



## Acceleron Announces Preliminary Results from Part 1 of the ACE-083 Phase 2 Trial in Patients with Charcot-Marie-Tooth Disease at the 2018 Annual Meeting of the Peripheral Nerve Society

July 23, 2018

- Mean total muscle volume increases of more than 12% seen in the tibialis anterior –

- Company plans to initiate Part 2 of the CMT Phase 2 trial in the third quarter of 2018 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 23, 2018-- Acceleron Pharma Inc. (Nasdaq:XLRN), a leading biopharmaceutical company in the discovery and development of TGF-beta therapeutics to treat serious and rare diseases, today announced positive preliminary results from Part 1 of the Phase 2 clinical trial with ACE-083 in patients with Charcot-Marie-Tooth (CMT) disease at the Peripheral Nerve Society (PNS) annual meeting held in Baltimore, Maryland. CMT is one of the most common inherited neurological diseases and is associated with significant focal muscle weakness. The Company plans to initiate Part 2 of the ACE-083 CMT Phase 2 trial in the third quarter of 2018.

"Preliminary Phase 2 results of ACE-083 in patients with CMT show robust mean increases in total and contractile muscle volume, reductions in fat fraction, and an encouraging safety profile," said Robert K Zeldin, M.D., Chief Medical Officer of Acceleron. "We now look forward to initiating the randomized, placebo-controlled portion of the Phase 2 trial in which we will evaluate ACE-083's potential to improve function over a six-month treatment period."

Part 1 of the trial was an open-label, dose-escalation study that enrolled a total of 18 patients (in three cohorts of six patients each) with CMT1 or CMTX who received ACE-083 at dose levels of 150 mg, 200 mg, or 240 mg. ACE-083 was administered by injection into the tibialis anterior (TA) muscle bilaterally once every three weeks for three months to evaluate safety and increases in muscle volume. The TA, which is located in the lower leg, is the primary muscle responsible for ankle dorsiflexion, or the ability to lift the front of the foot when taking a step. TA weakness can result in foot drop and increased risk of falls.

Muscle volume was measured by magnetic resonance imaging (MRI) three weeks after the last injection of ACE-083. Muscle volume and fat fraction are represented as the changes from baseline averaged for each side.

- Mean total muscle volume (TMV) increases ranged from 12.6% to 14.2%.
- Mean absolute decreases (improvement) in fat fraction ranged from 1.7% to 3.5%.

In addition, treatment with ACE-083 resulted in mean increases from baseline in contractile muscle volume (an MRI-derived calculation to measure viable, functional muscle volume as part of the TMV), ranging from 15.8% to 19.6%.

The most common adverse events—*injection-site reactions, muscle spasms, and myalgia*—were mild or moderate (grades 1-2).

"There are currently no FDA-approved therapies for patients with CMT with muscle weakness. The muscle volume and fat fraction changes demonstrated in Part 1 of the ACE-083 trial are encouraging," said Florian P. Thomas, M.D., neurologist and principal investigator at Hackensack Meridian School of Medicine at Seton Hall University. "We're hopeful that ACE-083 may become an important option for patients."

The 2018 PNS ACE-083 Part 1 oral and poster presentations are available in the "Science" section on Acceleron's website, [www.acceleronpharma.com](http://www.acceleronpharma.com).

The double-blind, placebo-controlled Part 2 of the CMT Phase 2 trial will enroll approximately 40 patients who will be randomized (1:1) to receive either placebo or ACE-083. Patients will be evaluated for changes in muscle volume, fat fraction, strength, function and safety over a six-month primary treatment period, followed by a six-month open-label treatment period. Preliminary results are expected by the end of 2019.

For additional information on this clinical trial, please visit [clinicaltrials.gov](http://clinicaltrials.gov), identifier NCT03124459.

### About ACE-083

ACE-083 is a locally-acting therapeutic candidate, based on the naturally-occurring protein follistatin, which utilizes the Myostatin+ approach to inhibit multiple TGF-beta ligands. It is designed to have a concentrated effect along targeted muscles to maximize growth and strength selectively in the muscles into which the drug is administered. Acceleron is developing ACE-083 for disorders such as CMT disease and facioscapulohumeral muscular dystrophy (FSHD), in which improved muscle strength in target muscles may provide a clinical benefit and enhance quality of life. For more information, please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### About Charcot-Marie-Tooth Disease (CMT)

CMT is one of the most common inherited neurologic diseases. It is estimated to affect more than 125,000 people in the United States. The primary clinical manifestations of CMT include muscle weakness in the lower legs and arms. The lower leg muscle weakness can result in foot drop leading to a high-stepped gait and frequent tripping or falls. The disease is typically diagnosed by the presence of a characteristic pattern of muscle weakness, nerve conduction studies, and genetic testing. There are no FDA-approved drug therapies for CMT.

### About Acceleron

Acceleron is a Cambridge-based, clinical-stage biopharmaceutical company dedicated to the discovery, development, and commercialization of

therapeutics to treat serious and rare diseases. The Company's leadership in the understanding of TGF-beta 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, neuromuscular, and pulmonary diseases. In hematology, the Company and its global collaboration partner, Celgene, are developing luspatercept for the treatment of chronic anemia in myelodysplastic syndromes, beta-thalassemia, and myelofibrosis. Acceleron is also advancing its neuromuscular franchise with two distinct Myostatin+ agents, ACE-083 and ACE-2494, and a Phase 2 pulmonary program with sotatercept in pulmonary arterial hypertension.

For more information, please visit [www.acceleronpharma.com](http://www.acceleronpharma.com). Follow Acceleron on Social Media: [@AcceleronPharma](#) and [LinkedIn](#).

### **Forward-Looking Statements**

This press release contains forward-looking statements about the Company's strategy, future plans and prospects, including statements regarding the development of the Company's compounds, the timeline for clinical development and regulatory approval of the Company's compounds and the expected timing for reporting of data from ongoing clinical trials. The words "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "may," "plan," "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 the Company'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 trial may not be predictive of the results or success of other clinical trials of the same product candidate, that the development of the Company's compounds will take longer and/or cost more than planned, that the Company will be unable to successfully complete the clinical development of the Company's compounds, that the Company may be delayed in initiating, enrolling or completing any clinical trials, and that the Company'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 the Company's most recent Annual Report on Form 10-K, and other filings that the Company 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 the Company does not undertake and specifically disclaims any obligation to update any forward-looking statements.

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