Travere Therapeutics to Present Abstracts at the American Society of Nephrology (ASN) Kidney Week 2023

October 13, 2023

Two late-breaking high-impact oral presentations of the Phase 3 PROTECT Study of FILSPARI® (sparsentan) in IgAN and Phase 3 DUPLEX Study of sparsentan in FSGS

11 total abstracts accepted for presentation highlight Travere's leadership and commitment in the field of rare kidney disease

SAN DIEGO, Oct. 13, 2023 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc. (Nasdaq: TVTX) today announced that the Company will present 11 abstracts, including two late-breaking oral presentations, at the upcoming American Society of Nephrology (ASN) Kidney Week 2023 in Philadelphia, PA, November 2-5, 2023.

Presentations will highlight the long-term efficacy and tolerability data of FILSPARI® (sparsentan) in IgA nephropathy (IgAN) from the PROTECT Study, as well as the potential for use of FILSPARI as a first-line treatment in newly diagnosed IgAN patients and in combination with SGLT2 inhibitors. The Company will also present data on the efficacy and tolerability of sparsentan in focal segmental glomerulosclerosis (FSGS) and pediatric proteinuric glomerular diseases, as well as provide insights into patient quality of life and the impact of proteinuria on kidney survival in rare kidney diseases.

"The data we and our collaborators are presenting at ASN are a testament to our collective dedication to enhance our scientific understanding of kidney diseases to improve patients' lives," said Jula Inrig, M.D., chief medical officer of Travere Therapeutics. "We look forward to presenting data that further demonstrate the clinical benefit of sparsentan in rare kidney diseases and sharing important advancements that have the potential to shape the future of patient care."

Late-Breaker Oral Presentations

Sparsentan vs Irbesartan in Patients with Focal Segmental Glomerulosclerosis (FSGS): Results from the Phase 3 DUPLEX Trial
Abstract: FR-OR108
Oral Abstract Session: High Impact Clinical Trials
Hall A; November 3, 10:30-10:45 a.m. ET

Pivotal Results of the Phase 3 PROTECT Trial of Sparsentan vs Irbesartan in Patients with Immunoglobulin A Nephropathy (IgAN)
Abstract: FR-OR109
Oral Abstract Session: High Impact Clinical Trials
Hall A; November 3, 10:45-11:00 a.m. ET

Oral Presentation

Preliminary Findings from the Phase 2 EPPIK Study of Sparsentan in Pediatric Patients with Selected Proteinuric Glomerular Diseases
Abstract: SA-OR84
Oral Abstract Session: Pediatric Nephrology: Clinical and Genetic Studies
Room 105; November 4, 5:24-5:33 p.m. ET

Poster Presentations

Humanistic Burden of Rare Kidney Diseases: Understanding the Impact of IgAN and FSGS on Patients & Care-partners Study (HONUS): Preliminary Results for FSGS in the United States (US)
Poster: TH-PO597
Poster Session: Glomerular Diseases: Clinical and Epidemiologic Studies
Exhibit Hall; November 2, 10:00 a.m.-12:00 p.m. ET

Predictors of Major Adverse Kidney Disease Events in a Real-world Population with IgA Nephropathy
Poster: TH-PO614
Poster Session: Glomerular Diseases: Clinical and Epidemiologic Studies
Exhibit Hall; November 2, 10:00 a.m.-12:00 p.m. ET

Comparing Proteinuria and Kidney Survival in FSGS and IgAN: A NEPTUNE Analysis
Poster: TH-PO622
Poster Session: Glomerular Diseases: Clinical and Epidemiologic Studies
Exhibit Hall; November 2, 10:00 a.m.-12:00 p.m. ET

Sparsentan as First-line Treatment of Incident Patients with IgA Nephropathy: Preliminary Findings from the SPARTAN Trial
Poster: SA-PO901
Poster Session: Glomerular Diseases: Therapeutics
Exhibit Hall; November 4, 10:00 a.m.-12:00 p.m. ET

Sparsentan Receptor Occupancy Modeling, Clinical Actions, and Safety

Poster: SA-PO276
Poster Session: Pharmacology: Kinetics, Genomics, Medication-Related Problems
Exhibit Hall; November 4, 10:00 a.m.-12:00 p.m. ET

Concomitant Sparsentan and Sodium-glucose Cotransporter-2 Inhibitors (SGLT2i) in Patients with IgA Nephropathy (IgAN) in the PROTECT Open-label Extension (OLE)
Poster: SA-PO903
Poster Session: Glomerular Diseases: Therapeutics
Exhibit Hall; November 4, 10:00 a.m.-12:00 p.m. ET

Rate of Loss of eGFR and Time-averaged Proteinuria in IgAN Patients Progressing from Early Stage Disease to Kidney Failure
Poster: SA-PO948
Poster Session: Glomerular Diseases: Translational Studies and Biomarkers
Exhibit Hall; November 4, 10:00 a.m.-12:00 p.m. ET

Sparsentan and Sodium-glucose Cotransporter 2 Inhibitors (SGLT2i) in the PROTECT Open-label extension (OLE) Substudy and SPARTACUS: Trials in Progress
Poster: SA-PO902
Poster Session: Glomerular Diseases: Therapeutics
Exhibit Hall; November 4, 10:00 a.m.-12:00 p.m. ET

About IgA Nephropathy

IgA nephropathy (IgAN), also called Berger's disease, is a rare progressive kidney disease 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), protein in the urine (proteinuria) and a progressive loss of kidney function. Other symptoms of IgAN may include swelling (edema) and high blood pressure.

IgAN is the most common type of primary glomerulonephritis worldwide and a leading cause of kidney failure due to glomerular disease. IgAN is estimated to affect up to 150,000 people in the U.S. and is one of the most common glomerular diseases in Europe and Japan.

About Focal Segmental Glomerulosclerosis

Focal segmental glomerulosclerosis (FSGS) is a rare proteinuric kidney disorder in both children and adults that is estimated to affect more than 40,000 patients in the US with similar prevalence in Europe. The disorder is defined by progressive scarring of the kidney and often leads to kidney failure. 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. There is currently no approved pharmacologic indicated for the treatment of FSGS.

About the PROTECT Study

The PROTECT Study is one of the largest interventional studies to date in IgA nephropathy (IgAN) and the only head-to-head trial in this rare kidney disease. It is a global, randomized, multicenter, double-blind, parallel-arm, active-controlled clinical trial evaluating the safety and efficacy of 400 mg of sparsentan, compared to 300 mg of irbesartan, in 404 patients ages 18 years and up with IgAN and persistent proteinuria despite receiving at least 50% of max label dose and maximally tolerated ACE or ARB therapy. In August 2021, the Company announced the PROTECT Study met its pre-specified interim primary efficacy endpoint with statistical significance. Based on the pre-specified, primary analyses set, after 36 weeks of treatment, patients receiving sparsentan achieved a mean reduction in proteinuria from baseline of 49.8%, compared to a mean reduction in proteinuria from baseline of 15.1% for irbesartan-treated patients ($p<0.0001$). The study's confirmatory secondary endpoint in the U.S. is eGFR total slope from day 1 to week 110 of treatment. The confirmatory secondary endpoint in the EU is eGFR chronic slope from week 6 to week 110 of treatment, following the initial acute effect of randomized treatment. Following the 110-week blinded treatment period, treatment with study medication is discontinued for 4 weeks -- at this time, the investigator resumes standard of care treatment. Patients that completed the PROTECT double-blind portion of the study on treatment were eligible to participate in the open-label portion of the trial.

About the DUPLEX Study

The 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. 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 (FPRE) endpoint 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% of patients receiving sparsentan achieved FPRE, compared to 26.0% 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. The study's primary efficacy endpoint in the U.S. is the eGFR total slope from day 1 to week 108 of treatment. The primary efficacy endpoint in Europe is the eGFR chronic slope, from week 6 to week 108 of treatment, following the initial acute effect of randomized treatment. Patients that completed the DUPLEX double-blind portion of the study on treatment were eligible to participate in the open-label portion of the trial.

About the SPARTACUS Study

The SPARTACUS Study aims to evaluate the safety and effect of sparsentan in combination with SGLT2 inhibitor therapy in approximately 60 adult IgAN patients at risk of disease progression to kidney failure. In this 28-week, open-label, multi-center, single-group Phase 2 exploratory study, eligible participants on stable SGLT2 inhibitor dosing are administered sparsentan (target dose of 400 mg) for 24 weeks after discontinuation of standard of care ACEI and/or ARB treatment, followed by a 4-week safety follow-up period. The study will evaluate safety and efficacy outcomes including change

in proteinuria from baseline and achievement of remission of proteinuria-based endpoints through week 24. Patient enrollment is ongoing and the study is anticipated to readout in 2025.

About the SPARTAN Study

The SPARTAN Study a multi-center, open-label, single-group trial exploring the safety and response to first-line sparsentan treatment in newly diagnosed, renin angiotensin system (RAS) blockade-naïve adult patients with biopsy-proven IgAN. The study is a collaboration between Travere Therapeutics and the University of Leicester (Study Sponsor) and is being conducted in 5 hospitals in the UK. Participants (n=12) are administered sparsentan (target dose of 400 mg) for 110 weeks, followed by a 4-week safety period. In addition to established safety and efficacy assessments, including incidence of adverse events, change in proteinuria and eGFR, the mechanistic actions of sparsentan are explored through renal MRI assessments and analyses comparing diagnostic biopsies with repeat biopsies performed at week 24. The study is fully enrolled, with final readout scheduled for 2025.

FILSPARI® (sparsentan) U.S. Indication

FILSPARI is an endothelin and angiotensin II receptor antagonist indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a UPCR ≥1.5 g/g.

This indication is granted under accelerated approval based on reduction in proteinuria. It has not been established whether FILSPARI slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

FILSPARI® (sparsentan) Important Safety Information

BOXED WARNING: HEPATOTOXICITY AND EMBRYO-FETAL TOXICITY
Because of the risks of hepatotoxicity and birth defects, FILSPARI is available only through a restricted program called the FILSPARI REMS. Under the FILSPARI REMS, prescribers, patients and pharmacies must enroll in the program.

Hepatotoxicity
Some Endothelin Receptor Antagonists (ERAs) have caused elevations of aminotransferases, hepatotoxicity, and liver failure. In clinical studies, elevations in aminotransferases (ALT or AST) of at least 3-times the Upper Limit of Normal (ULN) have been observed in up to 2.5% of FILSPARI-treated patients, including cases confirmed with rechallenge.

Measure transaminases and bilirubin before initiating treatment and monthly for the first 12 months, and then every 3 months during treatment. Interrupt treatment and closely monitor patients who develop aminotransferase elevations more than 3x ULN.

FILSPARI should generally be avoided in patients with elevated aminotransferases (>3x ULN) at baseline because monitoring for hepatotoxicity may be more difficult and these patients may be at increased risk for serious hepatotoxicity.

Embryo-Fetal Toxicity
FILSPARI can cause major birth defects if used by pregnant patients based on animal data. Therefore, pregnancy testing is required before the initiation of treatment, during treatment and one month after discontinuation of treatment with FILSPARI. Patients who can become pregnant must use effective contraception before the initiation of treatment, during treatment, and for one month after discontinuation of treatment with FILSPARI.

Contraindications: FILSPARI is contraindicated in patients who are pregnant. Do not coadminister FILSPARI with angiotensin receptor blockers (ARBs), ERAs, or aliskiren.

Warnings and Precautions

Hepatotoxicity: Elevations in ALT or AST of at least 3-fold ULN have been observed. To reduce the risk of potential serious hepatotoxicity, measure serum aminotransferase levels and total bilirubin prior to initiation of treatment, monthly for the first 12 months, then every 3 months during treatment.

Advise patients with symptoms suggesting hepatotoxicity (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching) to immediately stop treatment with FILSPARI and seek medical attention. If aminotransferase levels are abnormal at any time during treatment, interrupt FILSPARI and monitor as recommended.

Consider re-initiation of FILSPARI only when hepatic enzyme levels and bilirubin return to pretreatment values and only in patients who have not experienced clinical symptoms of hepatotoxicity.

Avoid initiation of FILSPARI in patients with elevated aminotransferases (>3x ULN) prior to drug initiation.

Embryo-Fetal Toxicity: FILSPARI can cause fetal harm. Advise patients who can become pregnant of the potential risk to a fetus. Obtain a pregnancy test and advise patients who can become pregnant to use effective contraception prior to, during, and one month after discontinuation of FILSPARI treatment.

FILSPARI REMS: FILSPARI is available only through a restricted program under a REMS called the FILSPARI REMS.

Important requirements include:

- Prescribers must be certified with the FILSPARI REMS by enrolling and completing training.
- All patients must enroll in the FILSPARI REMS prior to initiating treatment and comply with monitoring requirements.
- Pharmacies that dispense FILSPARI must be certified with the FILSPARI REMS and must dispense only to patients who are authorized to receive FILSPARI.

Further information is available at www.filsparirems.com or 1-833-513-1325.

Hypotension: There was a greater incidence of hypotension-associated adverse events, some serious, including dizziness, in patients treated with FILSPARI compared to irbesartan. In patients at risk for hypotension, consider eliminating or adjusting other antihypertensive medications and maintaining appropriate volume status. If hypotension develops, consider a dose reduction or dose interruption of FILSPARI.

Acute Kidney Injury: Monitor kidney function periodically. Patients whose kidney function may depend in part on the activity of the renin-angiotensin system (e.g., patients with renal artery stenosis, chronic kidney disease, severe congestive heart failure, or volume depletion) may be at particular risk of developing acute kidney injury on FILSPARI. Consider withholding or discontinuing therapy in patients who develop a clinically significant decrease in kidney function while on FILSPARI.

Hyperkalemia: Monitor serum potassium periodically and treat appropriately. Patients with advanced kidney disease, taking concomitant potassium-increasing drugs (e.g., potassium supplements, potassium-sparing diuretics), or using potassium-containing salt substitutes are at increased risk for developing hyperkalemia. Dosage reduction or discontinuation of FILSPARI may be required.

Fluid Retention: Fluid retention may occur with ERAs, and has been observed with FILSPARI. If clinically significant fluid retention develops, after evaluation, consider modifying the dose of FILSPARI.

Most common adverse reactions (5%) with FILSPARI are peripheral edema, hypotension (including orthostatic hypotension), dizziness, hyperkalemia, and anemia.

Drug interactions

- **Renin-Angiotensin System (RAS) Inhibitors and ERAs:** Do not coadminister FILSPARI with angiotensin receptor blockers (ARBs), ERAs, or aliskiren.
- **Strong and Moderate CYP3A Inhibitors:** Avoid concomitant use of FILSPARI with strong CYP3A inhibitors. Monitor blood pressure, serum potassium, edema, and kidney function regularly when used concomitantly with moderate CYP3A inhibitors.
- **Strong CYP3A Inducers:** Avoid concomitant use with a strong CYP3A inducer.
- **Antacids and Acid Reducing Agents:** Administer FILSPARI 2 hours before or after administration of antacids. Avoid concomitant use of acid reducing agents (histamine H2 receptor antagonist and PPI proton pump inhibitor) with FILSPARI**.**
- **Non-Steroidal Anti-Inflammatory Agents (NSAIDs), Including Selective Cyclooxygenase-2 (COX-2) Inhibitors:** Monitor for signs of worsening renal function.
- **CYP2B6, 2C9, and 2C19 Substrates:** Monitor for efficacy of the concurrently administered CYP2B6, 2C9, and 2C19 substrates and consider dosage adjustment in accordance with the Prescribing Information.
- **P-gp and BCRP Substrates: A**void concomitant use of sensitive substrates of P-gp and BCRP with FILSPARI.
- **Agents Increasing Serum Potassium:** Monitor serum potassium frequently. Concomitant use of FILSPARI with potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, or other drugs that raise serum potassium levels may result in hyperkalemia.

Use in specific populations

- **Pregnancy / Females and Males of Reproductive Potential:** FILSPARI can cause fetal harm, including birth defects and fetal death, when administered to a pregnant patient and is contraindicated during pregnancy.
    - **Pregnancy Testing / Contraception:** Verify the pregnancy status and effective method of contraception prior to, during, and one month after discontinuation of FILSPARI treatment. The patient should contact their physician immediately for pregnancy testing if onset of menses is delayed or pregnancy is suspected.
- **Lactation:** Advise patients not to breastfeed during treatment with FILSPARI.
- **Hepatic Impairment:** Avoid use of FILSPARI in patients with any hepatic impairment (Child-Pugh class A-C).

Please see Full Prescribing Information for FILSPARI here.

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 “anticipate,” “believe,” “expect,” “intend,” “may,” “might,” “objective,” “plan,” “will” 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 potential effect of FILSPARI (sparsentan) as a first-line treatment in newly diagnosed IgAN patients and in combination with SGLT2 inhibitors, references to data on the long-term efficacy and tolerability of FILSPARI in IgAN, references to data on the efficacy and tolerability of sparsentan in FSGS and pediatric proteinuric glomerular diseases, anticipated readout dates, and references to PROTECT, DUPLEX, and the other studies referenced herein. 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, risks associated with enrollment of clinical trials for rare diseases, and risks that ongoing or planned clinical trials may not succeed or may be delayed for safety, regulatory or other reasons. The Company faces risks related to the commercial launch of a new product; risks associated with market acceptance of FILSPARI and other current and future products, including efficacy, safety, price, reimbursement and benefit over competing therapies; the risk that the results of the Phase 3 PROTECT Study of sparsentan in IgAN will not be deemed sufficient by the FDA to serve as the basis for an sNDA submission for traditional approval of sparsentan; and the risk that the results from the Phase 3 DUPLEX study of sparsentan in FSGS will not serve as a basis for a regulatory submission for approval of sparsentan for FSGS. There is no guarantee that regulators will grant full approval of sparsentan for IgAN or FSGS. The Company also 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; risks 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; and 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.

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