# Celgene Corporation and Acceleron Pharma Announce Results of the Phase 3 BELIEVE Trial Evaluating Luspatercept in Adult Patients with Beta-Thalassemia at ASH 2018

December 1, 2018

*Pivotal phase 3 data demonstrated treatment with investigational luspatercept resulted in significant reduction of transfusion burden compared to placebo*

*Regulatory submissions planned in the United States and Europe in the first half of 2019*

SUMMIT, N.J. & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 1, 2018-- Celgene Corporation (NASDAQ: CELG) and Acceleron Pharma Inc. (NASDAQ: XLRN) today announced results from a pivotal, phase 3 trial (BELIEVE) evaluating the safety and efficacy of luspatercept for the treatment of adults with beta-thalassemia-associated anemia who require regular red blood cell (RBC) transfusions. The data were presented by Maria Domenica Cappellini, M.D. in an oral session of the 60$^{th}$American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego, CA (Abstract #163).

“Currently, the standard of care to help patients with beta-thalassemia manage their anemia is regular, lifelong red blood cell transfusions, which over time can result in iron overload and life-threatening co-morbidities,” said Professor Cappellini, M.D., Professor of Medicine, University of Milan - Fondazione IRCCS. “These findings from the BELIEVE study are exciting because they suggest that luspatercept may help patients reduce their dependence on red blood cell transfusions.”

BELIEVE met the primary endpoint of erythroid response, defined as a ≥33% reduction in RBC transfusion burden (with a reduction of ≥ 2 units of RBC) during weeks 13–24 compared to the baseline 12-week interval prior to randomization. The study also included secondary endpoints that evaluated the impact of treatment on RBC transfusion burden. Mean change in transfusion burden from baseline to weeks 13-24 (luspatercept vs. placebo) was -1.35 RBC units.

**RBC Transfusion Burden Reduction of ≥ 33% Response Rates[1]**

| Response Time Interval | Luspatercept | Placebo | P-value |
|---|---|---|---|
| Weeks 13-24 | 21.4% (48/224) | 4.5% (5/112) | < 0.0001 |
| Weeks 37-48 | 19.6% (44/224) | 3.6% (4/112) | < 0.0001 |
| Any 12 weeks during the entire treatment period | 70.5% (158/224) | 29.5% (33/112) | < 0.0001 |
| Any 24 weeks during the entire treatment period | 41.1% (92/224) | 2.7% (3/112) | < 0.0001 |

**RBC Transfusion Burden Reduction of ≥ 50% Response Rates[1]**

| Response Time Interval | Luspatercept | Placebo | P-value |
|---|---|---|---|
| Weeks 13-24 | 7.6% (17/224) | 1.8% (2/112) | 0.0303 |
| Weeks 37-48 | 10.3% (23/224) | 0.9% (1/112) | 0.0017 |
| Any 12 weeks during the entire treatment period | 40.2% (90/224) | 6.3% (7/112) | < 0.0001 |
| Any 24 weeks during the entire treatment period | 16.5% (37/224) | 0.9% (1/112) | < 0.0001 |

[1]RBC transfusion burden reduction response rates are calculated versus baseline (i.e., the 12 weeks prior to randomization)

**BELIEVE Safety Summary (Safety Population)**

Grade 3 or higher treatment-emergent adverse events (TEAEs) were reported in 29.1% (65/223) of patients receiving luspatercept and 15.6% (17/109) of patients receiving placebo. Serious adverse events were reported in 15.2% (34/223) of patients receiving luspatercept and 5.5% (6/109) of patients receiving placebo. A TEAE of acute cholecystitis resulted in death in one placebo-treated patient (0.9%). No luspatercept-treated patients died due to TEAEs.

**Grade 3 or 4 TEAEs in at least 1% of patients in either arm**

| | Luspatercept N= 223 | Placebo N= 109 |
|---|---|---|
| Anemia | 3.1% | 0.0% |
| Increased liver iron concentration | 2.7% | 0.9% |
| Hyperuricemia | 2.7% | 0.0% |
| Hypertension | 1.8% | 0.0% |

| | | |
|---|---|---|
| Syncope | 1.8% | 0.0% |
| Back pain | 1.3% | 0.9% |
| Bone pain | 1.3% | 0.0% |
| Blood uric acid increased | 1.3% | 0.0% |
| Increased aspartate aminotransferase | 1.3% | 0.0% |
| Increase alanine aminotransferase | 0.9% | 2.8% |
| Thromboembolic events* | 0.9% | 0.0% |

*All grades of thromboembolic events, including DVT, PE, portal vein thrombosis, ischemic stroke, thrombophlebitis, and superficial phlebitis were reported in 8 of 223 (3.6%) luspatercept-treated versus 1 of 109 (0.9%) placebo-treated patients

“The BELIEVE results demonstrate the potential of luspatercept to help adults living with beta-thalassemia better manage their anemia and reduce their transfusion burden,” said Alise Reicin, M.D., President, Global Clinical Development for Celgene. “These results further our understanding of the luspatercept clinical profile, which will continue to inform our plans to advance this promising investigational therapy.”

“These outcomes of the BELIEVE trial increase our confidence in the potential of luspatercept to become an important new treatment option for patients suffering from beta-thalassemia,” said Habib Dable, President and Chief Executive Officer of Acceleron. “Our focus now is to work diligently with health authorities to help ensure that this underserved patient population can gain access to luspatercept as quickly as possible.”

Luspatercept is not approved in any region for any indication. The companies are planning regulatory application submissions of luspatercept in the United States and Europe in the first half of 2019.

**About BELIEVE**

BELIEVE is a phase 3, randomized, double blind, placebo-controlled multicenter study comparing luspatercept + best supportive care (BSC) versus placebo + BSC in adult beta-thalassemia patients who require regular RBC transfusions. The median age of the patients was 30 years in both treatment arms. 336 patients were randomized 2:1 to receive either luspatercept 1.0 mg/kg + BSC (224 patients) or placebo + BSC (112 patients) every 3 weeks for up to 48 weeks. Patients in the luspatercept + BSC arm were able to be titrated up to 1.25 mg/kg of luspatercept every 3 weeks. BSC was defined as RBC transfusions and iron chelation therapy to maintain each patient’s baseline hemoglobin level. Crossover to the luspatercept treatment group was allowed after unblinding and assessment by an independent Data Safety Monitoring committee; patients receiving luspatercept + BSC will be followed for up to 3 years. The study was conducted at 65 sites in 15 countries.

**About Luspatercept**

Luspatercept is a first-in-class erythroid maturation agent (EMA) that is believed to regulate late-stage red blood cell maturation. Acceleron and Celgene are jointly developing luspatercept as part of a global collaboration. Phase 3 clinical trials continue to evaluate the safety and efficacy of luspatercept in patients with MDS (the MEDALIST trial) and in patients with beta-thalassemia (the BELIEVE trial). A COMMANDS phase 3 trial in first-line, lower-risk, MDS patients, the BEYOND phase 2 trial in non-transfusion-dependent beta-thalassemia, and a phase 2 trial in myelofibrosis are ongoing. For more information, please visit www.clinicaltrials.gov.

**About Celgene**

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit www.celgene.com.

Follow Celgene on Social Media: Twitter, Pinterest, LinkedIn, Facebook and YouTube.

**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. Follow Acceleron on Social Media: @AcceleronPharma and LinkedIn.

**FORWARD-LOOKING STATEMENTS**

*This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding the potential benefits of, and plans relating to the collaboration between Acceleron and Celgene; the potential of luspatercept as a therapeutic drug; and the benefit of each company’s strategic plans and focus. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “will,” “would,” “could,” “potential,” “possible,” “hope” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from current expectations and beliefs. For example, there can be no guarantee that luspatercept will be successfully developed or complete necessary clinical phases. Forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other important factors, including: results of clinical trials, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; the ability to obtain and maintain requisite regulatory approvals and to enroll patients in planned clinical trials; the ability to obtain, maintain and*

*enforce patent and other intellectual property protection for luspatercept; the ability to maintain key collaborations; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in each company's public filings with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and neither company has any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law.*

*Hyperlinks are provided as a convenience and for informational purposes only. Neither Celgene nor Acceleron bears responsibility for the security or content of external websites or websites outside of their respective control.*

View source version on businesswire.com: https://www.businesswire.com/news/home/20181201005028/en/

Source: Celgene Corporation

**Celgene Corporation**
Investors:
+1-908-673-9628
ir@celgene.com
or
Media:
+1-908-673-2275
media@celgene.com

**Acceleron Pharma Inc.**
Todd James, IRC, (617) 649-9393
Vice President, Investor Relations and Corporate Communications
or
Candice Ellis, (617) 649-9226
Manager, Investor Relations and Corporate Communications
or
Media:
Matt Fearer, (617) 301-9557
Director, Corporate Communications