



Magenta Therapeutics Presents Clinical and Preclinical Data on MGTA-456 Cell Therapy in Best Abstracts Sessions at Transplant and Cellular Therapy (TCT) Annual Meeting

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-- Additional follow-up on patients with cerebral adrenoleukodystrophy (cALD) treated with MGTA-456 in Phase 2 study in inherited metabolic disorders (IMDs) shows persistent resolution of brain inflammation on MRI and stable Loes disease scores --

-- Additional follow-up on patients with Hurler syndrome treated with MGTA-456 in Phase 2 IMD study shows correction of enzyme deficiency and decrease in toxic metabolites --

--Three presentations highlighted by TCT among best abstracts and best pediatric abstracts --

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 25, 2019-- [Magenta Therapeutics](#) (NASDAQ:MGTA), a clinical-stage biotechnology company developing novel medicines to bring the curative power of stem cell transplant to more patients, today announced that the Company presented Phase 2 clinical data and preclinical research on its MGTA-456 program at the TCT annual meeting.

MGTA-456 is a cell therapy designed to provide a high dose of hematopoietic stem cells that are well-matched to the patient. The Company plans to enroll 12 patients in the ongoing Phase 2 study in inherited metabolic disorders, which include cALD, metachromatic leukodystrophy and globoid cell leukodystrophy. The study previously enrolled patients with Hurler syndrome. The primary endpoint of the study is engraftment after transplantation. Both short- and long-term disease specific outcomes are also being collected. Data from the first five evaluable patients treated in this study were highlighted in an oral presentation in the Pediatric Best Abstracts Session by Paul Orchard, M.D., Medical Director, Inherited Metabolic & Storage Disease Bone Marrow Transplantation Program, University of Minnesota.

In a separate oral presentation in the Best Pediatric Abstracts Session, Kevin Goncalves, Ph.D., Magenta Therapeutics, highlighted data demonstrating that the high stem cell doses in MGTA-456 accelerate and improve engraftment of human microglia in the brains of transplanted mice. Tony Boitano, Ph.D., Magenta Therapeutics, presented a third data set in the TCT Meeting Best Abstracts session demonstrating that MGTA-456 contains large doses of the stem cells responsible for engraftment, which are also correlated with rapid neutrophil recovery in patients following transplant.

"Inherited metabolic disorders are rare diseases that cause progressive damage to multiple organs, including the brain, and are often fatal. Stem cell transplant is the only disease-modifying treatment option but delivering sufficient doses of stem cells has been a persistent challenge," said John Davis, M.D., M.P.H., chief medical officer, Magenta Therapeutics. "MGTA-456 provides patients with a large number of stem cells to help overcome these challenges, and we are pleased that all five evaluable patients treated with MGTA-456 thus far have met the primary endpoints with robust and consistent engraftment. Further, in patients with Hurler syndrome, the production of normal levels of enzyme was associated with reduction in toxic disease-related metabolites. In patients with cALD, we have seen persistent decrease in brain inflammation as measured by imaging. These are early signs that MGTA-456 may provide disease-modifying clinical benefit to these patients."

Robust Engraftment with MGTA-456, a CD34+ Expanded Cell Therapy Product in Patients with Inherited Metabolic Disorders (IMD): Preliminary Phase 2 Trial Results

Key results, as of January 30th, 2019, presented by Paul Orchard, M.D., University of Minnesota:

Transplant success outcomes:

- Five of five evaluable 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.

Early evidence of disease benefit:

- The two patients with cALD showed resolution of gadolinium enhancement on MRI, an indicator of brain inflammation, by day 28 post-transplant, and the resolution persisted at the most recent patient visits (Day 180 post-transplant and Day 100 post-transplant, respectively).
 - Durable resolution of gadolinium enhancement is correlated with long-term disease benefit in patients with cALD.
- The Loes score, a method for quantifying the severity of brain abnormalities and atrophy found on MRI, remained stable in both patients as of the most recent patient visits.
- Patients with Hurler syndrome achieved normal levels of blood leukocyte IDUA enzyme, the enzyme that is deficient in untreated patients with Hurler syndrome. This suggests that transplant with MGTA-456 is beginning to affect the disease in these patients.
 - Normalization of blood leukocyte IDUA enzyme after transplant has been significantly associated with improvement in disease.

- Patients with Hurler syndrome showed a marked decline in urine total glycosaminoglycan (GAG) levels as of the Day 100 post-transplant patient visit. This 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 with High Doses of CD34+ CD90+ Cells, Enhances Speed and Level of Human Microglia Engraftment in the Brains of NSG Mice

Key results presented by Kevin Goncalves, Ph.D., Magenta Therapeutics:

- Stem cell transplant is a standard of care in inherited metabolic disorders, and engraftment of microglial cells, which produce the deficient enzyme in the brain, after transplant is crucial for successful outcomes in patients.
- 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 controls ($p < 0.001$, $n = 8$ 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 in preclinical models 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.

MGTA-456 Contains Large Numbers of CD34+CD90+ Hematopoietic Stem Cells Which Contain the NSG Engraftment Activity and Correlate with Time to Neutrophil Recovery Following Transplant into Patients with Hematologic Malignancy

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

- To date 41 evaluable 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 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 successful 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.
- A Phase 2 study of MGTA-456 in patients with blood cancers is ongoing at the University of Minnesota.

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

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