Travere Therapeutics Announces Late-Breaking Data from Phase 3 DUPLEX Study of FILSPARI in FSGS Presented at the American Society of Nephrology (ASN) Kidney Week 2025

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New late-breaking data from DUPLEX Study show significantly more FILSPARI® (sparsentan)-treated patients achieved proteinuria below 0.7 g/g compared with irbesartan

FILSPARI treatment associated with a clinically meaningful lower risk of kidney failure events over five years compared with irbesartan in DUPLEX-aligned RaDaR cohort

Data support findings of PARASOL Project, reinforcing that reaching proteinuria below 0.7 g/g is associated with long-term kidney preservation

SAN DIEGO--(BUSINESS WIRE)-- Travere Therapeutics, Inc., (Nasdaq: TVTX) today announced new data from the Phase 3 DUPLEX Study demonstrating that patients with focal segmental glomerulosclerosis (FSGS) treated with FILSPARI® (sparsentan) were significantly more likely to reach proteinuria levels below 0.7 g/g compared to those receiving the maximum labeled dose of irbesartan, and achievement of this threshold correlated with reduced risk of kidney failure. The data were presented as a late-breaking poster at the American Society of Nephrology (ASN) Kidney Week 2025 in Houston, TX, November 6-9.

“We are pleased to present new data from the pivotal DUPLEX Study, highlighting the correlation between proteinuria reduction and the potential of FILSPARI to reduce long-term kidney failure events,” said Jula Inrig, M.D., chief medical officer of Travere Therapeutics. “People living with FSGS face a serious and progressive disease that often leads to kidney failure and dialysis. The PARASOL Project has determined that reducing proteinuria to the lowest possible levels is key to protecting kidney function in FSGS, and these analyses from the DUPLEX Study reinforce its findings."

The PARASOL Project previously identified urine protein-to-creatinine ratio (UPCR) below 0.7 g/g as a clinically meaningful proteinuria target in FSGS. This late-breaking poster reported the proportion of FILSPARI-treated patients reaching this threshold compared to the maximum labeled dose of irbesartan in the DUPLEX Study, and the effect of reaching this target on progression to kidney failure. A DUPLEX-aligned cohort of patients with FSGS (n=386) from the UK National Registry of Rare Kidney Disease (RaDaR) was then utilized to model the impact of achieving UPCR below 0.7 g/g on five-year kidney failure risk, during a 24-month period.

Key findings from the late-breaking analyses include:

- In DUPLEX, significantly more patients treated with FILSPARI achieved UPCR below 0.7 g/g earlier and more often than those treated with irbesartan at any time (37.5% vs. 21.4% relative risk [RR], 1.8 [95% CI, 1.3-2.4]) and at week 108 (19% vs. 11.2% (RR, 1.7 [95% CI, 1.03-2.8]).
- Irrespective of treatment with FILSPARI or irbesartan, patients who achieved UPCR below 0.7 g/g at any time were less likely to reach kidney failure than those who did not (3.6% vs. 11.2% (RR, 0.52 [95% CI, 0.2-1.8]).
- In the DUPLEX-aligned RaDaR cohort, achieving UPCR below 0.7 g/g at 24-months was associated with lower risk of kidney failure over an additional 60-months of follow up (hazard ratio [HR], 0.14 [95% CI, 0.05-0.38]). A similar lower risk was observed for those who achieved UPCR below 0.7 g/g at any time over 24-months (HR, 0.27 [95% CI, 0.16-0.45]).

In a separate oral presentation, the Company shared an analysis predicting the reduction in risk of kidney failure events at five-years for patients treated with FILSPARI based on the relative reduction in proteinuria from the DUPLEX Study. As previously published in the New England Journal of Medicine, the DUPLEX Study demonstrated that treatment with FILSPARI resulted in a clinically meaningful and durable reduction in proteinuria, with FSGS patients achieving a 50% reduction from baseline UPCR, compared to a 32% reduction with the maximum labeled dose of irbesartan. This translates to a 26% relative reduction in UPCR for FILSPARI-treated patients compared to the maximum labeled dose of irbesartan at 24 months. The analysis uses a DUPLEX-aligned cohort of patients from RaDaR to examine the correlation between reduction in proteinuria and the long-term risk of kidney failure.

Key findings from the RaDaR analysis include:

- Within the RaDaR cohort, robust reductions in the risk of kidney failure were observed for patients achieving complete remission (UPCR below 0.3 g/g) and proteinuria below 0.7 g/g at 24-months. These findings support the overall conclusions of the PARASOL Project.
- Any reduction in UPCR correlated to a reduction in risk of kidney failure events at 5-years (1-unit reduction of log-transformed UPCR HR, 0.41 [95% CI, 0.29-0.58]).
- When applied to the DUPLEX Study, the 26% relative reduction in UPCR for patients treated with FILSPARI compared to irbesartan, correlates to a

significant and clinically meaningful reduction in 5-year risk of kidney failure of 24% (HR, 0.76 [95% CI, 0.69-0.85]).

More information on Travere's presence at ASN can be found **here**.

About the DUPLEX Study

The Phase 3 DUPLEX Study is the largest interventional study to date in FSGS, and the only study in FSGS against a maximally dosed active comparator. While DUPLEX achieved its pre-specified interim FSGS partial remission of proteinuria (FPRE) endpoint with statistical significance at 36 weeks, it did not achieve the primary efficacy eGFR slope endpoint over 108 weeks of treatment. The two-year results from the study were published in the New England Journal of Medicine and showed that FILSPARI delivered clinically meaningful benefit at 108 weeks with significant proteinuria reduction, higher rates of partial and complete remission, and a lower rate of end-stage kidney disease compared to active control. FILSPARI was well-tolerated with a safety profile that was consistent across all clinical trials conducted to date and comparable to the maximally dosed active control, irbesartan, including no drug-induced liver injury and no fluid overload. Patients who completed the DUPLEX double-blind portion of the study on treatment were eligible to participate in the open-label extension of the trial.

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 U.S. 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. FILSPARI is not approved for use in FSGS. There are currently no FDA-approved pharmacologic therapies for FSGS.

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 risk of hepatotoxicity, 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 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 is contraindicated for use during pregnancy because it may cause fetal harm if used by pregnant patients. Therefore, in patients who can become pregnant, exclude pregnancy prior to initiation of FILSPARI. Advise use of effective contraception before the initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with FILSPARI. When pregnancy is detected, discontinue FILSPARI as soon as possible.

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 in clinical trials, 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 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) because monitoring hepatotoxicity in these patients may be more difficult and these patients may be at increased risk for serious hepatotoxicity.
- FILSPARI REMS: Due to the risk of hepatotoxicity, 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**).
- Embryo-Fetal Toxicity: Based on data from animal reproduction studies, FILSPARI may cause fetal harm when administered to a pregnant patient and is contraindicated during pregnancy. The available human data for ERAs do not establish the presence or absence of fetal harm related to the use of FILSPARI. Counsel patients who can become pregnant of the potential risk to a fetus. Exclude pregnancy before initiating treatment with FILSPARI. Advise patients who can become pregnant to use effective contraception prior to initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with FILSPARI. When pregnancy is detected, discontinue FILSPARI as soon as possible.
- 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: statements relating to the clinical studies, models and data described herein; statements regarding the potential of FILSPARI to reduce long-term kidney failure events; statements regarding FILSPARI as a potential treatment for FSGS; and statements related to the estimated sizes of patient populations. 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 related to the Company’s sNDA for FILSPARI in FSGS, including the timing and outcome thereof. There is no guarantee that the FDA will grant approval of FILSPARI for FSGS on the anticipated timeline, or at all. The Company also faces risks and uncertainties related to its business and finances in general, the success of its commercial products, risks and uncertainties associated with its preclinical and clinical stage pipeline, risks and uncertainties associated with the regulatory review and approval process, risks and uncertainties 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. Specifically, the Company faces risks associated with the ongoing commercial launch of FILSPARI in IgAN, the timing and potential outcome of its and its partners’ clinical studies, market acceptance of its commercial products including efficacy, safety, price, reimbursement, and benefit over competing therapies, risks related to the challenges of manufacturing scale-up, risks associated with the successful development and execution of commercial strategies for such products, including FILSPARI, and risks and uncertainties related to the new administration, including but not limited to risks and uncertainties related to tariffs and the funding, staffing and prioritization of resources at government agencies including the FDA. 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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