, pegtibatinase has been generally well-tolerated.

“Many people living with HCU are unable to adequately control toxic homocysteine levels with the limited available treatment options. As a result, they are living at high risk of developing long-term, serious complications from disease progression,” said Bill Rote, Ph.D., senior vice president of research and development at Travere Therapeutics. “Receiving Breakthrough Therapy Designation is a significant step forward in the development of our program and we look forward to continuing to work closely with the FDA as we seek to align on a pivotal Phase 3 program that will ultimately position pegtibatinase to potentially become the first disease-modifying therapy for HCU.”

Breakthrough Therapy Designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies on a clinically significant endpoint(s). Drugs that receive Breakthrough Therapy Designation are eligible for Fast Track designation features, intensive guidance on an efficient drug development program, and organizational commitment from the FDA.

The Company will report second quarter 2022 financial results tomorrow, Thursday, August 4, 2022, and host a conference call and webcast to discuss corporate updates and financial results at 8:00 a.m. ET.

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 FSGS and IgAN in the U.S. and 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 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 August of 2021, the Company announced that the ongoing PROTECT Study in IgAN 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 at the time of the interim assessment, sparsentan had been generally well tolerated and performed consistent with the observed safety profile to date. 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. An NDA for accelerated approval of sparsentan in IgAN is currently being evaluated by the FDA under Priority Review designation. If approved for both indications, sparsentan could potentially be the first medicine approved for both FSGS and IgAN.

About Pegtibatinase

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 ongoing Phase 1/2 COMPOSE Study to assess its safety, tolerability, pharmacokinetics, pharmacodynamics and clinical effects in patients with classical HCU. Pegtibatinase 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.

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 Company's goal of making sparsentan a new treatment standard for rare kidney disorders, if approved; references to the Company's expectations of working with the FDA during the review process; the ability to submit for traditional approval in FSGS following the completion of the DUPLEX Study and expectations regarding the timing thereof, as well as plans for regulatory submissions of sparsentan in Europe for IgAN and FSGS and the timings thereof; references to the efficacy, safety and tolerability profile of sparsentan based on the preliminary data from the DUPLEX and PROTECT Studies' interim analyses; 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 and DUPLEX studies and timing for topline results from the two-year endpoint analyses; the potential for sparsentan to become the first medicine approved for both FSGS and IgAN; the Company's plans for working with regulators this year to align on the design of a pivotal program that can enable pegtibatinase to potentially become the first disease modifying therapy for the HCU; and the expectation that Breakthrough Therapy designation for pegtibatinase for HCU will confer advantages on the program. 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 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; 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 traditional approval of sparsentan as planned; and the 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 review process for the sparsentan IgAN NDA will remain on

track for the FDA's assigned target action date, that the FDA will grant accelerated approval of sparsentan for IgAN within the assigned target action date, or at all, or that the DUPLEX Study will support an application for traditional review or that sparsentan will be approved for FSGS. There is also no guarantee that the results from the ongoing clinical study of pegtibatinase will be positive or that the Company will be able to align with regulators on the design of a pivotal program for pegtibatinase 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; 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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