February 17, 2023

Ligand's Partner Travere Therapeutics Announces FDA Accelerated Approval of FILSPARI™ (sparsentan), the First and Only Non-immunosuppressive Therapy for the Reduction of Proteinuria in IgA Nephropathy

First single molecule Dual Endothelin Angiotensin Receptor Antagonist (DEARA) approved for use in patients with IgA nephropathy (IgAN)

Interim results from the ongoing Phase 3 PROTECT head-to-head trial demonstrated a rapid, sustained and clinically meaningful reduction in proteinuria vs. active control, irbesartan

Ligand is entitled to receive a net $15.3 million milestone and net royalties of 9% on future sales

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announced that its partner Travere Therapeutics, Inc. (Nasdaq: TVTX) has received accelerated approval from the U.S. Food and Drug Administration (FDA) for FILSPARI™ (sparsentan) to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (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. The continued approval of FILSPARI may be contingent upon confirmation of a clinical benefit in the ongoing Phase 3 PROTECT Study, which is designed to demonstrate whether FILSPARI slows kidney function decline. Topline results from the two-year confirmatory endpoints in the PROTECT Study are expected by Travere in the fourth quarter of 2023 and are intended to support traditional approval of FILSPARI.

FILSPARI, a once-daily oral medication, is designed to selectively target two critical pathways in the disease progression of IgAN (endothelin-1 and angiotensin II) and is the first and only non-immunosuppressive therapy approved for the treatment of this condition. IgAN is a rare kidney disease and a leading cause of kidney failure due to glomerular disease, affecting up to 150,000 people in the U.S., with approximately 30,000 to 50,000 of such patients estimated to be addressable under the indication approved via accelerated approval. Travere expects FILSPARI to be available beginning the week of February 27, 2023, and has indicated it will be providing a comprehensive patient support program throughout the patient's treatment journey.

"We are delighted to see the approval of sparsentan, now FILSPARI, which represents a significant step forward in improving the lives of patients living with IgA nephropathy," said Todd Davis, CEO of Ligand Pharmaceuticals. "Our partnership with Travere has been a remarkable journey, and we are proud to have played a part in bringing this innovative treatment to market. Congratulations to the entire team at Travere on this accomplishment."

Under Ligand's license agreement with Travere for sparsentan, Ligand is entitled to receive a net $15.3 million milestone on this FDA approval, other potential milestone payments and net royalties of 9% on future global net product sales of sparsentan.

"The accelerated approval of FILSPARI is a significant milestone on our path to advancing a transformative treatment for the IgA nephropathy community," said Eric Dube, Ph.D., president and CEO of Travere Therapeutics. "As a first-of-its-kind, non-immunosuppressive therapy, we believe FILSPARI has the potential to ultimately become the new standard of care for IgA nephropathy and offer hope to those living with this condition who until now have had few treatment options. We are grateful to the patients, caregivers, clinical trial investigators, healthcare providers, and advocates who have worked alongside us to develop this innovative first-in-class therapy."

The approval of FILSPARI, granted under the FDA's accelerated approval pathway, is based on clinically meaningful and statistically significant improvements in proteinuria compared to an active comparator in the pivotal and ongoing Phase 3 PROTECT Study, the largest head-to-head interventional study to date in IgAN. The PROTECT Study is a global, randomized, multicenter, double-blind, active-controlled clinical trial evaluating the safety and efficacy of 400 mg of FILSPARI, compared to 300 mg of irbesartan, in 404 patients ages 18 years and up with IgAN and persistent proteinuria despite maximal tolerated ACE or ARB therapy.

In August 2021, Travere announced positive topline interim results that were based on the pre-specified, primary analyses set which showed that after 36 weeks of treatment, 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 ($p<0.0001$). Per request from the FDA, the efficacy data contained in the FDA-approved label is a post-hoc sensitivity analysis that evaluates the first 281 randomized patients, a subset of the full trial population. The mean reduction in proteinuria from baseline in the post-hoc sensitivity analysis is 45% for FILSPARI versus 15% for the active control, irbesartan. Both the pre-specified and post-hoc sensitivity analyses have demonstrated that FILSPARI achieves a rapid and sustained reduction in proteinuria, with statistically significant and clinically meaningful improvement compared to the active comparator irbesartan. Per the study protocol, patients continue in a blinded manner in the PROTECT Study to fully assess the treatment effect on eGFR slope over 110 weeks in the confirmatory endpoint analysis. Results from the confirmatory endpoint analysis are expected in the fourth quarter of 2023.

Results from the interim assessment in 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. In PROTECT, the most common adverse reactions (≥ 5%) are peripheral edema, hypotension (including orthostatic hypotension), dizziness, hyperkalemia, and anemia. Because of the risks of liver injury and birth defects, FILSPARI is available only through a Risk Evaluation and Mitigation Strategy (REMS) approved by the FDA.

Travere announced that together with their collaborator CSL Vifor, they expect a review decision by the European Medicines Agency (EMA) in the second half of 2023 on the potential approval of the Conditional Marketing Authorization (CMA) application for sparsentan for the treatment of IgAN in Europe.

Travere expects to report topline results from the two-year confirmatory endpoints in the ongoing Phase 3 DUPLEX Study of sparsentan in focal segmental glomerulosclerosis (FSGS) in the second quarter of 2023. Pending supportive data, Travere announced an anticipated submission of a supplemental NDA for traditional approval for an FSGS indication in the second half of 2023 and a subsequent variation to the CMA of sparsentan for the treatment of patients with FSGS in Europe is targeted for submission by the end of 2023. Sparsentan has been granted Orphan Drug Designation for the treatment of IgAN and FSGS in the U.S. and Europe.

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 FILSPARI (sparsentan)

FILSPARI (sparsentan) is a once-daily, oral medication designed to selectively target two critical pathways in the disease progression of IgAN (endothelin-1 and angiotensin II) and is the first and only non-immunosuppressive therapy approved for the treatment of this condition. FILSPARI is a prescription medicine indicated to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression, generally a UPCR ≥1.5 g/g.

About the PROTECT Study

The ongoing PROTECT Study is one of the largest interventional studies to date in IgAN. It is a global, randomized, multicenter, double-blind, parallel-arm, active-controlled clinical trial evaluating the safety and efficacy of 400mg of sparsentan, compared to 300mg of irbesartan, in 404 patients ages 18 years and up with IgAN and persistent proteinuria despite available ACE or ARB therapy. In August 2021, Travere 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 percent, compared to a mean reduction in proteinuria from baseline of 15.1 percent for irbesartan-treated patients ($p<0.0001$). Travere believes that preliminary eGFR data available at the time of the interim analysis are indicative of a potential clinically meaningful treatment effect after two years of treatment. Preliminary results at the time of the interim assessment suggested that sparsentan had been generally well-tolerated to date in the study and

consistent with its overall observed safety profile. The PROTECT Study is fully enrolled and is scheduled to continue as planned on a blinded basis to assess the treatment effect on eGFR slope over 110 weeks in the confirmatory endpoint analysis. Topline results from the confirmatory endpoint analysis are expected in the fourth quarter of 2023.

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company focused on funding, enabling and supporting clinical development that allows pharmaceutical companies to create high impact medicines. Ligand does this by licensing our platform technologies, providing project financing or both. Our business model creates value for stockholders by providing 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 while mitigating the binary clinical risk associated with developing a single program. Our business model is based on funding mid to late-stage drug development in return for economic rights and licensing our technology platforms 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) ultimately 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. For our Captisol partners, our team supplies our Captisol material needed for their programs. Our Pelican Expression Technology is a robust, validated, cost-effective and scalable platform for recombinant protein production that is especially well-suited for complex, large-scale protein production where traditional systems are not. 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.

Disclaimer

The information in this press release regarding FILSPARI comes from Travere. 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 milestone payments and royalties Ligand may receive in connection with the commercialization of FILSPARI and the timing for expected study results and 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'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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