September 21, 2023

# Ligand's Partner Travere Therapeutics Announces Confirmatory Data from the Phase 3 PROTECT Study of FILSPARI® Demonstrating Long-Term Kidney Function Preservation in IgA Nephropathy; Narrowly Missing eGFR Total Slope Endpoint versus Active Control

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announced that its partner Travere Therapeutics, Inc. (Nasdaq: TVTX) ("Travere") today released topline, two-year confirmatory secondary endpoint results from its pivotal, head-to-head Phase 3 PROTECT Study of FILSPARI® (sparsentan) in IgA nephropathy (IgAN) versus irbesartan. FILSPARI demonstrated long-term kidney function preservation and achieved a clinically meaningful difference in estimated glomerular filtration rate (eGFR) total and chronic slope versus irbesartan, narrowly missing statistical significance in eGFR total slope while achieving statistical significance in eGFR chronic slope for purposes of regulatory review in the EU. FILSPARI is currently available under accelerated approval in the U.S. Travere will engage with regulators and expects to submit a supplemental New Drug Application (sNDA) in 1H 2024 for full approval in the U.S.

Under Ligand's license agreement with Travere for FILSPARI, Ligand is entitled to receive net royalties of 9% on global net product sales of FILSPARI.

"We are encouraged by the results from the Phase 3 study reported by Travere today," said Todd Davis, CEO of Ligand Pharmaceuticals. "The PROTECT study showed all topline efficacy endpoints favored FILSPARI, and patients treated with FILSPARI over two years exhibited one of the slowest annual rates of kidney function decline seen in clinical trials to-date. In addition, FILSPARI was well-tolerated with a consistent safety profile comparable to irbesartan across all clinical trials conducted to-date, supporting long-term use."

**PROTECT Study Results**

In the PROTECT Study, a total of 404 patients with persistent proteinuria despite active angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB) treatment, were randomized 1:1 to receive once daily oral doses of either FILSPARI or irbesartan, the active control. eGFR total and chronic slope are the secondary confirmatory endpoints for the U.S. and the EU, respectively. All topline efficacy endpoints favored FILSPARI as compared to irbesartan.

| | FILSPARI (N=202) | Irbesartan (N=202) | Difference (FILSPARI - Irbesartan) |
|---|---|---|---|
| **eGFR total slope,** mL/min/1.73m$^2$ per year[a] | **-2.9** | **-3.9** | **1.0, p=0.058** (-0.03, 1.94) |
| **eGFR chronic slope,** mL/min/1.73m$^2$ per year[b] | **-2.7** | **-3.8** | **1.1, p=0.037** (0.07, 2.12) |
| **UP/C (g/g)** Mean % change from baseline at week 110[c] | **-42.8** | **-4.4** | **GMR: 0.60** (0.50, 0.72) |
| **Absolute change in eGFR** Mean change from baseline at week 110[d] | **-5.8** | **-9.5** | **3.7** (1.45, 5.99) |
| **Absolute change in eGFR** Mean change from baseline at week 114[e] following 4 weeks post treatment (Patients who completed blinded treatment period) | **-6.1** | **-9.0** | **2.9** (0.45, 5.25) |
| **Confirmed 40% Reduction in eGFR, ESRD, or Death during the Study** n (%) | **18** (8.9) | **26** (12.9) | **RR: 0.68** (0.37, 1.24)[f] |

a LS Means and 95% CI from a random coefficient analysis including available on-treatment eGFR data from Week 6 through Week 110 with multiple imputation; mL/min/1.73m2 per year

b LS Means and 95% CI from a random coefficient analysis including available on-treatment eGFR data through Week 110 with multiple imputation; mL/min/1.73m2 per year

c Geometric LS Means, Geometric LS Mean Ratio (GMR), and 95% CI from MMRM analysis including on-treatment data through Week 110 with multiple imputation

d LS Means and 95% CI from MMRM analysis including on-treatment data through Week 110; mL/min/1.73m2

e ANCOVA adjusted for eGFR at baseline; mL/min/1.73m2

f Relative risk (RR) of events and 95% CI from Poisson regression model

A preliminary review of the safety results through 110 weeks of treatment indicates FILSPARI was generally well-tolerated, and the overall safety profile in the study has been consistent between treatment groups.

Eric Dube, Ph.D., president and CEO of Travere Therapeutics, commented, “The confirmatory results of the PROTECT Study demonstrated treatment with FILSPARI resulted in the largest sustained reduction in proteinuria and one of the slowest rates of eGFR decline in a controlled study of IgAN patients, to date. This outcome is incredibly important for IgAN patients, who face the risk of progression to kidney failure in their lifetime. We’re proud of the high bar we’ve set in delivering the only head-to-head study in IgAN, which compares FILSPARI against maximally tolerated dose of irbesartan. Since our accelerated approval, we’ve continued to hear inspiring stories of the impact this medicine is having on people

living with IgAN. While eGFR total slope narrowly missed statistical significance, the overall evidence from PROTECT suggest potential long-term benefit of FILSPARI as a foundational treatment for patients with IgAN. FILSPARI has the potential to transform the treatment paradigm in this rare kidney disease, and we look forward to engaging with FDA to discuss our planned sNDA submission."

Travere will complete a full evaluation of the data from the PROTECT Study and work with the study investigators on future presentations and publications of the results at an upcoming medical meeting and in a peer-reviewed publication.

In August 2022, the European Medicines Agency (EMA) accepted for review the Conditional Marketing Authorization (CMA) application of sparsentan for the treatment of IgAN. Together with Travere's partner CSL Vifor, Travere anticipates a review opinion by the Committee for Medicinal Products for Human Use (CHMP) on the CMA application for sparsentan for the treatment of IgAN in the EU around year-end.

**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 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 maximum 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 Europe 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.

## 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.

## About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company enabling scientific advancement through supporting the clinical development of high-value medicines. Ligand does this by providing financing, licensing our technologies or both. Our business model generates value for stockholders by creating a diversified portfolio of biotech and pharmaceutical product revenue streams that are supported by an efficient and low corporate cost structure. Our goal is to offer investors an opportunity to participate in the promise of the biotech industry in a profitable and diversified manner. Our business model is based on funding programs in mid- to late-stage drug development in return for economic rights and licensing our technology to help partners discover and develop medicines. We partner with other pharmaceutical companies to leverage what they do best (late-stage development, regulatory management and commercialization) in order to generate our revenue. Our Captisol® platform technology is a chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. We have established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Amgen, Merck, Pfizer, Jazz, Takeda, Gilead Sciences and Baxter International. For more information, please visit www.ligand.com.

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## Disclaimer

The information in this press release regarding FILSPARI comes from Travere Therapeutics. Ligand is not responsible for, and has no role in, the development of such product.

## Forward-Looking Statements

This news release contains forward-looking statements by Ligand that involve risks and uncertainties and reflect Ligand's judgment as of the date of this release. Words such as "plans," "believes," "expects," "anticipates," and "will," and similar expressions, are intended to identify forward-looking statements. These forward-looking statements include: the efficacy and safety of FILSPARI, the timing and amount of royalties Ligand may receive in connection with the commercialization of FILSPARI and the timing for future regulatory

submissions and approvals related to FILSPARI. Actual events or results may differ from Ligand's or its partner's expectations due to risks and uncertainties inherent in Ligand's and its partner's business, including, without limitation: risks relating to the regulatory approval process, including traditional approval of FILSPARI; changes in the size and nature of the market for FILSPARI, including potential competition, patient and payer perceptions and reimbursement determinations; that FILSPARI will continue to demonstrate requisite safety and efficacy following commercial launch; Ligand is dependent on Travere for the development and commercialization of FILSPARI; Ligand or its partners may not be able to protect their intellectual property, and patents covering certain products and technologies may be challenged or invalidated; and other risks described in Ligand and Travere's prior press releases and filings with the Securities and Exchange Commission available at www.sec.gov. Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this release. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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