Travere Therapeutics and CSL Vifor Announce Sparsentan Receives Positive CHMP Opinion for the Treatment of IgA Nephropathy

February 23, 2024

Committee for Medicinal Products for Human Use (CHMP) recommends approval of the conditional marketing authorization (CMA) for sparsentan for the treatment of IgA nephropathy (IgAN) in Europe

Positive CHMP opinion is based on pivotal Phase 3 PROTECT Study results

European Commission decision is expected in Q2 2024

SAN DIEGO, Feb. 23, 2024 (GLOBE NEWSWIRE) -- Travere Therapeutics, Inc., (NASDAQ: TVTX) and CSL Vifor today announced that the European Medicines Agency's (EMA) CHMP has recommended approval of sparsentan for the treatment of adults with primary IgA nephropathy (IgAN) with a urine protein excretion >1.0 g/day (or urine protein-to-creatinine ratio ≥0.75 g/g). IgAN is a rare kidney disease and a leading cause of kidney failure. The CHMP opinion provides the basis for the European Commission's final decision regarding CMA for sparsentan. If approved in Europe, sparsentan will be the first non-immunosuppressive, single-molecule, dual endothelin angiotensin receptor antagonist for the treatment of IgAN.

"The positive recommendation from the CHMP represents a significant advancement toward the delivery of new treatment options for people living with IgAN in Europe, who face the risk of progression to kidney failure and who currently have no approved non-immunosuppressive treatment options. The PROTECT Study is the only head-to-head study in IgAN against a maximally labeled dose of irbesartan, a current standard of care. The study demonstrated treatment with sparsentan resulted in a rapid and sustained reduction in proteinuria and has the potential to preserve kidney function and significantly delay time to kidney failure compared to an active comparator, suggesting long-term benefits in IgAN," said Eric Dube, Ph.D., president and chief executive officer of Travere Therapeutics. "Together with CSL Vifor, we look forward to the European Commission's decision in the second quarter of 2024."

"The positive CHMP opinion for sparsentan is one step closer to bringing this treatment option to patients in Europe with IgAN, a rare and serious condition that can cause kidney disease," said Emmanuelle Lecomte Brisset, senior vice president and head of global regulatory affairs at CSL. "We look forward to the European Commission decision and to continuing to advance CSL's promise to provide innovative treatments for patients with kidney disease."

The positive CHMP opinion is based on results from the pivotal Phase 3 PROTECT Study of sparsentan in IgAN.

In August 2022, Travere Therapeutics and CSL Vifor announced they had submitted a Marketing Authorization Application (MAA) for CMA to the EMA. The European Commission previously granted Orphan Medicinal Product Designation to sparsentan for the treatment of IgAN.

If approved, sparsentan would receive a CMA in all member states of the European Union, as well as in Iceland, Liechtenstein and Norway. Sparsentan is currently marketed in the U.S. and granted accelerated approval by the U.S. Food and Drug Administration under the brand name FILSPARI® based on reduction in proteinuria.

In 2021, Travere Therapeutics granted CSL Vifor exclusive commercialization rights for sparsentan in Europe, Australia and New Zealand.

About IgA Nephropathy (IgAN)

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 glomerular disease worldwide and a leading cause of kidney failure. IgAN is estimated to affect up to 250,000 people in the licensed territories.

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.

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

About CSL Vifor

CSL Vifor is a global partner of choice for pharmaceuticals and innovative, leading therapies in iron deficiency and nephrology. We specialize in strategic global partnering, in-licensing and developing, manufacturing and marketing pharmaceutical products for precision healthcare, aiming to help patients around the world lead better, healthier lives. Headquartered in St. Gallen, Switzerland, CSL Vifor also includes the joint company Vifor Fresenius Medical Care Renal Pharma (with Fresenius Medical Care).

The parent company, CSL (ASX: CSL; USOTC: CSLLY), headquartered in Melbourne, Australia, employs 32,000 people and delivers its lifesaving therapies to people in more than 100 countries. For more information about CSL Vifor visit, www.cslvifor.com.

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**: Avoid 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.

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 our strategies, intentions or plans are also forward-looking statements. Such forward-looking statements include, but are not limited to, references to: statements regarding the potential conditional marketing authorization of sparsentan for the treatment of IgAN in the European Union, Iceland, Liechtenstein and Norway and the anticipated timing thereof, including the potential timing and outcome of the European Commission’s decision; and the potential for sparsentan to be the first non-immunosuppressive, single-molecule, dual endothelin angiotensin receptor antagonist for the treatment of IgAN in the EU. 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 the Company’s preclinical and clinical stage pipeline. Specifically, the Company faces risks associated with 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. Specifically, the Company faces risks related to the timing and potential outcome of the European Commission’s decision regarding conditional marketing authorization of sparsentan for IgAN. There is no guarantee that the European Commission will grant conditional marketing authorization of sparsentan for IgAN or that regulators will grant full approval of sparsentan for IgAN. 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.

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