Magenta Conditioning Lead Clinical Candidate MGTA-117 Demonstrates Broad Tolerability and High Therapeutic Index in Non-human Primates

February 24, 2020

– MGTA-117 ADC clinical candidate for conditioning showed broad tolerability and wide pre-clinical safety margins –
– MGTA-117 demonstrated robust anti-tumor activity in xenograft models from patients with refractory leukemia –
– Magenta plans to move MGTA-117 into the clinic with initial clinical data in 2021 –
– Landmark data with tool CD117-ADC demonstrate first successful gene therapy transplant without chemotherapy in non-human primates, awarded Best Oral Abstract by TCT –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 24, 2020--

Magenta Therapeutics (NASDAQ: MGTA), a clinical-stage biotechnology company developing novel medicines to bring the curative power of immune reset to more patients, today announced data from its newest clinical development candidate for conditioning, MGTA-117, at the Transplant and Cellular Therapy (TCT) Annual Meeting in Orlando, Florida. The company also announced additional results with a tool CD117-ADC molecule, which were recognized by TCT with an award for Best Oral Abstract.

Magenta has created a new stem cell biology discovery platform to harness the curative power of immune reset through stem cell transplant for more patients, and is developing a comprehensive portfolio of novel therapeutics to allow more patients to benefit through a more precise stem cell transplant process. This portfolio includes targeted, disease-modifying antibody drug conjugates (ADCs), such as MGTA-117, that are designed to precisely and rapidly remove the disease-causing cells in the body and enable immune system reset and long-term engraftment without the need for chemotherapy or radiation. MGTA-117, a CD117-targeted antibody engineered for the transplant setting and conjugated to amanitin, is an antibody drug conjugate being developed for patients undergoing immune reset through either autologous or allogeneic stem cell transplant. MGTA-117 precisely depletes hematopoietic stem and progenitor cells. It was developed under a partnership with Heidelberg Pharma that grants Magenta exclusive worldwide development and marketing rights for ADCs using an amanitin payload and targeting CD117.

“There is a significant opportunity to allow more patients to benefit from immune reset through stem cell transplant with novel, targeted medicines for conditioning. We are excited to present the first results from our MGTA-117 clinical candidate for targeted patient preparation for stem cell transplant or gene therapy. These new data highlight the potency, safety and broad pre-clinical therapeutic index of 30 fold of MGTA-117. We believe that MGTA-117 is the optimal agent for depleting stem cells to enable safe immune reset, and we look forward to moving this product candidate into the clinic, with initial clinical data expected in 2021,” said John Davis, M.D., M.P.H., Chief Medical Officer, Magenta. “The additional impressive results with the tool CD117-ADC in the NIH gene therapy study provide further validation of the safety and potency of the ADC approach and underscore Magenta’s leadership in the field of conditioning.”

Magenta is scaling up manufacturing of MGTA-117 and completing IND-enabling studies in 2020. The Company intends to move this new product candidate into the clinic with initial clinical data in 2021.

MGTA-117 ADC Clinical Candidate for Pre-Transplant Conditioning

Magenta presented new data at TCT demonstrating that MGTA-117, with its optimized linker-payload, potently depleted stem and progenitor cells with an improved therapeutic index over prior molecules: potency ratio of 30 fold (therapeutic index; typical range for approved ADCs at this stage is two to six fold). The antibody in use remains unchanged from prior molecules, and both the antibody and linker-payload are advancing in GMP manufacture.

Title: A Non-Genotoxic Anti-CD117 Antibody Drug Conjugate (ADC) Designed for Patient Conditioning Prior to Stem Cell Transplant and HSC-Based Gene Therapy Has a Broad Therapeutic Window across Species (Abstract #44)

Presenter: Bradley Pearse, Ph.D., Magenta Therapeutics

Results:

- MGTA-117 is an ADC purposefully designed with:
  - High selectivity and potency against CD117-expressing hematopoietic stem cells (HSCs) and disease-causing cells
  - Short half-life following target cell depletion, with clearance appropriate for the transplant setting
  - Effector function modified to focus therapeutic impact of payload delivery
  - A linker-payload optimized for tolerability while maintaining potency and stability
- MGTA-117 exhibited a broad therapeutic dose range across mouse and primate models and thus could have broad applications in stem cell transplant for malignant and non-malignant diseases.
- MGTA-117 demonstrated potent cytotoxicity on target disease-causing CD117+ cells and robust anti-tumor activity in xenograft models of acute myeloid leukemia.
- These results show that ADC-based conditioning for precise depletion of disease-causing cells may represent an improved approach to allow more patients to benefit from a potentially curative stem cell transplant.

First-Ever CD117-ADC Transplant in Non-human Primates

The results with MGTA-117 build on additional data presented at TCT with a tool CD117-ADC molecule. This study showed the first-ever successful transplant of gene-modified cells in non-human primates using a tool CD117-targeted, single-agent ADC, without the use of chemotherapy or

radiation. These data were awarded Best Oral Abstract by TCT.

Title: A Single Dose of CD117 Antibody Drug Conjugate Enables Autologous Gene-Modified Hematopoietic Stem Cell Transplant (Gene Therapy) in Nonhuman Primates (Abstract #5)

Presenter: Naoya Uchida, M.D., Ph.D., Cellular and Molecular Therapeutics Branch; National Heart, Lung, and Blood Institute; National Institutes of Health

Results:

- A single dose of a tool CD117-ADC fully depleted human HSCs in humanized mouse models.
- A single dose of CD117-ADC selectively depleted HSCs in non-human primates while sparing immune cells, which are important for recovery following transplant.
- CD117-ADC was engineered to have a short half-life to clear the body quickly and enabled transplant of the gene-modified cells within days of dosing in non-human primates.
- A single dose of CD117-ADC in non-human primates enabled successful transplant and long-term engraftment of HSCs modified with a lentiviral vector encoding the β-globin gene, the gene that causes sickle cell disease and β-thalassemia.
- CD117-ADC was well tolerated in non-human primates with no evidence of the often severe side effects seen with busulfan conditioning, including veno-occlusive disease, weight loss, diarrhea, mucositis, vomiting, pulmonary fibrosis or seizures.
- These proof-of-concept studies validate the use of CD117-ADC for targeted stem cell depletion prior to transplant and support its use as a new conditioning agent for gene therapy and stem cell transplant without toxic chemotherapy or radiation.

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 and information within the meaning of The Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “will,” “could”, “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “seeks,” “endeavor,” “potential,” “continue” or the negative of such words or other similar expressions can be used to identify forward-looking statements. The express or implied forward-looking statements included in this press release are only predictions and are subject to a number of risks, uncertainties and assumptions, including, without limitation risks set forth under the caption “Risk Factors” in Magenta’s Registration Statement on Form S-1, as updated by Magenta’s most recent Quarterly Report on Form 10-Q and its other filings with the Securities and Exchange Commission. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this press release may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although Magenta believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, except as required by law, neither Magenta nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements included in this press release. Any forward-looking statement included in this press release speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

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