



Magenta Therapeutics Presents Preclinical Data on Targeted Non-Genotoxic Conditioning Programs, Including First Conditioning Development Candidate

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-- Data in non-human primates from C100 program show potent stem and immune cell depletion with anti-CD45 amanitin ADC that is well tolerated at efficacious doses --

-- C200 development candidate, anti-CD117 amanitin ADC, showed potent and selective stem cell depletion and immune system preservation in non-human primates and was well tolerated --

-- Additional poster highlights preclinical data on anti-leukemia survival benefit with C100 and C200 targeted conditioning programs --

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 highlighted preclinical research on its targeted conditioning programs in four presentations and posters at the Transplant and Cellular Therapy (TCT) annual meeting.

Patients currently undergoing stem cell 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 process is associated with significant side effects, including infertility and mortality risks, which can prevent many eligible patients from undergoing a stem cell 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 needed to enable a successful transplant or gene therapy procedure without the toxicities of chemotherapy and radiation. Magenta's C100 program targets CD45, expressed on both stem and immune cells, with the goal of enabling stem cell transplant in blood cancer and autoimmune diseases. Magenta's C200 program targets CD117, expressed on stem cells, with potential applicability as a conditioning agent before gene therapy for genetic diseases and stem cell transplant for blood cancers.

"Stem cell transplant and gene therapy are potential cures for many diseases, including sickle cell disease, blood cancers, and autoimmune diseases, such as multiple sclerosis and systemic sclerosis. However, the toxicity of the current conditioning regimens prevents a significant percentage of patients from considering a transplant or gene therapy and requires the patients who do undergo the procedure to trade their disease for the prospect of infertility, organ damage, secondary cancers and even death," said Michael Cooke, Ph.D., Chief Scientific Officer, Magenta Therapeutics. "Data in non-human primates from Magenta's two distinct lead conditioning programs show potent and selective depletion of the target cells, and the ADCs were well tolerated. Based on these promising data, we selected a development candidate for the C200 program and have moved into IND-enabling studies. We expect to declare a candidate for the C100 program this year and move into IND-enabling studies in 2020."

Non-Genotoxic Conditioning Using Amanitin Antibody-Drug Conjugates Targeting CD45 Effectively Deplete Human and Non-Human Primate Hematopoietic Stem Cells and Immune Cells (C100 Program)

Key results, presented by Rahul Palchadhuri, Ph.D., Magenta Therapeutics:

- A single dose of an anti-CD45 ADC achieved efficient depletion of immune cells in the periphery and hematopoietic stem cells in the bone marrow in preclinical models.
- An anti-CD45 amanitin ADC with engineered fast half-life demonstrated potent depletion of peripheral immune cells as well as immune cells and hematopoietic stem cells in the bone marrow of non-human primates.
- An anti-CD45 amanitin ADC with engineered fast half-life demonstrated potent stem and immune cell depletion and rapid clearance, providing optimal pharmacokinetics for patient preparation for stem cell transplant.
- These ADCs were well tolerated at the efficacious doses.
- Simultaneous depletion of immune and hematopoietic stem cells using an anti-CD45 ADC with rapid clearance may enable safer conditioning for allogeneic transplant and enable an immune-reset in autoimmune disease transplantation, broadening patient access to this potentially curative therapy.
- Magenta plans to optimize the anti-CD45 ADC and select a development candidate in 2019, with IND-enabling studies to begin in 2020.
 - Magenta is testing anti-CD45 ADCs in preclinical models of autoimmune disease, with data expected later in 2019.

A CD117-Amanitin Antibody Drug Conjugate Effectively Depletes Human and Non-Human Primate Hematopoietic Stem and Progenitor Cells: Targeted Non-Genotoxic Conditioning for Bone Marrow Transplant (C200 Program)

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

- An anti-CD117 ADC conjugated with amanitin potently depleted both human and non-human primate hematopoietic stem cells and progenitors *in vivo*.
- An anti-CD117 amanitin ADC with engineered fast half-life demonstrated potent stem cell depletion and rapid clearance, representing optimal pharmacokinetics and pharmacodynamics for patient preparation for stem cell transplant or gene therapy.

- The ADCs were well tolerated at the efficacious doses.
- Potent and selective depletion of stem cells with rapid clearance of the ADC has the potential to provide a significant improvement over current approaches to patient preparation prior to stem cell transplant and gene therapies, broadening patient access to curative therapies.
- Magenta has declared a lead for development for the C200 program and moved into IND-enabling studies.
 - Magenta is undertaking studies of C200 in preclinical models for gene therapy conditioning, with data expected later this year.

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

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 in many blood cancers.
- Both the anti-CD117 amanitin ADC and the anti-CD45 amanitin ADC demonstrated potent killing of human hematopoietic stem cells and leukemia cell lines *in vitro*.
- A single dose of either ADC demonstrated potent *in vivo* anti-leukemia activity in mice bearing established human leukemia cell lines.
- Both ADCs significantly improved the survival of mice engrafted with human leukemia cells from AML patients, which included leukemias that were resistant to multiple lines of therapy.
- 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.
- Magenta continues to progress ADC-based conditioning approaches targeting CD45 and CD117 toward the clinic.

CD45-Targeted Antibody-Drug Conjugate Plus Post-Transplant Cytosan is Sufficient to Enable Allogeneic Bone Marrow Transplant in a Minor Mismatch Mouse Model (C100 Program)

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

- ADCs targeted to mouse CD45 have been shown to effectively condition immunocompetent mice for autologous stem cell transplant.
- To investigate the utility of a murine-specific tool ADC conjugated to saporin to enable allogeneic transplant, Magenta assessed this ADC as a single agent or in combination with immunosuppressive agents to facilitate transplant in a murine allogeneic transplant model.
- A single dose of anti-CD45 saporin ADC, when combined with post-transplant cyclophosphamide to prevent graft-versus-host-disease, enabled successful engraftment across minor histocompatibility antigens.
- The anti-CD45 saporin ADC was more effective than an unconjugated anti-CD45 antibody, pre-transplant cyclophosphamide, or sublethal irradiation in combination with post-transplant cyclophosphamide.
- Magenta continues to investigate additional linker-toxins as well as ADC-based conditioning in multiple allogeneic mouse models.

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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