Acceleron Presents Preliminary Interim Data from the SPECTRA Phase 2 Trial of Sotatercept in Pulmonary Arterial Hypertension (PAH) at the 2020 American Heart Association Scientific Sessions

November 13, 2020

– Treatment with sotatercept in first set of patients in the ongoing SPECTRA Phase 2 trial was associated with substantial improvements in hemodynamics, exercise tolerance and exercise capacity at week 24 –

– Sotatercept was generally well tolerated, consistent with the previously reported safety profile in PAH and in other diseases –

– Acceleron to host investor and analyst conference call and webcast with guest PAH key opinion leaders today, Friday, November 13, at 11:00 a.m. EST –

CAMBRIDGE, Mass.-(BUSINESS WIRE)--Nov. 13, 2020--Acceleron Pharma Inc. (Nasdaq: XLRN), a leading biopharmaceutical company in the discovery, development, and commercialization of TGF-beta superfamily therapeutics to treat serious and rare diseases, today presented a set of preliminary interim data from the ongoing SPECTRA Phase 2 trial of sotatercept in patients with pulmonary arterial hypertension (PAH).

Initial data from the trial, which is designed to assess resting and exercise hemodynamics and peak oxygen uptake—as recorded by invasive cardiopulmonary exercise testing (iCPET)—show that patients treated with sotatercept experienced substantial improvements in multiple hemodynamic measures as well as in exercise tolerance and exercise capacity. These early outcomes, obtained from the first 10 patients participating in the trial, were shared as part of an Invited Talk entitled, “SPECTRA and Beyond: Signs of Disease Modification?” presented virtually during the American Heart Association (AHA) 2020 Scientific Sessions.

Among the largest resting hemodynamic improvements observed were reductions in pulmonary vascular resistance (PVR; as measured in dyne-sec/cm$^5$) from a mean of 576 at baseline to 369 at week 24 (35.9% reduction) and mean pulmonary arterial pressure (mPAP) as measured in mmHg from 43.4 to 30.6 (29.5% reduction).

“The SPECTRA trial’s innovative design is meant to help us better understand and detect sotatercept’s potential effects on underlying disease pathology,” said Aaron Waxman, M.D., Ph.D.*, Director, Pulmonary Vascular Disease Program at Boston’s Brigham and Women’s Hospital, who delivered the Invited Talk at the AHA. “Despite the limited number of patients evaluated to date, it is difficult not to be encouraged by the range and extent of positive changes seen in key hemodynamic and exercise capacity measures thus far.”

In this single-arm, open-label multi-center exploratory study, a total of up to 25 patients with advanced PAH (classified as WHO functional class III) on stable combination background therapy are to be treated with an initial cycle of 0.3 mg/kg of sotatercept delivered subcutaneously, followed by subsequent cycles of 0.7 mg/kg of sotatercept through a 24-week treatment period. The protocol includes iCPET at baseline and at week 24 to assess change from peak oxygen uptake or VO$_2$ max (the primary endpoint) as well as changes from baseline in a range of secondary endpoints, including mPAP and VO$_2$ at anaerobic threshold.

During his AHA talk, Dr. Waxman also provided an in-depth profile of the first patient treated in the SPECTRA trial: a 25-year-old woman diagnosed with idiopathic PAH nearly five years prior to enrollment. This patient, who was classified as WHO functional class III and on combination background therapy, experienced substantial hemodynamic and functional improvements. Perhaps most notably, this patient was reclassified from WHO functional class III at baseline to class I at week 24. The patient retained functional class I status in follow-up testing at 48 weeks.

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

“We’re thrilled to see such positive preliminary outcomes from the SPECTRA trial, which serves as another important exploration of sotatercept and the potential of its unique mechanism to alter the course and treatment of PAH,” said Habib Dable, President and Chief Executive Officer of Acceleron. “These results, combined with new PULSAR trial data presented at AHA and the topline PULSAR findings announced earlier this year, position us well to initiate a robust Phase 3 development program to realize our vision of sotatercept as a backbone therapy for patients with PAH across all stages of disease.”

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

The presentation referenced above is available on the “Publications” page under the “Science & Pipeline” section of Acceleron’s website, www.acceleronpharma.com.

*Dr. Waxman is the principal investigator of the SPECTRA trial and a paid consultant to Acceleron.

About the SPECTRA Trial

The SPECTRA Phase 2 trial is a single arm, open-label, multi-center exploratory study to determine the effects of sotatercept plus standard of care in adults with WHO functional class III PAH. The primary endpoint of the trial is the change from baseline in peak oxygen uptake (VO$_2$ max) at 24 weeks, as recorded by invasive cardiopulmonary exercise testing (iCPET). Secondary hemodynamic endpoints as well as endpoints of exercise capacity and tolerance assessed via iCPET and right heart catheterization include change from baseline at 24 weeks in: ventilatory efficiency (VE/VO$_2$ slope); cardiac index (L/min/m$^2$); mean pulmonary artery pressure (mPAP); pulmonary vascular resistance (PVR); arteriovenous oxygen content difference (Ca-vO$_2$); ventilatory efficiency; “dead space” assessment (VE/VO$_2$ slope); and oxygen consumption at anaerobic threshold (VO$_2$ at AT).
A total of up to 25 patients are to receive stable background combination PAH therapy plus sotatercept at a starting dose level of 0.3 mg/kg delivered subcutaneously for one cycle, escalating to 0.7 mg/kg at cycle 2 for the remainder of the treatment period. Following the 6-month open-label treatment period, participants in the trial are eligible to continue in the 18-month extension period, which includes iCPET conducted at 48 weeks.

Conference Call and Webcast Information

The Company will host a webcast and conference call today, November 13, 2020, at 11:00 a.m. EST, to review the presentations of sotatercept at AHA.

The webcast will be accessible under “Events & Presentations” in the Investors/Media page of the company’s website at www.acceleronpharma.com. Individuals can participate in the live conference call by dialing 877-312-5848 (domestic) or 253-237-1155 (international) and referring to the “AHA Sotatercept Conference Call.”

A replay of the webcast will be available on the Acceleron website approximately two hours after the event.

About Sotatercept

Sotatercept is an investigational reverse-remodeling 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. The PULSAR Phase 2 trial evaluating sotatercept in combination with approved PAH-specific medicines in patients with PAH achieved its primary endpoint of improvement in pulmonary vascular resistance and its key secondary endpoint of improvement in 6-minute walk distance. 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. Following the PULSAR results, sotatercept was granted Breakthrough Therapy designation from the FDA and Priority Medicines designation from the EMA in PAH. Sotatercept is also being evaluated in the SPECTRA Phase 2 exploratory trial.

In preclinical research published in Science Translational Medicine, sotatercept exhibited consistent effects across multiple components of disease, including suppressed proliferation of pulmonary arterial smooth muscle and microvascular endothelial cells, reduced pulmonary pressures, lessened right ventricular hypertrophy, improved right ventricular function, and attenuated vascular remodeling.

The Company recently presented details of its Phase 3 development plan, including the design for the registrational STELLAR trial, which is expected to be initiated before the end of 2020. Acceleron is planning two additional Phase 3 studies in patients with PAH: the HYPERION trial, exploring early intervention with sotatercept, and the ZENITH trial assessing later-stage intervention.

Sotatercept is an investigational therapy that is not approved for any use in any country. Sotatercept is part of a licensing agreement with Bristol Myers Squibb.

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 commercialization, research, and development efforts in hematologic and pulmonary diseases. In hematology, REBLOZYL® (luspatercept-aamt) is the first and only erythroid maturation agent approved in the United States, Europe, and Canada for the treatment of anemia in certain blood disorders. REBLOZYL is part of a global collaboration partnership with Bristol Myers Squibb. The Companies co-promote REBLOZYL in the United States and are also developing luspatercept for the treatment of anemia in patient populations of MDS, beta-thalassemia, and myelofibrosis. In pulmonary, Acceleron is developing sotatercept for the treatment of pulmonary arterial hypertension (PAH), having recently presented positive topline results of the PULSAR Phase 2 trial. The Company is currently planning multiple Phase 3 trials with the potential to support its long-term vision of establishing sotatercept as a backbone therapy for patients with PAH at all stages of the 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 of sotatercept in PAH, the timeline for clinical development and regulatory approval of sotatercept in PAH, 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 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, and that Breakthrough Therapy or PRIME designation may not expedite the development or review of sotatercept. 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, Quarterly Report on Form 10-Q, 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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