Retrophin Initiates Pivotal Phase 3 Clinical Trial of Sparsentan for the Treatment of Focal Segmental Glomerulosclerosis

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SAN DIEGO, April 03, 2018 (GLOBE NEWSWIRE) -- Retrophin, Inc. (NASDAQ:RTRX) today announced that the first patient has been enrolled in the DUPLEX Study, a global, pivotal Phase 3 clinical trial evaluating the long-term nephroprotective potential of sparsentan for the treatment of focal segmental glomerulosclerosis (FSGS), a rare kidney disorder that often leads to end-stage renal disease, with no approved pharmacologic treatment available.

“Patients with FSGS currently face a progressive decline that often results in end-stage renal disease and our hope is that the DUPLEX Study will enable us to deliver a first-in-class treatment to these patients in need,” said Bill Rote, PhD, senior vice president and head of research and development for Retrophin. “Developed in alignment with the FDA, the design of our pivotal DUPLEX Study builds upon the promising results from the Phase 2 DUET Study of sparsentan and positions us to pursue Subpart H accelerated approval with the inclusion of our interim endpoint assessing modified partial remission of proteinuria. We look forward to working closely with the FSGS community and investigators as we continue to enroll participants in this pioneering study.”

About the DUPLEX Study

The pivotal DUPLEX Study is a global, randomized, multicenter, double-blind, parallel-arm, active-controlled Phase 3 clinical trial evaluating the safety and efficacy of sparsentan for the treatment of FSGS. Approximately 300 patients, aged 8 to 75 years, are expected to be randomized to receive either sparsentan (initial dose of 400 mg daily for two weeks, titrating up to a target dose of 800 mg daily) or an active control - irbesartan (initial dose of 150 mg daily for two weeks, titrating up to a target dose of 300 mg daily).

In concurrence with U.S. Food and Drug Administration (FDA) feedback, the DUPLEX Study protocol provides for an unblinded analysis of at least 190 patients (approximately 95 per treatment group) to be performed after 36 weeks of treatment to evaluate the interim efficacy endpoint – the proportion of patients achieving a modified partial remission of proteinuria (urine protein-to-creatinine ratio (Up/C) ≤1.5 g/g and a >40 percent reduction in Up/C from baseline) at Week 36. Retrophin expects that successful achievement of this endpoint will serve as the basis for Subpart H accelerated approval of sparsentan in the United States and Conditional Marketing Authorization (CMA) consideration in Europe. The primary endpoint of the study is the change in slope of estimated glomerular filtration rate (eGFR) after 108 weeks of treatment. Secondary endpoints include the percent change in eGFR from Week 6 to Week 108, as well as the percent change from baseline in Up/C at Week 36 assessed at the final analysis. Top-line data from the 36-week interim efficacy endpoint analysis are expected in the second half of 2020.

About Focal Segmental Glomerulosclerosis

FSGS is a rare kidney disorder without an 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 appears 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 in proteinuria from baseline, appears to be associated with long-term preservation of renal function in patients with FSGS. Symptoms of FSGS are currently managed with angiotensin receptor blockers, angiotensin converting enzyme inhibitors, steroids or calcineurin inhibitors.

About Sparsentan

If approved, sparsentan could be the first FDA-approved pharmacologic treatment for FSGS; its 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. Sparsentan has been granted orphan drug designation for the treatment of FSGS by the FDA and European Commission.

The Phase 2 DUET Study of sparsentan met its primary efficacy endpoint for the combined treatment group, demonstrating a greater than two-fold reduction in proteinuria compared to irbesartan, after the eight-week, double-blind treatment period. Irbesartan is part of a class of drugs used to manage FSGS in the absence of an FDA-approved pharmacologic treatment. In April 2018, Retrophin initiated the pivotal Phase 3 DUPLEX Study of sparsentan for the treatment of FSGS. The study includes an interim efficacy endpoint based on proteinuria to serve as the basis for a New Drug Application (NDA) filing for Subpart H accelerated approval of sparsentan in FSGS.

About Retrophin

Retrophin is a biopharmaceutical company specializing in identifying, developing and delivering life-changing therapies to people living with rare diseases. The Company’s approach centers on its pipeline featuring late-stage assets targeting rare diseases with significant unmet medical needs, including fosmetpantotenate for pantothenate kinase-associated neurodegeneration (PKAN), a life-threatening neurological disorder that typically begins in early childhood, and sparsentan for focal segmental glomerulosclerosis (FSGS) and IgA nephropathy (IgAN), disorders characterized by progressive scarring of the kidney often leading to end-stage renal disease. Research in additional rare diseases is also underway, including a joint

development arrangement evaluating the potential of CNSA-001 in phenylketonuria (PKU), a rare genetic metabolic condition that can lead to neurological and behavioral impairment. Retrophin's R&D efforts are supported by revenues from the Company's commercial products Chenodal®, Cholbam® and Thiola®.

Retrophin.com

Forward-Looking Statements

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, these statements are often identified by the words "may", "might", "believes", "thinks", "anticipates", "plans", "expects", "intends" or similar expressions. In addition, expressions of our strategies, intentions or plans are also forward-looking statements. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties associated with the Company's business and finances in general, success of its commercial products as well as risks and uncertainties associated with the Company's preclinical and clinical stage pipeline. Specifically, the Company faces risks associated with market acceptance of its marketed products including efficacy, safety, price, reimbursement and benefit over competing therapies. The risks and uncertainties the Company faces with respect to its preclinical and clinical stage pipeline include risk that the Company's clinical candidates will not be found to be safe or effective and that ongoing or planned clinical trials will not proceed as planned. Specifically, with respect to sparsentan, the Company faces the risk that the Phase 3 clinical trial of sparsentan in FSGS (the "DUPLEX Study") will not demonstrate that sparsentan is safe or effective or serve as a basis for accelerated approval of sparsentan as planned; and more generally, risk that the Company's product candidates will not be approved for efficacy, safety, regulatory or other reasons, and for each of the programs, risk associated with enrollment of clinical trials for rare diseases and risk that ongoing or planned clinical trials may not succeed, may not progress as expected, or may be delayed for safety, regulatory or other reasons. The Company faces risk that it will be unable to raise additional funding that may be required to complete development of any or all of its product candidates; risk relating to the Company's dependence on contractors for clinical drug supply and commercial manufacturing; uncertainties relating to patent protection and exclusivity periods and intellectual property rights of fourth parties; and risks and uncertainties relating to competitive products and technological changes that may limit demand for the Company's products. You are cautioned not to place undue reliance on these forward-looking statements as there are important factors that could cause actual results to differ materially from those in forward-looking statements, many of which are beyond our control. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Investors are referred to the full discussion of risks and uncertainties as included in the Company's most recent Form 10-K and other filings with the Securities and Exchange Commission.

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