# Magenta Therapeutics Presents Preclinical Data on Targeted Non-Genotoxic Conditioning Programs Demonstrating Potent Stem Cell Depletion and Anti-Leukemia Survival Benefit

December 3, 2018

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 preclinical research on its targeted conditioning programs at the 60th annual meeting of the American Society of Hematology (ASH).

Patients undergoing bone marrow transplant or stem cell gene therapy are first prepared, or conditioned, with non-specific, genotoxic chemotherapy alone or in combination with total body irradiation. This conditioning process is associated with significant toxicity, including development of cancers, infertility, organ toxicities, or even death. As a result, many patients do not consider undergoing a bone marrow transplant or gene therapy. Magenta is developing a portfolio of targeted antibody drug conjugates (ADCs), including non-genotoxic agents, that selectively remove the specific cells to enable a successful transplant or gene therapy procedure.

“This year’s five ASH data presentations from our portfolio of targeted conditioning programs give further insight into our progress in addressing one of the major challenges of the transplant and gene therapy process: the genotoxic conditioning that leaves patients infertile and puts them at risk for malignancies and organ toxicity,” said Michael Cooke, Ph.D., chief scientific officer, Magenta Therapeutics. “Our most advanced targeted conditioning program, C200, is focused on ADCs directed at CD117, a target expressed on stem cells and many types of leukemia cells. Preclinical data at ASH this year show potent and selective depletion of human and non-human primate stem cells with our non-genotoxic CD117 ADC conjugated to amanitin. In addition, both this ADC and our CD45-targeted ADC from our C100 program demonstrated the additional benefit of anti-leukemia activity and survival advantage in patient-derived leukemia models. Based on these promising data, we are finalizing the CD117 and CD45 ADCs, and we expect to select a lead for development for the CD117 program to launch IND-enabling studies in 2019.”

***CD117-Amanitin Antibody Drug Conjugates Effectively Deplete Human and Non-Human Primate HSCs: Proof of Concept as a Targeted Strategy for Conditioning Patients for Bone Marrow Transplant, Abstract #3314***

Key results, presented by Brad Pearse, Ph.D., Magenta Therapeutics:

- An anti-CD117 ADC conjugated with amanitin potently depleted human and non-human primate hematopoietic stem cells and progenitors *in vivo*.
- An anti-CD117 amanitin ADC with engineered fast half-life showed potent stem cell depletion and rapid clearance, providing appropriate pharmacokinetics for patient preparation for bone marrow transplant.
- The ADCs were well tolerated at the efficacious doses.
- Potent and selective depletion of stem cells with rapid clearance of the ADC could provide a significant improvement over current approaches to patient preparation with an acceptable safety profile prior to BMT for malignancies, autoimmune diseases and gene therapies, broadening patient access to these potentially curative therapies.
- Magenta will next finalize the linker-toxin construct and select a lead for development in 2018, then begin IND-enabling studies in 2019.

***Single Doses of Antibody Drug Conjugates (ADCs) Targeted to CD117 or CD45 Have Potent In Vivo Anti-Leukemia Activity and Survival Benefit in Patient-Derived AML Models, Abstract #3316***

Key results, presented by Jennifer Proctor, Magenta Therapeutics:

- CD117 is expressed on human hematopoietic stem and progenitor cells and on leukemia cells in 80% of patients with acute myeloid leukemia (AML) and in 65% of patients with myelodysplastic syndromes (MDS); CD45 is expressed on all lympho-hematopoietic cells and in nearly all blood cancers, other than multiple myeloma.
- Both the anti-CD117 amanitin ADC (C200 program) and the anti-CD45 amanitin ADC (C100 program) showed potent killing of human hematopoietic stem cells and human leukemia cell lines expressing these targets *in vitro*.
- A single dose of either ADC showed potent *in vivo* anti-leukemia activity in mice bearing established human leukemia cell lines.
- Both ADCs also significantly improved the survival of mice engrafted with human leukemia cells from AML patients, including leukemias that were resistant to multiple lines of therapy including previous allogeneic bone marrow transplant.
- Magenta Therapeutics’ C200 and C100 programs are designed with the dual intent of selectively eliminating the necessary cells to enable a successful transplant and reducing disease burden in patients with active disease or in patients who are at high risk of disease relapse.
- Magenta will next finalize the linker-toxin constructs, select anti-CD117 and anti-CD45 leads for development and continue to progress ADC-based conditioning approaches targeting CD45 and CD117 toward clinical development.

***Antibody Drug Conjugates Targeted to CD45 or CD117 Enable Allogeneic Hematopoietic Stem Cell Transplantation in Animal Models, Abstract #3324***

Key results, presented by Sharon Hyzy, M.S., Magenta Therapeutics:

- ADCs targeted to mouse CD45 or mouse CD117 have been shown to effectively condition immunocompetent mice for autologous bone marrow transplant.
- To investigate the utility of these murine-specific tool ADCs conjugated to saporin to enable allogenic transplant, Magenta assessed these ADCs as single agents or in combination with immunosuppressive agents to facilitate transplant in a murine allogeneic transplant model.
- Both anti-CD45 and anti-CD117 saporin ADCs, when combined with additional immunosuppressants, enabled successful minor mismatch whole bone marrow transplants in mouse models.
- Conditioning with the anti-CD45 saporin ADC plus post-transplant cyclophosphamide to prevent graft vs. host disease enabled successful engraftment across minor histocompatibility antigens.
- The ADCs were more effective than an unconjugated anti-CD45 antibody, pre-transplant cyclophosphamide, or sublethal irradiation in combination with post-transplant cyclophosphamide.
- Magenta will next investigate other linker-toxins as well as ADC-based conditioning in various allogeneic mouse models.

***Non-genotoxic conditioning facilitates robust HSPC engraftment and multi-lineage development in a dose dependent manner in Fanconi anemia, Abstract #2041***

Key results, presented by Meera Srikanthan, Ph.D., Fred Hutchinson Cancer Research Center:

- Conditioning with genotoxic chemotherapy in patients with Fanconi anemia is currently utilized to open the bone marrow niche prior to infusion of hematopoietic stem cells in a bone marrow transplant but is often associated with genotoxic effects.
- ADCs targeting hematopoietic stem cells are an emerging non-genotoxic method of conditioning, particularly in diseases associated with DNA damage and cancer predisposition, such as Fanconi anemia.
- Researchers at the Fred Hutchinson Cancer Research Center sought to study the application of non-genotoxic ADC-based conditioning targeting hematopoietic stem cells to eliminate leukemogenic host HSCs and to facilitate the engraftment of donor cells.
- Results showed that the immunotoxin-based conditioning drugs from Magenta are of similar if not superior efficacy compared to cyclophosphamide, facilitating multi-lineage engraftment of autologous stem cells, as would be used in gene therapy.
- Researchers at the Fred Hutchinson Cancer Research Center will next determine whether immunotoxin conditioning facilitates engraftment of gene-modified stem cells using FancA (-/-) mice and optimize dosing of immunotoxin platform to completely eliminate host hematopoiesis in order to decrease the risk of leukemogenesis.

***Targeting CD45 with an Amanitin Antibody-Drug Conjugate Effectively Depletes Human HSCs and Immune Cells for Transplant Conditioning, Abstract #4526***

Key results will be presented by Rahul Palchaudhuri, Ph.D., Magenta Therapeutics, on Monday, December 3, 2018.

- A human/primate cross-reactive anti-CD45 amanitin ADC potently depletes human hematopoietic stem cells and immune cells in culture.
- The anti-CD45 ADC achieved efficient depletion of immune cells in the periphery and hematopoietic stem cells in the bone marrow of humanized mice.
- Simultaneous depletion of immune and hematopoietic stem cells using an anti-CD45 ADC may enable safer conditioning for allogeneic transplant and enable immune-reset in autoimmune disease transplantation.
- Magenta plans to optimize the anti-CD45 ADC and select a development candidate in 2019, with IND-enabling studies to begin in 2020.

**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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