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Ligand Partner Travers Therapeutics Announces Achievement of Interim Proteinuria Endpoint in the Ongoing Phase 3 DUPLEX Study of Sparsentan in Focal Segmental Glomerulosclerosis

Sparsentan achieved statistically significant response on interim proteinuria endpoint compared to irbesartan after 36-weeks of treatment

To date in the study, sparsentan has been generally well-tolerated and has shown a safety profile comparable to irbesartan

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** partner Travers Therapeutics, Inc. (NASDAQ: TVTX) today announced that their ongoing pivotal Phase 3 DUPLEX Study of sparsentan in focal segmental glomerulosclerosis (FSGS) achieved its pre-specified interim FSGS partial remission of proteinuria endpoint (FPRE) after 36 weeks of treatment. Sparsentan, an investigational product candidate, demonstrated a statistically significant response on FPRE compared to the active control, irbesartan ($p=0.0094$). Preliminary results from the interim analysis suggest that to date in the study, sparsentan has been generally well-tolerated and has shown a comparable safety profile to irbesartan. Based on the data from the interim analysis, Travers intends to pursue submissions for accelerated approval of sparsentan for FSGS and plans to continue its engagement with regulators in the first half of 2021 to discuss the ongoing study and to establish next steps for filing with the available data set.

Under Ligand's license agreement with Travers for sparsentan, Ligand is entitled to receive a net \$5.9 million milestone on NDA submission, other potential milestone payments and net royalties of 9% on future worldwide sales by Travers. The royalty term is expected to be 10 years following the first commercial sale.

"Travers has reported impressive top-line results from the Sparsentan DUPLEX trial, and we commend their team for the success in this study," said John Higgins, CEO of Ligand Pharmaceuticals. "We are proud of our partnership and the early collaborative work we did to help support this program. Sparsentan is one of Ligand's top partnered portfolio assets, and we are very pleased to see this asset progress."

"For decades people living with FSGS have faced daily challenges in controlling proteinuria and a fear of progressing to transplant or dialysis because current treatment options are not enough," said Eric Dube, Ph.D., chief executive officer of Travers Therapeutics. "Today, we are very pleased to announce interim proteinuria results from the ongoing DUPLEX Study that demonstrate treatment with sparsentan can lead to significantly greater reductions in

proteinuria compared to current standard of care. As we move ahead, our organization will be focused on maintaining high quality in this ongoing study, and on continuing our engagement with regulators to enable submissions for accelerated approval with the available data set.”

Traverse is providing limited data from the interim analyses to maintain trial integrity in the ongoing study. In the DUPLEX Study, a total of 371 patients were randomized 1:1 to receive either sparsentan or irbesartan, the active control. The study protocol provided for an unblinded analysis to evaluate the interim efficacy endpoint – the proportion of patients achieving FPPE, which is a clinically meaningful endpoint defined as urine protein-to-creatinine ratio (UP/C) ≤ 1.5 g/g and a >40 percent reduction in UP/C from Baseline, at Week 36 – following the first approximately 190 patients reaching 36 weeks of treatment. After 36 weeks of treatment, 42.0 percent of patients receiving sparsentan achieved FPPE, compared to 26.0 percent of irbesartan-treated patients ($p=0.0094$).

The confirmatory primary endpoint of the DUPLEX Study to support full regulatory approval is the rate of change in eGFR over 108 weeks of treatment. As of the time of the interim analyses, available long-term eGFR data for the confirmatory endpoint were limited. Consistent with the DUPLEX Study protocol, patients will continue in a blinded manner to assess the treatment effect on eGFR slope over 108 weeks in the confirmatory endpoint analysis.

A preliminary review of the interim safety results indicate sparsentan has been generally well-tolerated and the overall safety profiles in the study to date have been generally comparable between treatment groups.

The DUPLEX Study is fully enrolled and is scheduled to continue as planned on a blinded basis to assess the confirmatory eGFR endpoint after 108 weeks of treatment. Topline results from the confirmatory endpoint are expected in the first half of 2023. Traverse is also evaluating sparsentan for the treatment of IgA nephropathy in the ongoing pivotal Phase 3 PROTECT Study, and topline efficacy data from the 36-week interim proteinuria endpoint analysis from that study are anticipated in the third quarter of 2021.

About the DUPLEX Study

The ongoing DUPLEX Study is the largest interventional study to date in FSGS. It is a global, randomized, multicenter, double-blind, parallel-arm, active-controlled Phase 3 clinical trial assessing the efficacy and safety of sparsentan in 371 patients ages 8 to 75 years with primary FSGS. After a two-week washout period, patients are randomized 1:1 to receive either sparsentan or irbesartan, the active control, and subsequently dose titrated to the maximum dose of 800 mg of sparsentan or 300 mg of irbesartan, as tolerated. The DUPLEX Study protocol provides for an unblinded analysis of at least 190 patients to be performed after 36 weeks of treatment to evaluate the interim efficacy endpoint – the proportion of patients achieving a FSGS partial remission of proteinuria endpoint (FPPE), which is defined as urine protein-to-creatinine ratio (UP/C) ≤ 1.5 g/g and a >40 percent reduction in UP/C from baseline, at Week 36. The confirmatory endpoint of the study is the change in slope of estimated glomerular filtration rate (eGFR) from baseline after 108 weeks of treatment.

About Focal Segmental Glomerulosclerosis

FSGS is a rare proteinuric kidney disorder that is estimated to affect up to 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 end-stage kidney disease (ESKD). 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.

Reduction in proteinuria appears to be beneficial in the treatment of FSGS and may be associated with a decreased risk of progression to ESKD. Achieving FPRE appears to be associated with long-term preservation of renal function in patients with FSGS. FSGS is currently managed with angiotensin receptor blockers, angiotensin converting enzyme inhibitors, steroids or calcineurin inhibitors.

About Sparsentan

Sparsentan is a novel investigational product candidate, that functions as a high affinity dual-acting antagonist of both the endothelin type A and angiotensin II type 1 receptors, in a single molecule. Pre-clinical data have shown that blockade of both pathways in forms of rare chronic kidney disease, reduces proteinuria, protects podocytes and prevents glomerulosclerosis and mesangial cell proliferation. Sparsentan has been granted Orphan Drug Designation for the treatment of FSGS in the U.S. and Europe. Sparsentan has also been granted Orphan Drug Designation for the treatment of IgAN in the U.S. and has received a positive opinion from the European Medicines Agency Committee for Orphan Medicinal Products on the company's application for Orphan Drug Designation for IgAN in Europe.

Sparsentan is currently being evaluated in the pivotal Phase 3 DUPLEX Study for the treatment of FSGS and the pivotal Phase 3 PROTECT Study for the treatment of IgAN. In the Phase 2 DUET Study of sparsentan in FSGS, the combined treatment group met its primary efficacy endpoint, demonstrating a greater than two-fold reduction in proteinuria compared to irbesartan, and was generally well tolerated after the eight-week, double-blind treatment period. Irbesartan is part of a class of drugs used to manage FSGS and IgAN in the absence of an approved pharmacologic treatment. If approved for both indications, sparsentan could potentially be the first medicine approved for both FSGS and IgAN.

About Ligand Pharmaceuticals

Ligand is a revenue-generating biopharmaceutical company focused on developing or acquiring technologies that help pharmaceutical companies discover and develop medicines. Ligand's 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. Ligand's goal is to offer investors an opportunity to participate in the promise of the biotech industry in a profitable, diversified and lower-risk business than a typical biotech company. Ligand's business model is based on doing what Ligand does best: drug discovery, early-stage drug development, product reformulation and partnering. Ligand partners with other pharmaceutical companies to leverage what they do best (late-stage development, regulatory management and commercialization) to ultimately generate our revenue. Ligand's OmniAb[®] technology platform is a patent-protected transgenic animal

platform used in the discovery of fully human mono- and bispecific therapeutic antibodies. The Captisol platform technology is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Ligand's Protein Expression Technology[®] is a robust, validated, cost-effective and scalable approach to recombinant protein production, and is especially well-suited for complex, large-scale protein production that cannot be made by more traditional systems. Ab Initio[™] technology and services for the design and preparation of customized antigens enable the successful discovery of therapeutic antibodies against difficult-to-access cellular targets. Ligand has established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Amgen, Merck, Pfizer, Sanofi, Janssen, Takeda, Gilead Sciences and Baxter International. For more information, please visit www.ligand.com.

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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. These forward-looking statements include, without limitation, statements regarding: the timing and amount of milestone payments Ligand expects; the potential to receive royalties, and the potential royalty term, from future worldwide sales of sparsentan, if approved by the U.S. Food and Drug Administration (FDA) or other regulatory agencies; Traveire Therapeutics' expectations around the timeline for continuing its engagement with regulators, expectations regarding anticipated accelerated approval regulatory submissions for sparsentan in FSGS based on the available data set from the DUPLEX interim analysis, and the potential for sparsentan to become the first medicine approved for both FSGS and IgAN. Actual events or results may differ from Ligand's expectations due to risks and uncertainties inherent in Ligand's business, including, without limitation: the FDA may not accept Traveire Therapeutics' NDA submission for review; the risk that the Phase 3 DUPLEX Study of sparsentan in FSGS will not demonstrate that sparsentan is safe or effective or serve as a basis for accelerated approval of sparsentan as planned; the FDA may not agree with Traveire's interpretation of results from the DUPLEX trial or other clinical trial data; the FDA may request additional data in connection with its review of the sparsentan NDA; Ligand is dependent on Traveire on the development and, if approved, commercialization of sparsentan and Traveire may not generate net sales to generate royalties payable to Ligand; and other risks described in Ligand's prior press releases and filings with the SEC. The failure to meet expectations with respect to any of the foregoing matters may reduce Ligand's stock price. Ligand disclaims any intent or obligation to update these forward-looking statements after the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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Ligand Pharmaceuticals Incorporated

Patrick O'Brien

investors@ligand.com

(858) 550-7893

Twitter: @Ligand_LGND

LHA Investor Relations

Bruce Voss

bvoss@lhai.com

(310) 691-7100

Source: Ligand Pharmaceuticals Incorporated