Acceleron Presents Topline Results of the PULSAR Phase 2 Trial of Sotatercept in Patients with Pulmonary Arterial Hypertension

June 24, 2020

- Data presented during 'Breaking News' Session of the American Thoracic Society 2020 Virtual Conference (ATS 2020 Virtual) show the PULSAR trial achieved its primary endpoint: a statistically significant mean reduction in pulmonary vascular resistance (PVR) -

- Patients on stable background therapy who were treated with 0.3 mg/kg or 0.7 mg/kg of sotatercept experienced mean PVR reductions of approximately 21% and 34%, respectively -

- The trial also achieved a statistically significant all-dose mean improvement from baseline of 54 meters in the key secondary endpoint of six-minute walk distance (6MWD) and a placebo corrected improvement of 25 meters (all doses combined) -

- Sotatercept was generally well tolerated; adverse events were consistent with previously published data on sotatercept in clinical trials in other patient populations -

- Company-hosted investor and analyst conference call and webcast with guest PAH key opinion leaders to be held today, Wednesday, June 24th at 4:30 p.m. EDT -

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 24, 2020-- Acceleron Pharma Inc. (NASDAQ:XLRN), a biopharmaceutical company dedicated to the discovery, development, and commercialization of TGF-beta superfamily therapeutics to treat serious and rare diseases, today presented topline results of the PULSAR Phase 2 trial of sotatercept in patients with pulmonary arterial hypertension (PAH).

During the "Breaking News: Clinical Trials in Pulmonary Medicine" session of ATS 2020 Virtual, study investigators reported that patients on stable background PAH-specific therapies treated with sotatercept experienced a statistically significant reduction in pulmonary vascular resistance (PVR), the trial's primary endpoint, at week 24 versus placebo.

"We're thrilled to report the impressive magnitude of the positive effects that sotatercept, in combination with current therapies, was able to achieve in patients with PAH," said Habib Dable, President and Chief Executive Officer of Acceleron. "Although the introduction over the past two decades of more than a dozen treatments for PAH has driven the development of today's combination-therapy strategies, the substantial morbidity still associated with PAH clearly signals the need for a new approach. As we work now with health authorities to move sotatercept into Phase 3 testing, we are increasingly encouraged that we will be able to deliver a truly innovative therapy to patients with this debilitating disease."

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, including mono, double, and triple therapy over a 24-week treatment period. Of the 106 patients participating in the trial, 35% were receiving double background PAH-specific therapies and 56% were receiving triple background PAH-specific therapies. The trial achieved its primary endpoint, key secondary endpoint, and showed concordance of results across multiple additional endpoints and regardless of baseline characteristics.

Primary Endpoint:

Treatment*	**% Reduction in PVR**	**P-Value**
Sotatercept 0.3 mg/kg (n=32)	20.5%	0.0027
Sotatercept 0.7 mg/kg (n=42)	33.9%	<0.0001
Placebo (n=32)	2.1%	

**All cohorts include stable background PAH-specific therapies*

The trial also achieved the protocol-defined improvement in the key secondary endpoint of 6MWD at 24 weeks. Both sotatercept dose groups achieved at least a 50-meter (LS mean) increase from baseline, as demonstrated in the 0.3 mg/kg group (58 meters) and the 0.7 mg/kg group (50 meters), allowing for a pre-specified pooled analysis. Overall, treatment with sotatercept (pooled analysis) achieved a 54-meter (LS mean) change from baseline and a placebo-corrected (LS mean) difference of 25 meters (nominal p=0.03).

"These results, seen on top of existing therapies in heavily pretreated patients, are consistent with sotatercept exerting its effects through a mechanism distinct from currently approved agents," said Dr. David Badesch†, Professor of Medicine and Clinical Director of the Pulmonary Hypertension Center at the University of Colorado.

Badesch, who presented the PULSAR trial data during today's ATS 2020 Virtual session, continued: "By selectively binding ligands of the TGF-beta superfamily, sotatercept is designed to rebalance key signaling pathways whose disruption has been shown to be important in PAH biology. If

sotatercept's efficacy and safety are confirmed in the next phase of clinical development, I believe it has the potential to substantially alter the way we treat patients with PAH."

Treatment with sotatercept also demonstrated improvement across multiple exploratory study endpoints at week 24, including a 51% reduction in amino-terminal brain natriuretic propeptide (NT-proBNP), and 20% reduction in mean pulmonary arterial pressure. In addition, 23% of subjects improved their World Health Organization (WHO) functional class.

Sotatercept was generally well tolerated in the trial. Adverse events observed in the study were generally consistent with previously published data on sotatercept in clinical trials in other patient populations. Serious treatment-emergent adverse events (TEAEs) were reported in 6% (2/32) of patients receiving 0.3 mg/kg of sotatercept plus background therapy, 24% (10/42) of patients receiving 0.7 mg/kg of sotatercept plus background therapy, and in 9% (3/32) of patients receiving placebo plus background therapy.

Hemoglobin increase was reported in one patient (3%) in the 0.3 mg/kg sotatercept dose group and in 6 patients (14%) in the 0.7 mg/kg sotatercept dose group. No patient in the placebo group experienced an increase in hemoglobin. Two patients (6%) in the 0.3 mg/kg sotatercept dose group and 5 patients (12%) in the 0.7 mg/kg sotatercept dose group experienced thrombocytopenia. TEAEs occurring in 10% or more of all patients in any arm were headache, diarrhea, peripheral edema, dizziness, fatigue, hypokalemia, and nausea.

As of June 22, 2020, 94 of 97 patients who opted to participate in the 18-month extension period of the trial were still enrolled; 64 patients have now been treated with sotatercept for at least 12 months.

Dr. Badesch's presentation from ATS 2020 Virtual is available in the Publications section under "Science & Pipeline" on the Company's website at acceleronpharma.com.

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

†Dr. Badesch is the principal investigator of the PULSAR trial and a paid consultant 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 exploratory analyses 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; mean pulmonary arterial pressure, a hemodynamic measure of average pressure in the main pulmonary arteries, which is elevated in PAH patients; 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 June 24, 2020, at 4:30 p.m. EDT.

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 conference call by dialing 877-312-5848 (domestic) or 253-237-1155 (international) and referring to the "Acceleron ATS 2020 Conference Call."

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 research recently 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. Sotatercept, which is part of a licensing agreement with Bristol Myers Squibb, is also being evaluated in the exploratory, open-label SPECTRA Phase 2 trial in patients with PAH. For more information, please visit www.clinicaltrials.gov.

Sotatercept, which has been granted Breakthrough Therapy designation from the U.S. Food and Drug Administration and Priority Medicine (PRIME) designation from the European Medicines Agency in PAH, 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 commercialization, research, and development efforts in hematologic and pulmonary diseases. In hematology, Acceleron and its global collaboration partner, Bristol Myers Squibb, are co-promoting REBLOZYL® (luspatercept-aamt), the first and only approved erythroid maturation agent, in the United States for the treatment of anemia in certain blood disorders. The Companies 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.

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 may take longer and/or cost more than planned, that Acceleron may 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 may 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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