Reata Announces Initial Phase 2 Pulmonary Arterial Hypertension Data for Bardoxolone Methyl and Planned Initiation of Phase 3 Study

October 27, 2015 12:50 PM ET

Montreal, Quebec – October 27, 2015 – Reata Pharmaceuticals announced initial data from the LARIAT trial evaluating bardoxolone methyl in pulmonary arterial hypertension (PAH) patients at the annual meeting of the 2015 American College of Chest Physicians (CHEST) in Montreal, Canada. The presentation, "Initial Data Report from 'LARIAT': a Phase 2 Study of Bardoxolone Methyl in PAH Patients on Stable Background Therapy," was presented by Ronald Oudiz, M.D., Professor of Medicine, David Geffen School of Medicine at UCLA. Dr. Oudiz is Director of the Pulmonary Hypertension Center and a Faculty Cardiologist at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center in Southern California.

All patients in the study were on stable doses of background PAH therapies at baseline and throughout the study. Efficacy analyses showed that bardoxolone methyl increased 6-minute walk distance (6MWD) at doses of 2.5 to 10 mg through 16 weeks of treatment. Patients treated with bardoxolone methyl demonstrated a statistically significant mean increase in 6MWD compared to baseline of 22 m and a placebo-corrected difference of 21.4 m ($p = 0.037$). Many current therapies have shown a limited ability to improve 6MWD in patients who have baseline 6MWD values greater than 450 m. However, 6MWD changes in patients with baseline values greater than 450 m were similar to those with baseline values less than 450 m. Changes in 6MWD were associated with improvements in metabolic parameters, including mean weight loss of 3 kg relative to placebo and reductions in creatine kinase, a marker of muscle inflammation.

Notably, patients with connective tissue disease associated PAH (CTD-PAH), who typically experience less therapeutic benefit from approved PAH therapies, demonstrated a mean increase from baseline in 6MWD of 30 m and a placebo-corrected change of 44 m. This change may reflect the novel anti-inflammatory, metabolic, and mitochondrial effects of bardoxolone methyl.

Safety analyses from LARIAT demonstrated that bardoxolone methyl was well-tolerated with relatively fewer discontinuations in bardoxolone methyl-treated patients compared to those who received placebo. No drug-related serious adverse events were reported, and the adverse event profile was manageable. Importantly, unlike previous observations in a subset of patients with advanced kidney disease, no fluid retention events or less severe manifestations of fluid retention were observed in the LARIAT PAH subjects. No meaningful or dose-related changes in blood pressure, heart rate, other measures of fluid status, and echocardiographic parameters were noted.

Reata completed an end of phase 2 interaction with the FDA in October, and the FDA concurred with Reata's proposal for an initial phase 3 study in CTD-PAH patients using 6MWD as the primary endpoint. The primary endpoint will be assessed after 24 weeks of treatment. Reata plans to initiate this first phase 3 study in 2016 and is considering additional studies in other subtypes of PAH.

"The initial data from LARIAT are very encouraging and indicate that bardoxolone methyl's novel mechanism of action may provide a new approach to PAH therapy. Clinically, these effects may acutely translate to increased muscular function, and as we have observed in preclinical models, may reduce pathological cardiovascular remodeling in the long-term," said Colin Meyer, M.D., Reata's Chief Medical Officer. "This pharmacology is particularly meaningful to PAH patients with connective tissue disease. These patients have autoimmune disease that causes their PAH, and their inflammatory disease processes often involve more remodeling than other subtypes. This explains why these patients often do not respond well to approved vasodilator therapy relative to idiopathic PAH patients and represent a subset of the PAH population with significant unmet need. On the basis of these data and recent interactions with the FDA, we are excited to announce that we are planning to initiate a phase 3 study of bardoxolone methyl in patients with CTD-PAH in 2016."

About Bardoxolone Methyl

Bardoxolone methyl is an experimental, oral once daily antioxidant inflammation modulator (AIM) that has received orphan drug designation for the treatment of PAH by the US Food and Drug Administration. Bardoxolone methyl directly targets the bioenergetic and inflammatory components of PH. PH patients experience mitochondrial dysfunction, increased production of NF-κB and related inflammatory pathways involved in ROS signaling, cellular proliferation, and fibrosis. Bardoxolone methyl, through the combined effect of Nrf2 activation and NF-κB suppression, has the potential to inhibit inflammatory and proliferative signaling, suppress ROS production and signaling, reduce the production of enzymes related with fibrosis and tissue remodeling, and increase ATP production and cellular respiration.

About the LARIAT Study

LARIAT (A Dose-Ranging Study of the Efficacy and Safety of Bardoxolone Methyl in Patients with Pulmonary Hypertension) is a Phase 2 dose ranging study examining the safety, tolerability, and efficacy of bardoxolone methyl in patients with PAH on stable background therapy. To determine if bardoxolone methyl could complement approved PAH therapies, the Phase 2 study was designed to assess efficacy through exercise capacity.

This initial data report is from analysis performed on the initial 3 cohorts (24 patients). World Health Organization (WHO) Group 1 PAH patients (n = 24) were randomized in cohorts of 8 patients in a 1:3 ratio to receive once-daily placebo or bardoxolone methyl at doses of 2.5, 5, or 10 mg for 16 weeks. Each dosing cohort completed week 4 assessments before the next dosing cohort opened. Patients were WHO functional class II or III and using stable doses of at least one approved PAH therapy were included in the study. The primary efficacy variable, 6-minute walk distance (6MWD), was collected at baseline and every 4 weeks post-randomization. A Safety Review Committee monitored the study, and all eligible participants were offered open-label extension therapy after the initial 16 weeks. For more details on the LARIAT study visit https://www.clinicaltrials.gov/ct2/show/NCT02036970.

About Pulmonary Arterial Hypertension

Pulmonary arterial hypertension (PAH) is a multi-organ condition characterized by an abnormally high pressure in the network of arteries and veins that lead to and from the lungs due, in part, to narrowing of the pulmonary vasculature as a result of inflammation, remodeling, proliferation, and endothelial dysfunction. Mitochondrial dysfunction has also been implicated in PAH. PAH patients experience increased pressure on the right side of the heart, ultimately leading to ventricular failure and death. Although PAH does not involve metastasis or disruption of tissue boundaries, it shares some features with cancer, including hyperproliferation and resistance to apoptosis, or programmed cell death, of vascular smooth muscle and other cells. Further, impaired energetics of skeletal muscle is a common feature of PAH.

About Reata Pharmaceuticals, Inc.

Reata Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company located in Irving, Texas, focused on the development of drugs that target proteins involved in the cellular biology of oxidative stress, inflammation, and mitochondrial function to address the unmet medical needs of patients with serious or life threatening diseases. We focus on drugs with novel mechanisms of action that modulate important regulatory proteins, called transcription factors, that coordinate the cellular response to stressors by activating or suppressing the activity of many target proteins. The effects of AIM pharmacology have been documented in more than 200 scientific papers and are potentially relevant to a wide range of diseases.

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