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Ligand Partner Retrophin Reports Additional Positive Data from Phase 2 DUET Study of Sparsentan in Focal Segmental Glomerulosclerosis at ASN Kidney Week 2016

Significant reduction of proteinuria compared to irbesartan

Statistically significant difference in modified partial remission; complete remission also observed

Further analysis supports sparsentan generally safe and well-tolerated

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ:LGND)** partner Retrophin, Inc. today announced additional results from the Phase 2 DUET study of sparsentan for the treatment of focal segmental glomerulosclerosis (FSGS), a rare kidney disorder without an FDA-approved pharmacologic treatment that often leads to end-stage renal disease. These new findings are being presented today in the late-breaking High-Impact Clinical Trials oral session at the American Society of Nephrology (ASN) Kidney Week 2016 in Chicago.

“The prevalence of FSGS is on the rise and without an approved therapy, many patients diagnosed with the disorder face a progressive decline and the high likelihood of end-stage renal disease,” said Howard Trachtman, MD, Professor of Pediatrics; Director, Division of Pediatric Nephrology, NYU School of Medicine, NYU Langone Medical Center. “These findings from the DUET study underscore the potential of sparsentan as a first-in-class treatment for FSGS.”

As announced in September, top-line data from DUET showed the sparsentan treatment group achieved statistical significance in the study’s primary efficacy endpoint, reduction of proteinuria. These results showed a greater than two-fold reduction of proteinuria compared to irbesartan, after an eight-week, double-blind treatment period.

An analysis of the secondary endpoint presented today showed that a significantly greater proportion of patients receiving sparsentan achieved modified partial remission of proteinuria, compared to irbesartan-treated patients. Modified partial remission, defined as proteinuria levels of less than or equal to 1.5 g/g and greater than 40 percent reduction of proteinuria from baseline, is associated with long-term preservation of renal function in FSGS. In addition, four patients receiving sparsentan achieved complete remission, compared to zero irbesartan-treated patients. Also presented today was a post-hoc, intention-to-treat (ITT) analysis showing that the sparsentan treatment group again

demonstrated a greater than two-fold reduction of proteinuria, compared to irbesartan. Further analysis of the safety database from the initial eight-week, double-blind treatment period presented today showed sparsentan was generally safe and well-tolerated.

“These new results add to the growing body of evidence from the DUET study, reinforcing our confidence that sparsentan may represent a significant advancement in the treatment of FSGS,” said Stephen Aselage, chief executive officer of Retrophin. “We thank the DUET investigators for their diligence, as well as the patients and their families for their commitment to finding new and better treatment options for FSGS.”

New findings from the DUET study presented at ASN Kidney Week include:

- An analysis of the secondary endpoint, which showed that after the eight-week, double-blind treatment period, 28.1 percent of patients receiving sparsentan (n=64) achieved modified partial remission of proteinuria, compared to 9.4 percent of irbesartan-treated patients (n=32, p=0.040).
- The proportion of patients achieving modified partial remission increased during the open label period. After 48 weeks of treatment with sparsentan (n=26), 57.7 percent of patients achieved modified partial remission. In addition, 50.0 percent of patients that transferred from irbesartan to sparsentan at the beginning of the open label period achieved modified partial remission after 40 weeks of treatment (n=12).
- Complete remission, defined as proteinuria less than 0.3 g/g, was achieved by four patients receiving sparsentan during the eight-week, double-blind treatment period, compared to zero irbesartan-treated patients.
- A post-hoc ITT analysis (imputing zero change in proteinuria for the 13 patients missing baseline or week 8 data) showed a statistically significant difference in the mean reduction of proteinuria from baseline for the sparsentan treatment group (n=73), compared to the irbesartan group (n=36), after the study’s eight-week, double-blind treatment period. The sparsentan group achieved a 42.7 percent mean reduction of proteinuria compared to 15.7 percent for the irbesartan group (p=0.004).
- The ITT analysis also showed that after eight weeks of treatment with 400 mg and 800 mg of sparsentan (n=60), the mean reduction of proteinuria from baseline was 44.8 percent, compared to 15.9 percent for the irbesartan-treated patients in these two cohorts (n=28, p=0.008).
- During the eight-week, double-blind period, the incidence of treatment-emergent adverse events (TEAE) for the sparsentan group was similar to the irbesartan group, except for edema. The severity of edema did not significantly worsen from baseline and no patients withdrew from the study as a result of edema during the eight-week, double-blind treatment period. The most common TEAEs in the study were headache, hypotension, dizziness, edema, nausea, diarrhea, vomiting and upper abdominal pain. The incidence of serious adverse events was similar across both groups.
- 84 percent of patients who completed the eight-week, double blind treatment period continue to receive sparsentan in the open-label extension.

About the DUET Study

The DUET study is an international, randomized, double-blind, Phase 2 clinical trial assessing the safety and efficacy of sparsentan in 109 patients with primary focal segmental glomerulosclerosis (FSGS), of which 96 qualified for the evaluable efficacy database. The primary endpoint is the reduction of proteinuria, as compared to irbesartan, which is part of a class of drugs used to manage FSGS in the absence of an FDA-approved pharmacologic treatment. After a two-week washout period, patients were randomized to receive daily oral doses of 200 mg, 400 mg, and 800 mg of sparsentan or 300 mg of irbesartan. After completing an initial eight weeks of randomized treatment, all patients were eligible to receive sparsentan as part of the study's open-label extension.

About Focal Segmental Glomerulosclerosis (FSGS)

Focal segmental glomerulosclerosis, or FSGS, is a rare disorder without an FDA-approved pharmacologic treatment option 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 renal disease. FSGS is characterized by proteinuria, where protein is found in the urine due to a breakdown of the normal filtration mechanism in the kidney. 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 is widely regarded to be beneficial in the treatment of FSGS, and may be associated with a decreased risk of progression to end-stage renal disease. Achieving modified partial remission of proteinuria, defined as proteinuria levels of less than or equal to 1.5 g/g and greater than 40 percent reduction of proteinuria from baseline, is associated with long-term preservation of renal function in patients with FSGS. In the absence of an FDA-approved pharmacologic treatment, patients with FSGS are currently managed with angiotensin receptor blockers, angiotensin converting enzyme inhibitors, calcineurin inhibitors, and steroids.

About Sparsentan

Sparsentan could be the first FDA-approved pharmacologic treatment for focal segmental glomerulosclerosis, or FSGS, a rare kidney disorder that often leads to end-stage renal disease. Sparsentan's dual mechanism of action combines angiotensin receptor blockade with endothelin receptor type A blockade. In several forms of chronic kidney disease, endothelin receptor blockade has been shown to have an additive beneficial effect on proteinuria in combination with renin-angiotensin blockade via angiotensin receptor blockade or angiotensin converting enzyme inhibitors.

The Phase 2 DUET study of sparsentan met the primary efficacy endpoint for the combined treatment group, demonstrating a greater than two-fold reduction of proteinuria compared to irbesartan, after the eight-week, double-blind treatment period. Retrophin is working with the FDA to determine the most expeditious path forward to advance the development of sparsentan towards approval. In 2015, the FDA and European Commission each granted sparsentan orphan drug designation for the treatment of FSGS.

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company focused on developing or acquiring technologies that help pharmaceutical companies discover and develop medicines. 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, diversified and lower-risk business than a typical biotech company. Our business model is based on doing what we do best: drug discovery, early-stage drug development, product reformulation and partnering. We partner with other pharmaceutical companies to leverage what they do best (late-stage development, regulatory management and commercialization) to ultimately generate our revenue. Ligand's Captisol® platform technology is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. OmniAb® is a patent-protected transgenic animal platform used in the discovery of fully human mono-and bispecific therapeutic antibodies. Ligand has established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Novartis, Amgen, Merck, Pfizer, Celgene, Gilead, Janssen, Baxter International and Eli Lilly.

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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 include statements regarding the possible use of sparsentan as a treatment options for FSGS, the timing and results of review by the Food and Drug Administration (FDA) of sparsentan, Retrophin's plans to present the DUET study results at an upcoming medical meeting or in a peer-reviewed publication, and the ability of patients to continue in an open-label study of sparsentan. Actual events or results may differ from our expectations. For example, Ligand has no control whether Retrophin terminates the open-label study of sparsentan, including due to adverse events reported by patients, there can be no assurance that success in a Phase 2 clinical trial will result in success in future clinical trials; the safety and tolerability data from a new clinical trial in sparsentan may conflict with the results of the Phase 2 DUET clinical trial; and the number of patients diagnoses with FSGS may be more or fewer than Retrophin believes. The failure to meet expectations with respect to any of the foregoing matters may reduce Ligand's stock price. Additional information concerning these and other important risk factors affecting Ligand can be found in Ligand's prior press releases available at www.ligand.com as well as in Ligand's public periodic 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 press release, except as required by law. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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