Magenta Therapeutics Presents New Data from Phase 2 Study of MGTA-456 Cell Therapy in Patients with Inherited Metabolic Disorders

December 3, 2018

-- All five patients with inherited metabolic disorders (IMDs) treated with MGTA-456 in ongoing Phase 2 study met the primary endpoint of successful engraftment --

-- Patients with cerebral adrenoleukodystrophy (cALD) showed resolution of brain inflammation on MRI as early as one month post-treatment --

-- Patients with Hurler’s syndrome showed increase in corrected enzyme and decrease in disease-related metabolites --

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 2, 2018-- Magenta Therapeutics (NASDAQ:MGTA), a clinical-stage biotechnology company developing novel medicines to bring the curative power of bone marrow transplant to more patients, today announced that the Company presented initial Phase 2 clinical data and preclinical research on its MGTA-456 program at the 60th annual meeting of the American Society of Hematology (ASH).

MGTA-456 is a cell therapy providing a high dose of hematopoietic stem cells that are well-matched to the patient, administered through a transplant procedure. The ongoing Phase 2 study in inherited metabolic disorders aims to enroll 12 patients with cerebral adrenoleukodystrophy (cALD), metachromatic leukodystrophy or globoid cell leukodystrophy, and previously also enrolled patients with Hurler’s syndrome. The primary endpoint of the study is engraftment after transplantation and the secondary endpoint is transplant-related safety and tolerability. Early data from this Phase 2 study were highlighted in a poster presentation by John Wagner, M.D., Director, Blood and Marrow Transplantation Division, University of Minnesota. In a separate oral presentation, Kevin Goncalves, Ph.D., Magenta Therapeutics, highlighted data showing that MGTA-456 significantly improves engraftment and the number of human microglia in the brains of transplanted mice; Tony Boitano, Ph.D., Magenta Therapeutics, presented a third data set showing that MGTA-456 contains large doses of the cells responsible for engraftment, which are also correlated with rapid neutrophil recovery in patients following transplant.

“Inherited metabolic disorders are rare and often fatal diseases. The only disease-modifying treatment option is bone marrow transplant, which can be challenging for patients without a matched sibling donor. MGTA-456 is a cell therapy with a high dose of stem cells that are well matched to the patient and may represent a promising treatment option for these patients,” said John Davis, M.D., M.P.H., chief medical officer, Magenta Therapeutics. “We are pleased to see robust and consistent engraftment, the primary endpoint of the study, in all five of the evaluable patients treated thus far. We are also very encouraged by the changes in early disease biomarkers and brain imaging evidence that are correlated with positive long-term disease outcomes. In addition to leukodystrophies, we are developing MGTA-456 for patients with a broad range of diseases where we believe it has the potential to deliver transformative benefit. A Phase 2 investigator-initiated study of MGTA-456 in blood cancers will begin in late 2018, and we will start a Phase 2 study of MGTA-456 in sickle cell disease in the first half of 2019.”

**Preliminary Phase 2 Results Demonstrate Engraftment with Minimal Neutropenia with MGTA-456, a CD34+ Expanded Cord Blood Product in Patients Transplanted for Inherited Metabolic Disorders, Abstract #3467**

Key results, as of November 2, 2018:

- Five patients treated and evaluable: two with cALD, three with Hurler’s syndrome
- Five of five patients treated with MGTA-456 met the primary endpoint of successful engraftment by day 42 following the transplant procedure.
  - In recent historical cohorts of patients undergoing regular cord blood transplantation with identical pre-transplant conditioning, up to 32% did not engraft at comparable time points.
- The patients treated with MGTA-456 had minimal neutropenia, lasting for a median of 1 day.
  - In the historical cohort, neutropenia lasted for a median of 8 days.
- The two patients with cALD showed resolution/reduction of gadolinium enhancement on MRI, an indicator of brain inflammation, by day 28 post-transplant. Resolution of gadolinium enhancement is correlated with long-term disease benefit in patients with cALD.
- Patients with Hurler’s syndrome showed an increase in blood leukocyte Idua enzyme, the enzyme that is deficient in untreated patients with Hurler’s syndrome, suggesting that transplant with MGTA-456 is beginning to affect the disease in these patients.
- Patients with Hurler’s syndrome showed a marked decline in urine total glycosaminoglycan (GAG) levels, which is correlated with improved long-term disease outcomes.
- Two treatment-related adverse events were observed: one grade 1 vomiting and one grade 3 nausea, both of which were transient.

**Preclinical Data, MGTA-456 Stem Cell Expansion Program**

_MGTA-456, A First-in-Class Cell Therapy Produced from a Single Cord Blood Unit, Enables A Reduced Intensity Conditioning Regimen and Enhances Speed and Level of Human Microglia Engraftment in the Brains of NSG Mice, Abstract #115_

Key results presented by Kevin Goncalves, Ph.D., Magenta Therapeutics:
• NSG mice were transplanted with MGTA-456 or unexpanded cord blood after being conditioned with total body irradiation or either high- or low-dose busulfan, and engraftment of microglial cells in the brain was measured.
• In sublethally-irradiated animals, MGTA-456 led to an 11-fold increase in hematopoietic engraftment and a 24-fold increase in microglial engraftment in the brain (p<0.001, n=8 mice) relative to standard of care, with histology consistent with engrafting microglia in the brain.
• In busulfan-conditioned animals, MGTA-456 led to a 25-fold increase in hematopoietic engraftment and a 60-fold increase in microglial engraftment in the brain relative to standard of care (p<0.001, n=8 mice).
• MGTA-456 led to faster microglial engraftment: a 28-fold increase in microglial engraftment was demonstrated as early as 2 weeks post-transplant with MGTA-456 (p<0.001, n=8 mice). The number of engrafting hematopoietic cells in the periphery correlated with number of engrafting microglia in the brain (p<0.0001).
• Subpopulations of MGTA-456 were evaluated to determine the source of microglial engraftment. Only CD34+CD90+ cells, but not CD34+CD90- or CD34- cells, led to brain engraftment, consistent with the subpopulation of cells that result in hematopoietic engraftment following transplant of unexpanded cells (Radtke et al., Sci Trans Med 2017 and Goncalves et al., Blood 2017 130:659).
• These data demonstrate that microglial engraftment is faster and greater in recipients of MGTA-456 even after lower dose busulfan conditioning, that microglial engraftment correlates with peripheral blood recovery, and that microglia cells are derived from CD34+CD90+ cells.

“Inherited metabolic disorders are characterized by defective enzyme function in the brains of patients, and engraftment of microglial cells in the brain after transplant is crucial for successful correction of the disease,” said Michael Cooke, Ph.D., chief scientific officer, Magenta Therapeutics. “These preclinical data provide compelling proof of mechanism for potential transformative benefit with MGTA-456 in patients with inherited metabolic disorders.”

**MGTA-456 Contains Large Numbers of Expanded Cord Blood (CB) CD34+CD90+ Hematopoietic Stem Cells (HSC) Which Confer All Engraftment Activity and Correlate with Accelerated Neutrophil Recovery after Myeloablative Conditioning in Patients with Hematologic Malignancy, Abstract #2083**

Key results, presented by Tony Boitano, Ph.D., Magenta Therapeutics:

• To date 41 patients have been treated with MGTA-456 (36 with blood cancers; 5 with inherited metabolic disorders), and all have engrafted at a significantly faster rate than what was seen in historical controls.
• Magenta scientists sought to fully characterize the expanded CD34+ cell fraction of MGTA-456 phenotypically and functionally and identify the cell population that correlates with time to neutrophil recovery.
• MGTA-456 was found to contain large doses of CD34+CD90+ hematopoietic stem cells and progenitors, which are responsible for engraftment in mouse models.
• The dose of CD34+CD90+ cells was also found to have the strongest correlation with faster time to neutrophil recovery in patients.
• Of the 36 patients with blood cancers treated with MGTA-456, 100% of patients engrafted in a median of 14 days, with 67 percent overall survival at 2 years in this high-risk disease setting.

**About Magenta Therapeutics**

Headquartered in Cambridge, Mass., Magenta Therapeutics is a clinical-stage biotechnology company developing novel medicines for patients with autoimmune diseases, blood cancers and genetic diseases. By creating a platform focused on critical areas of unmet need, Magenta Therapeutics is pioneering an integrated approach to allow more patients to receive one-time, curative therapies by making the process more effective, safer and easier.

**Forward-Looking Statement**

This press release may contain forward-looking statements, including express or implied statements regarding Magenta’s future expectations, plans and prospects, including projections regarding future revenues and financing performance, our long-term growth, the anticipated timing of our clinical trials and regulatory filings, the development of our product candidates and advancement of our preclinical programs, as well as other statements containing the words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “project,” “should,” “target,” “will” or “would” and similar expressions that constitute forward-looking statements under the Private Securities Litigation Reform Act of 1995. Although Magenta’s forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Magenta. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Magenta’s programs and operations are described in additional detail in its registration statement on Form S-1, its Quarterly Report on Form 10-Q and its other filings made with the Securities and Exchange Commission from time to time. Any forward-looking statement made in this press release speaks only as of the date on which it is made. Magenta undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise.

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