

August 16, 2021



Ligand Partner Travers Therapeutics Announces Positive Topline Interim Results from the Ongoing Phase 3 PROTECT Study of Sparsentan in IgA Nephropathy

Sparsentan treatment demonstrated a statistically significant mean reduction of proteinuria from baseline after 36 weeks, more than threefold the reduction of active comparator irbesartan ($p < 0.0001$)

Sparsentan has been generally well-tolerated and consistent with the previously observed safety profile to date

EMERYVILLE, Calif.--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces that its partner Travers Therapeutics, Inc. (NASDAQ: TVTX) today announced positive topline interim results from the ongoing pivotal Phase 3 PROTECT Study of sparsentan, an investigational product candidate for the treatment of IgA nephropathy (IgAN). The PROTECT Study met its pre-specified interim primary efficacy endpoint with statistical significance, demonstrating a greater than threefold reduction of proteinuria from baseline after 36 weeks of treatment, compared to the active control irbesartan ($p < 0.0001$). Preliminary results from the interim analysis suggest that to date in the study, sparsentan has been generally well-tolerated and consistent with the observed safety profile to date. Based on the results from the interim analysis, Travers plans to submit an application for accelerated approval in the U.S. in the first half of 2022 and also plans to submit an application for conditional marketing authorization in Europe.

Under a license agreement with Travers for sparsentan, Ligand is entitled to receive a net \$5.9 million milestone upon NDA submission, other potential milestone payments and net royalties of 9% on future worldwide sales by Travers.

"Travers is reporting impressive topline results from the sparsentan PROTECT trial, and we commend their team for the success so far in this study," said John Higgins, CEO of Ligand Pharmaceuticals. "Sparsentan is one of Ligand's most important partnered assets and we are very pleased to see the growing body of evidence in treating rare kidney disorders."

"IgAN is a leading cause of end-stage kidney disease and there is a clear need for novel treatment options to slow the progression of this devastating rare kidney disorder," said Eric Dube, Ph.D., chief executive officer of Travers Therapeutics. "These data from the PROTECT Study further demonstrate sparsentan's ability to significantly reduce proteinuria and support its potential to become a new foundational treatment for people living with IgAN, if approved. We will continue our efforts to maintain high quality in this ongoing study, and

we look forward to engaging with regulators as we prepare for accelerated approval submissions beginning in the first half of next year.”

To maintain integrity in the ongoing study, Travele is providing limited data from the interim analyses. In the PROTECT Study, a total of 404 patients with persistent proteinuria despite active ACE or ARB treatment, were randomized 1:1 to receive once daily oral doses of either sparsentan or irbesartan, the active control. The study protocol provided for an unblinded analysis to evaluate the interim efficacy endpoint – the change in proteinuria (urine protein-to-creatinine ratio, or UPCR) at Week 36 from baseline – following the first approximately 280 patients reaching 36 weeks of treatment. After 36 weeks of treatment, patients receiving sparsentan experienced a 49.8 percent mean reduction of proteinuria from baseline after 36 weeks, more than threefold the mean reduction in proteinuria from baseline of 15.1 percent for irbesartan-treated patients ($p=0.0001$).

The secondary endpoints of the PROTECT Study include the rate of change in estimated glomerular filtration rate (eGFR) following the initiation of randomized treatment over 58-week and 110-week periods, as well as the rate of change in eGFR over 52-week and 104-week periods following the first six weeks of randomized treatment. Travele said they believe 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. Consistent with the PROTECT Study protocol, patients will 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. Topline results from the confirmatory endpoint analysis are expected in the second half of 2023.

A preliminary review of the interim safety results indicate sparsentan has been generally well-tolerated and consistent with the previously observed safety profile with no new safety signals emerging.

Travele is also evaluating sparsentan for the treatment of focal segmental glomerulosclerosis (FSGS) in the ongoing pivotal Phase 3 DUPLEX Study and remains on track to provide a regulatory update during the third quarter of 2021.

About the PROTECT Study

The PROTECT Study 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. The PROTECT Study protocol provides for an unblinded interim analysis of at least 280 patients to be performed after 36 weeks of treatment to evaluate the primary efficacy endpoint – the change in proteinuria (urine protein-to-creatinine ratio) at Week 36 from baseline. Secondary efficacy endpoints include the rate of change in eGFR following the initiation of randomized treatment over 58-week and 110-week periods, as well as the rate of change in eGFR over 52-week and 104-week periods following the first six weeks of randomized treatment.

About IgA Nephropathy

IgA nephropathy (IgAN), also called Berger's disease, is a rare kidney disorder 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) and protein in the urine (proteinuria). Other symptoms of IgAN may include kidney pain, swelling (edema) and high blood pressure.

IgAN is the most prevalent primary chronic glomerular disease worldwide and a leading cause of ESKD. IgAN is estimated to affect more than 100,000 people in the U.S. and is one of the leading causes of acute nephritis in Europe and Japan. There are currently no approved treatments indicated for IgAN.

About Sparsentan

Sparsentan, a Dual Endothelin Angiotensin Receptor Antagonist (DEARA), is a novel investigational product candidate. Pre-clinical data have shown that blockade of both endothelin type A and angiotensin II type 1 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 IgAN and FSGS in the U.S. and Europe.

Sparsentan is currently being evaluated in the pivotal Phase 3 DUPLEX Study for the treatment of focal segmental glomerulosclerosis (FSGS) and the pivotal Phase 3 PROTECT Study for the treatment of IgAN. In February 2021, Travers announced that the ongoing pivotal Phase 3 DUPLEX Study of sparsentan in FSGS achieved its pre-specified interim FSGS partial remission of proteinuria endpoint (FPRE) with statistical significance. FPRE 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. After 36 weeks of treatment, 42.0 percent of patients receiving sparsentan achieved FPRE, compared to 26.0 percent of irbesartan-treated patients ($p=0.0094$). Preliminary results from the interim analysis suggest that at the time of the interim assessment, sparsentan had been generally well-tolerated and shown a comparable safety profile to irbesartan. 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 affairs and commercialization) to ultimately generate our revenue. Ligand's OmniAb[®] technology platform is a patent-protected technology stack 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 Pelican 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 traditional systems. Ligand has established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Amgen, Merck, Pfizer, Roche, Jazz Pharmaceuticals, Sanofi, Janssen, Takeda, Gilead Sciences, GSK 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 submitting an application for accelerated approval regulatory submissions for sparsentan in IgAN based on the available data set from the PROTECT interim analysis, the potential for sparsentan to become the first medicine approved for both FSGS and IgAN and references to the efficacy, safety and tolerability profile of Sparsentan based on the preliminary data from the PROTECT Study interim analysis. 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 PROTECT Study of sparsentan in IgAN 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 PROTECT 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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Source: Ligand Pharmaceuticals