Acceleron Announces Sotatercept Achieved Primary and Secondary Endpoints in the PULSAR Phase 2 Placebo-Controlled Trial in Patients with Pulmonary Arterial Hypertension

January 27, 2020

- The PULSAR trial achieved its primary endpoint: a statistically significant reduction in pulmonary vascular resistance -

- The trial also achieved statistically significant improvements in the key secondary endpoint of six-minute walk distance (6MWD) and other secondary endpoints, including amino-terminal brain natriuretic propeptide (NT-proBNP), and World Health Organization (WHO) functional class -

- Sotatercept was generally well tolerated in the trial and adverse events were consistent with previously published data on sotatercept in other diseases -

- Conference call and webcast with guest pulmonary key opinion leaders to be held today, Monday, January 27th at 5:00 p.m. EST -

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 27, 2020-- Acceleron Pharma Inc. (NASDAQ:XLRN), a leading biopharmaceutical company in the discovery and development of TGF-beta superfamily therapeutics to treat serious and rare diseases, today announced that the PULSAR Phase 2 trial of sotatercept met its primary and key secondary endpoints in patients with pulmonary arterial hypertension (PAH).

In patients on stable background PAH-specific therapies, sotatercept demonstrated a statistically significant reduction in pulmonary vascular resistance (PVR), the trial's primary endpoint, at week 24 versus placebo. The trial also achieved a statistically significant improvement in the key secondary endpoint of 6MWD, as well as other secondary endpoints, including NT-proBNP, and WHO functional class.

"We're thrilled to report such positive topline results from the PULSAR trial," said Habib Dable, President and Chief Executive Officer of Acceleron. "PAH is a debilitating disease of high unmet medical need, so we're encouraged by these data that signal that sotatercept could deliver added benefit to patients. We look forward to upcoming interactions with health authorities as we plan to globally develop and, if approved, commercialize sotatercept in PAH."

In this Phase 2 double-blind, placebo-controlled study, 106 patients were randomized to receive placebo, 0.3 mg/kg of sotatercept, or 0.7 mg/kg of sotatercept subcutaneously every 21 days in combination with stable background PAH-specific therapies over a 24-week treatment period.

Sotatercept was generally well tolerated in the trial. Adverse events observed in the study were generally consistent with previously published data on sotatercept in other diseases.

"Approved therapies for patients with PAH target three main pathways of endothelial cell dysfunction to primarily promote pulmonary vasodilation," said Dr. Marc Humbert*, Professor of Medicine and Director of the French Pulmonary Hypertension Reference Center at the Université Paris-Saclay. "As a selective ligand trap for members of the TGF-beta superfamily, sotatercept is designed to rebalance BMPR-II signaling, which is a key molecular driver of PAH. The PULSAR data demonstrate that this novel approach has the potential to provide significant benefit on top of currently available therapies."

"These results are particularly impressive given the patient population, the majority of whom were on background combination therapy, including parenteral prostacyclins, had advanced hemodynamics and lengthy duration of disease," said Dr. Vallerie McLaughlin*, Professor of Medicine and Director of the Pulmonary Hypertension Program at the University of Michigan. "Exceptionally notable was the concordance of the effects across the prespecified subgroups. These clinically meaningful data raise the exciting possibility that sotatercept could potentially shift the treatment paradigm for patients with PAH."

97 out of the 106 patients who enrolled in the PULSAR trial are currently participating in the 18-month extension period of the trial. To date, no patients have discontinued participation in the extension trial.

Acceleron plans to present a detailed review of the topline results from the PULSAR Phase 2 trial of sotatercept at a medical conference later this year.

Sotatercept is an investigational therapy that is not approved for any use in any country.

**Drs. McLaughlin and Humbert are investigators in the PULSAR trial and are paid consultants to Acceleron.*

About the PULSAR Trial

The PULSAR Phase 2 trial is a randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of sotatercept in PAH patients. The primary endpoint of the trial is the change from baseline in pulmonary vascular resistance (PVR) over a 24-week treatment period. PVR, as measured by right heart catheterization, is the resistance that the heart must overcome to pump blood through the pulmonary circulatory system. The key secondary endpoint was six-minute walk distance (6MWD; a measure of functional capacity/endurance). Other secondary endpoints included change in amino-terminal brain natriuretic propeptide (NT-proBNP; a hormone secreted by cardiac muscle cells in response to stretching caused by increased blood volume in the heart), and WHO functional class. A total of 106 patients were randomized in a 3:3:4 ratio to receive placebo, sotatercept 0.3 mg/kg, or sotatercept 0.7 mg/kg subcutaneously every 21 days with standard-of-care therapies in combination. The trial was powered to detect an 18% reduction in the primary endpoint of PVR and a 24-meter improvement in the secondary endpoint of 6MWD.

Following the 6-month double-blind treatment period, participants in the trial were eligible to continue in the 18-month extension period.

Conference Call and Webcast

The Company will host a webcast and conference call to discuss the topline results from the PULSAR Phase 2 trial on January 27, 2020, at 5:00 p.m. EST.

The webcast will be accessible under "Events & Presentations" in the Investors/Media page of the Company's website at acceleronpharma.com. Individuals can participate in the conference call by dialing 877-312-5848 (domestic) or 253-237-1155 (international) and referring to the "Acceleron PULSAR Phase 2 Trial Results."

The archived webcast will be available for replay on the Acceleron website approximately two hours after the event.

About Sotatercept

Sotatercept is an investigational agent designed to be a selective ligand trap for members of the TGF-beta superfamily to rebalance BMPR-II signaling, which is a key molecular driver of PAH. In preclinical studies of PAH, sotatercept reversed pulmonary vessel muscularization and improved indicators of right heart failure. Recent topline analysis of the PULSAR Phase 2 trial of sotatercept in patients with PAH revealed the trial met the primary as well as key and other secondary endpoints. Sotatercept is also being evaluated in the SPECTRA Phase 2 trial in patients with PAH. For more information, please visit www.clinicaltrials.gov

Sotatercept is an investigational therapy that is not approved for any use in any country.

About PAH

PAH is a rare and chronic, rapidly progressing disorder characterized by the constriction of small pulmonary arteries and elevated blood pressure in the pulmonary circulation. PAH results in significant strain on the heart, often leading to limited physical activity, heart failure, and reduced life expectancy. The 5-year survival rate for patients with PAH is approximately 57%. Available therapies generally act by promoting the dilation of pulmonary vessels without addressing the underlying cause of the disease. As a result, PAH often progresses rapidly for many patients despite standard of care treatment. A growing body of research has implicated imbalances in BMP and TGF-beta signaling as a primary driver of PAH in familial, idiopathic, and acquired forms of the disease.

About Acceleron

Acceleron is a biopharmaceutical company dedicated to the discovery, development, and commercialization of therapeutics to treat serious and rare diseases. Acceleron's leadership in the understanding of TGF-beta superfamily biology and protein engineering generates innovative compounds that engage the body's ability to regulate cellular growth and repair.

Acceleron focuses its research and development efforts in hematologic, pulmonary, and neuromuscular diseases. In hematology, Acceleron and its global collaboration partner, Bristol-Myers Squibb, are co-promoting newly approved REBLOZYL® (luspatercept-aamt), the first and only approved erythroid maturation agent, in the United States and are developing luspatercept for the treatment of chronic anemia in myelodysplastic syndromes and myelofibrosis. Acceleron is developing sotatercept for the treatment of pulmonary arterial hypertension, having recently reported positive topline results of the Phase 2 PULSAR trial and actively enrolling patients in the Phase 2 SPECTRA trial. The company is also advancing its neuromuscular program with ACE-083, a locally-acting Myostatin+ agent in Phase 2 development in Charcot-Marie-Tooth disease.

For more information, please visit www.acceleronpharma.com. Follow Acceleron on Social Media: @AcceleronPharma and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements about Acceleron's strategy, future plans and prospects, including statements regarding the development and commercialization of sotatercept in PAH and of Acceleron's other compounds, the timeline for clinical development and regulatory approval of sotatercept in PAH and Acceleron's other compounds, the expected timing for reporting of data from ongoing clinical trials, and the potential of Acceleron's compounds as therapeutic drugs. The words "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "may," "plan," "possible," "potential," "project," "should," "target," "will," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Actual results could differ materially from those included in the forward-looking statements due to various factors, risks and uncertainties, including, but not limited to, that preclinical testing of Acceleron's compounds and data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials, that the results of any clinical trials may not be predictive of the results or success of other clinical trials, that regulatory approval of Acceleron's compounds in one indication or country may not be predictive of approval in another indication or country, that the development of Acceleron's compounds will take longer and/or cost more than planned, that Acceleron will be unable to successfully complete the clinical development of Acceleron's compounds, that Acceleron may be delayed in initiating, enrolling or completing any clinical trials, that Acceleron's compounds will not receive regulatory approval or become commercially successful products. These and other risks and uncertainties are identified under the heading "Risk Factors" included in Acceleron's most recent Annual Report on Form 10-K, and other filings that Acceleron has made and may make with the SEC in the future.

The forward-looking statements contained in this press release are based on management's current views, plans, estimates, assumptions, and projections with respect to future events, and Acceleron does not undertake and specifically disclaims any obligation to update any forward-looking statements.

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