Travere Therapeutics Announces Full FDA Approval of FILSPARI® (sparsentan), the Only Non-Immunosuppressive Treatment that Significantly Slows Kidney Function Decline in IgA Nephropathy

September 5, 2024

FDA approves expanded indication making FILSPARI available to patients with IgA nephropathy (IgAN) at risk of progression; updated label includes data showing long-term durable benefit on proteinuria and kidney function preservation that accrued over two years

Conversion to full approval based on results from the PROTECT Study, where FILSPARI delivered superior long-term kidney function preservation compared to the active comparator irbesartan in the only Phase 3 head-to-head trial conducted in IgAN

As an oral, non-immunosuppressive and dual acting, once-daily medicine with superior long-term results vs. irbesartan, FILSPARI has the potential to become foundational care in IgAN

Company to host conference call September 5, 2024, at 6 p.m. ET

SAN DIEGO, Sept. 05, 2024 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc., (Nasdaq: TVTX) today announced that the U.S. Food and Drug Administration (FDA) has granted full approval to FILSPARI® (sparsentan) to slow kidney function decline in adults with primary IgAN who are at risk of disease progression. FILSPARI was granted accelerated approval in February 2023 based on the surrogate marker of proteinuria. Full approval is based on positive long-term confirmatory results from the PROTECT Study demonstrating that FILSPARI significantly slowed kidney function decline over two years compared to irbesartan.

“We know that most people living with IgAN are at risk of disease progression and are seeking a safe, effective and convenient treatment option that can help preserve their kidney function. Full approval now enables physicians to confidently prescribe FILSPARI more broadly as a once-daily, oral, non-immunosuppressive treatment, that can provide superior preservation of kidney function and replace current standard of care,” said Eric Dube, Ph.D., president and chief executive officer of Travere Therapeutics. “With KDIGO’s recent draft guidelines recommending FILSPARI as a foundational kidney-targeted therapy and lowering the targeted proteinuria level for all IgAN patients to under 0.5 g/day or 0.3 g/day – FILSPARI is well positioned to become foundational care for IgAN as the treatment landscape evolves. We are grateful to the patients, caregivers, clinical trial investigators, healthcare providers, and advocates who have worked alongside our team at Travere for so many years to help raise the bar on protecting and preserving kidney health for those living with rare kidney disease.”

FILSPARI is the only oral, once-daily, non-immunosuppressive medication that directly targets glomerular injury in the kidney by blocking two critical pathways of IgAN disease progression (endothelin-1 and angiotensin II).

The two-year efficacy data contained in the FDA-approved label is a modified intention to treat (ITT) analysis, and as preferred by the FDA, evaluates data from all patients regardless of treatment discontinuation. In the final analysis of the 404 randomized patients, FILSPARI significantly reduced the rate of decline in kidney function from baseline to Week 110 compared to irbesartan. In the ITT analysis included in the label, the mean eGFR slope from baseline to Week 110 was -3.0 mL/min/1.73 m^2/year for FILSPARI and -4.2 mL/min/1.73 m^2/year for irbesartan, corresponding to a statistically significant treatment effect of 1.2 mL/ min/1.73 m^2/year (p=0.0168). The positive treatment effects on proteinuria compared to the active control irbesartan that were observed at Week 36 were durable out to the two-year measurement period. Additional results from the PROTECT Study demonstrated the benefit of FILSPARI on absolute eGFR accrued over time and by Week 110 resulted in a 3.8 mL/min/1.73 m^2 difference in the mean change from baseline between FILSPARI and irbesartan.

Results from the PROTECT Study showed that FILSPARI was well tolerated with a clearly defined safety profile that has been consistent across all clinical trials conducted to date. Following engagement with the FDA, the Company expects to submit an sNDA for a potential modification to the liver-monitoring REMS.

“As a physician who has dedicated my career to treating patients with glomerular diseases, I believe the full approval of FILSPARI for IgAN provides us with a critically important tool for patient management,” said Brad Rovin, M.D., medical director at The Ohio State University Center for Clinical Research Management, director, Division of Nephrology, and steering committee member for the PROTECT Study. “This approval should facilitate patient access to a medication that targets injury directly in the kidney, reduces proteinuria, even to the point of complete remission in some patients, and is more effective than current standard-of-care treatment in preserving kidney function over time. This is a very exciting milestone in the evolution of treating IgAN.”

“Today’s full approval of FILSPARI brings new hope to the IgAN community, and I’m grateful for the progress that has been made in giving patients a new treatment option that can help protect their kidneys,” said Bonnie Schneider, executive director and co-founder of the IgA Nephropathy Foundation.

“The expanded indication and full approval of FILSPARI is welcome news for the rare kidney disease community,” said Josh Tarnoff, chief executive officer of NephCure. “We have waited a long time for a medicine to slow the irreversible kidney damage from IgAN and appreciate Travere’s leadership in championing new endpoints for IgAN that have spurred significant innovation for this rare kidney disease.”

Travere Therapeutics has a comprehensive patient support program, Travere TotalCare®, to enable a smooth experience for patients, their caregivers, and healthcare providers. This program provides services, assistance, and resources that can help patients understand IgAN, manage the insurance process, fill their prescriptions and initiate treatment. Patients or providers can call 833-FILSPARI (833-345-7727) or visit TravereTotalCare.com to learn more.

Conference call information

Travere Therapeutics will host a conference call and webcast today, Thursday, September 5, 2024 at 6 p.m. ET to discuss the FDA full approval of FILSPARI. To participate in the conference call, dial +1 (888) 394-8218 (U.S.) or +1 +1 (323) 994-2093 (International), confirmation code 1966916. The webcast can be accessed on the Investor page of Travere's website at ir.travere.com/events-presentations. Following the live webcast, an archived version of the call will be available for 30 days on the Company's website.

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 the PROTECT Study

The PROTECT Study is one of the largest interventional studies to date in IgA nephropathy (IgAN) and the only Phase 3 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 FILSPARI (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.

The primary efficacy endpoint for the interim analysis was the change from baseline in urine protein/creatinine ratio at Week 36. The key secondary efficacy endpoint for the final analysis was the rate of change in eGFR over a 110-week period following initiation of randomized therapy.

The trial met the pre-specified primary endpoint which showed that after 36 weeks patients receiving FILSPARI 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 two-year efficacy data contained in the FDA-approved label is a modified intention to treat (ITT) analysis, and as preferred by the FDA, evaluates data from all patients regardless of treatment discontinuation. In the final analysis of 404 randomized patients, FILSPARI reduced the rate of decline in kidney function from baseline to Week 110 compared to irbesartan. The mean eGFR slope from baseline to Week 110 was -3.0 mL/min/1.73 m^2/year for FILSPARI and -4.2 mL/min/1.73 m^2/year for irbesartan, corresponding to a statistically significant treatment effect of 1.2 mL/ min/1.73 m^2/year ($p=0.0168$).

Additional results from the PROTECT Study demonstrated the benefit of FILSPARI on absolute eGFR accrued over time and by Week 110 resulted in a 3.8 mL/min/1.73 m^2 difference in the mean change from baseline between FILSPARI and irbesartan.

Patients who completed the PROTECT double-blind portion of the study on treatment were eligible to participate in the open-label extension of the trial.

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.

FILSPARI® (sparsentan) U.S. Indication

FILSPARI (sparsentan) is indicated to slow kidney function decline in adults with primary immunoglobulin A nephropathy (IgAN) who are at risk for disease progression.

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 3.5% 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 in up to 3.5% of FILSPARI-treated patients, including cases confirmed with rechallenge. While no concurrent elevations in bilirubin >2-times ULN or cases of liver failure were observed in FILSPARI-treated patients, some ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure. To reduce the risk of potential serious hepatotoxicity, measure serum aminotransferase levels and total bilirubin prior to initiation of treatment and 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 because monitoring hepatotoxicity in these patients may be more difficult and these patients may be at increased risk for serious hepatotoxicity.

- **Embryo-Fetal Toxicity:** FILSPARI can cause fetal harm when administered to a pregnant patient and is contraindicated during pregnancy. Advise patients who can become pregnant of the potential risk to a fetus. Obtain a pregnancy test prior to initiation of treatment with FILSPARI, monthly during treatment, and one month after discontinuation of treatment. Advise patients who can become pregnant to use effective contraception prior to initiation of treatment, during treatment, and for one month after discontinuation of treatment with FILSPARI.

- **FILSPARI REMS:** Due to the risk of hepatotoxicity and embryo-fetal toxicity, FILSPARI is available only through a restricted program called the FILSPARI REMS. Prescribers, patients, and pharmacies must be enrolled in the REMS program and comply with all requirements (www.filsparirems.com).

- **Hypotension:** Hypotension has been observed in patients treated with ARBs and ERAs. 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, despite elimination or reduction of other antihypertensive medications, consider a dose reduction or dose interruption of FILSPARI. A transient hypotensive response is not a contraindication to further dosing of FILSPARI, which can be given once blood pressure has stabilized.

- **Acute Kidney Injury:** Monitor kidney function periodically. Drugs that inhibit the renin-angiotensin system (RAS) can cause kidney injury. Patients whose kidney function may depend in part on the activity of the RAS (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 in clinical studies with FILSPARI. FILSPARI has not been evaluated in patients with heart failure. If clinically significant fluid retention develops, evaluate the patient to determine the cause and the potential need to initiate or modify the dose of diuretic treatment then consider modifying the dose of FILSPARI.

Most common adverse reactions

The most common adverse reactions (≥5%) are hyperkalemia, hypotension (including orthostatic hypotension), peripheral edema, dizziness, anemia, and acute kidney injury.

Drug interactions

- **Renin-Angiotensin System (RAS) Inhibitors and ERAs:** Do not coadminister FILSPARI with ARBs, ERAs, or aliskiren due to increased risks of hypotension, syncope, hyperkalemia, and changes in renal function (including acute renal failure).

- **Strong and Moderate CYP3A Inhibitors:** Avoid concomitant use of FILSPARI with strong CYP3A inhibitors. If a strong CYP3A inhibitor cannot be avoided, interrupt FILSPARI treatment. When resuming treatment with FILSPARI, consider dose titration. Monitor blood pressure, serum potassium, edema, and kidney function regularly when used concomitantly with moderate CYP3A inhibitors. Concomitant use with a strong CYP3A inhibitor increases sparsentan exposure which may increase the risk of FILSPARI adverse reactions.

- **Strong CYP3A Inducers:** Avoid concomitant use with a strong CYP3A inducer. Concomitant use with a strong CYP3A inducer decreases sparsentan exposure which may reduce FILSPARI efficacy.

- **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. Sparsentan exhibits pH-dependent solubility. Antacids or acid reducing agents may decrease sparsentan exposure which may reduce FILSPARI efficacy.

- **Non-Steroidal Anti-Inflammatory Agents (NSAIDs), Including Selective Cyclooxygenase-2 (COX-2) Inhibitors:** Monitor for signs of worsening renal function with concomitant use with NSAIDs (including selective COX-2 inhibitors). In patients with volume depletion (including those on diuretic therapy) or with impaired kidney function, concomitant use of NSAIDs (including selective COX-2 inhibitors) with drugs that antagonize the angiotensin II receptor may result in deterioration of kidney function, including possible kidney failure.

- **CYP2B6, 2C9, and 2C19 Substrates:** Monitor for efficacy of concurrently administered CYP2B6, 2C9, and 2C19 substrates and consider dosage adjustment in accordance with the Prescribing Information. Sparsentan decreases exposure of these substrates, which may reduce efficacy related to these substrates.

- **P-gp and BCRP Substrates:** Avoid concomitant use of sensitive substrates of P-gp and BCRP with FILSPARI. Sparsentan may increase exposure of these transporter substrates, which may increase the risk of adverse reactions related to these substrates.

- **Agents Increasing Serum Potassium:** Monitor serum potassium frequently in patients treated with FILSPARI and other agents that increase serum potassium. 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.

Please see the full Prescribing Information, including BOXED WARNING, for additional Important Safety Information.

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 “on-track,” “positioned,” “look forward to,” “will,” “would,” “may,” “might,” “believes,” “anticipates,” “plans,” “expects,” “intends,” “potential,” or similar expressions. In addition, expressions of strategies, intentions or plans are also forward-looking statements. Such forward-looking statements include, but are not limited to, references to: the positioning of FILSPARI to potentially become foundational care in IgAN and to potentially replace the current standard of care; expectations regarding the continuing commercial launch of FILSPARI, expectations regarding prescribing behavior, patient access and matters related thereto; statements regarding planned engagement with the FDA and plans to submit an sNDA for a potential modification to the liver-monitoring REMS; and statements relating to KDIGO guidelines. 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, as well as risks and uncertainties associated with the Company’s business and finances in general, the success of its commercial products and risks and uncertainties associated with its preclinical and clinical stage pipeline. Specifically, the Company faces risks associated with the ongoing commercial launch of FILSPARI, market acceptance of its commercial products including efficacy, safety, price, reimbursement, and benefit over competing therapies, as well as risks associated with the successful development and execution of commercial strategies for such products, including FILSPARI. The risks and uncertainties the Company faces with respect to its preclinical and clinical stage pipeline include risk that the Company’s clinical candidates will not be found to be safe or effective and that current or anticipated future clinical trials will not proceed as planned. The Company also faces the 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.

Contact Info

Media:
888-969-7879
mediarelations@travere.com

Investors:
888-969-7879
IR@travere.com

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/21920774-d9c9-4c88-9a02-3a33a53714e8

Source: Travere Therapeutics, Inc.

FILSPARI (sparsentan)

FILSPARI (sparsentan)