NEWS RELEASE

Acceleron Presents Preliminary Data from the SPECTRA Phase 2 Trial of Sotatercept in Pulmonary Arterial Hypertension (PAH) at the American Thoracic Society 2021 International Conference

5/19/2021

– Treatment with sotatercept in the ongoing SPECTRA Phase 2 trial was associated with improvements in resting and exercise hemodynamics at week 24 –

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

- Company-hosted investor and analyst conference call and webcast with guest PAH key opinion leader to be held today, Wednesday, May 19th at 10:30 a.m. EDT –

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- 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 at the American Thoracic Society 2021 International Conference (ATS 2021) preliminary interim data from the SPECTRA Phase 2 trial of sotatercept in patients with pulmonary arterial hypertension (PAH).

The findings, presented during the session “Clinical Advances in Pulmonary Hypertension: Lessons from Best Abstracts,” included outcomes obtained from the first 10 patients evaluated among a total of 21 trial participants. These preliminary data from the ongoing 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 improvements in multiple key hemodynamic measures.

“Despite the relatively small number of patients evaluated to date, the consistency and scale of improvements seen in a range of clinically meaningful measures are very encouraging,” said Aaron Waxman, M.D., Ph.D.*, Director,

Pulmonary Vascular Disease Program at Boston's Brigham and Women's Hospital, who presented at ATS 2021. "Our analyses are ongoing, but observing such beneficial changes among heavily pretreated patients with fairly advanced disease suggests that sotatercept may be affecting the underlying pathology of PAH."

In this single-arm, open-label multi-center exploratory study, a total of 21 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.

As measured by iCPET at baseline and at week 24, investigators recorded improvements in peak oxygen uptake or VO2 max (the primary endpoint) as well as in a range of secondary endpoints, including ventilatory efficiency, total workload, and arteriovenous oxygen content. Previously reported improvements in resting hemodynamics included reductions in pulmonary vascular resistance (PVR; as measured in dynes-sec/cm5) 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).

In addition, six-minute walk distance (6MWD) increased by an average of 72.4 meters from baseline to week 24 in nine patients for whom data were available.

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. As of an interim data cut-off of February 25, 2021, treatment-emergent adverse events (TEAEs) were reported in 16 of 21 patients (76%). Serious TEAEs were reported in three patients (14%), but none was considered related to the study drug and none required dose interruption or reduction.

"It's exciting to be able to add these positive results from the SPECTRA trial to the growing body of clinical and preclinical evidence showing that sotatercept has the potential to transform the lives of patients with PAH by introducing a novel mechanism of action to the treatment paradigm," said Habib Dable, President and Chief Executive Officer of Acceleron. "With our comprehensive Phase 3 clinical program now underway, we are on track to achieve our vision of developing 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.

Dr. Waxman's detailed presentation 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 (VO2 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/VCO2 slope); cardiac index (L/min/m2); mean pulmonary artery pressure (mPAP); pulmonary vascular resistance (PVR); arteriovenous oxygen content difference (Ca-vO2); ventilatory efficiency; “dead space” assessment (VE/VCO2 slope); and oxygen consumption at anaerobic threshold (VO2 at AT).

A total of 21 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, May 19, 2021, at 10:30 a.m. EDT, to discuss results of the presentations at ATS 2021.

The webcast will be accessible under "Events & Presentations" in the Investors & Media page of the Company’s website at **www.acceleronpharma.com**. To participate in the conference call, please dial 833-494-1483 (domestic) or 236-714-2620 (international) and reference code #6565123.

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 signaling in the BMP pathway, which is a key molecular driver of PAH. In preclinical studies, sotatercept was shown to reverse the vascular remodeling that is a hallmark 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, which were published in a recent edition of the New England Journal of Medicine, 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.

The Company recently presented details of its Phase 3 development plan, including the design for the registrational **STELLAR** trial, which is currently enrolling patients with PAH. Acceleron is planning two additional Phase 3 studies in patients with PAH: the HYPERION trial in newly diagnosed patients and the ZENITH trial assessing intervention in patients diagnosed with World Health Organization (WHO) functional class IV disease.

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 research, development, and commercialization efforts in pulmonary and hematologic diseases. In pulmonary, Acceleron is developing sotatercept for the treatment of pulmonary arterial hypertension (PAH), having reported 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. Acceleron is also investigating the potential of its early-stage pulmonary candidate, ACE-1334, which it plans to advance into a Phase 1b/Phase 2 trial in systemic sclerosis-associated interstitial lung disease (SSc-ILD) this year.

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 myelodysplastic syndromes, beta-thalassemia, and myelofibrosis.

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 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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