Magenta Therapeutics Presents Positive MGTA-117 Clinical Data at the American Society of Hematology (ASH) Annual Meeting and Provides Program Updates

December 12, 2022

– MGTA-117 preliminary clinical results from 15 patients across three dose-escalation cohorts of the ongoing Phase 1/2 clinical trial shows single-agent activity with no dose-limiting toxicities; transition to patients with transplant-eligible AML/MDS expected in H1 2023 pending regulatory alignment –

– CD45 antibody-drug conjugate (CD45-ADC) IND-enabling studies are advancing –

– MGTA-145 clinical trial for stem cell mobilization in sickle cell disease patients is progressing with data now expected to be shared H1 2023 –

– Conference call and webcast scheduled for 8:30am ET / 7:30am CT on December 13, 2022 –

CAMBRIDGE, Mass., Dec. 12, 2022 (GLOBE NEWSWIRE) -- Magenta Therapeutics (Nasdaq: MGTA), a clinical-stage biotechnology company developing novel medicines designed to bring the curative power of stem cell transplant to more patients, highlights updated clinical data from the ongoing MGTA-117 Phase 1/2 dose-escalation clinical trial made in an oral presentation today at the American Society of Hematology 2022 Annual (ASH) Meeting in New Orleans and provides program updates across the portfolio.

"We have shown that a single dose of MGTA-117 binds target cells, depletes target cells, clears the body quickly as designed, and does so with a favorable tolerability profile in our ongoing Phase 1/2 clinical trial. We believe that these positive clinical data establishes proof-of-mechanism, and that we have reached an active dose. Target cell depletion is a critical measurement of success for MGTA-117, and we are encouraged by the levels of depletion we have observed in both the blood and the bone marrow of relapsed/refractory acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patients. We are excited about our planned next steps to take MGTA-117 into transplant-eligible AML and MDS patients as well as into patients who are receiving gene therapy. We are thankful to all of the patients and families who have participated in our trial to date as well as our investigators and the clinical site staff, all of whom have contributed greatly to the advancement of MGTA-117 for patients," said Jason Gardner, President and Chief Executive Officer of Magenta Therapeutics. "Together with the progress we are making on CD45-ADC and MGTA-145, we are pleased with the momentum across our portfolio and the multiple anticipated inflection points for Magenta in the coming year."

MGTA-117 Clinical Data and Continued Development
MGTA-117 is Magenta's most advanced targeted conditioning product candidate designed to deplete CD117-expressing target cells in the blood and/or bone marrow prior to a patient undergoing stem cell transplant or receiving an ex vivo gene therapy product. MGTA-117 is an anti-CD117 antibody conjugated to an amanitin payload. CD117, also known as c-Kit receptor, is highly expressed on hematopoietic stem cells, progenitor cells and cancer blast cells.

Current Phase 1/2 Patient Population and Potential Significance for Clinical Development
The ongoing Phase 1/2 clinical trial is in relapsed/refractory (R/R) AML and MDS. These patients are deemed ineligible for transplant due to active disease characterized by high numbers of cancer blast cells present in the bone marrow and in the bloodstream. Over 80% of patients with AML and MDS express the CD117 receptor on the surface of their cancer cells. In these patients, CD117+ target cells are a combination of cancer blast cells in the blood and bone marrow and non-malignant stem and progenitor cells in the bone marrow. MGTA-117 is designed to target all of these cells, and clinical evidence of depletion in this patient population provides valuable support that MGTA-117 will robustly deplete target cells in the proposed next phase of development in (i) transplant-eligible AML and MDS patients who have significantly lower numbers of cancer blast cells and (ii) gene therapy patients who have no cancer blast cells. Therefore, Magenta expects MGTA-117 to bind and deplete target cells in the bone marrow in these patient populations, and potentially achieve greater levels of depletion, at the same dose levels studied in R/R AML and MDS patients.

MGTA-117 Proof-of-Mechanism and Potential Active Dose

- *Participants Dosed & Available Data*. As of December 1, 2022, a total of 15 participants have been dosed with MGTA-117 in Cohorts 1, 2 and 3. All dosed participants contributed data in whole or in part to the preliminary data set depending on an individual's availability for collecting assessments. Eleven of the 15 dosed participants completed the dose-limiting toxicity safety observation period of 21 days. None of the four participant discontinuations were deemed to be related to MGTA-117.

- *Target Cell Binding*. MGTA-117 bound to CD117-expressing target cells within 15 minutes after dosing in all participants as measured by a receptor occupancy (RO) assay. RO increased with higher dose levels of MGTA-117. The percentage of occupied CD117 receptors was greater, and the receptor occupancy was more durable at the higher dose levels of Cohorts 2 and 3 as compared to Cohort 1 as expected.

- *Target Cell Depletion*.
    - *Depletion in Blood and Bone Marrow*. MGTA-117 showed greater depletion of target cancer blast cells in the blood of participants in Cohorts 2 and 3 compared to Cohort 1. In addition, three out of the four participants in Cohort 3 for whom paired bone marrow samples were collected at baseline and post-dosing had depletion of cancer blast cells in both blood and bone marrow. This matched depletion response in the blood and bone marrow provides evidence of an active dose and dose-dependent depletion of CD117-expressing cells.

- *Two Transplant-Ineligible Participants Became Transplant-Eligible*. Participants entering the clinical trial were considered ineligible for stem cell transplant and had active and persistent AML/MDS after receiving one or more anti-leukemic therapies. One relapsed/refractory MDS participant in Cohort 3 had a reduction of bone marrow cancer blast cells to a level that enabled the participant to become eligible for transplant. This is the trial's second participant who became eligible for transplant after a single dose of MGTA-117. The first participant, from Cohort 1, had relapsed/refractory AML and was previously disclosed.

- *Clearance*. MGTA-117 was shown to be rapidly cleared from the body as expected. No MGTA-117 was detectable in the blood 48 hours after dosing in Cohorts 1 and 2, and over 95% of MGTA-117 was cleared in the blood 48 hours after dosing at the higher dose level of Cohort 3. Rapid clearance of MGTA-117 was engineered into the molecule to ensure avoidance of depleting newly transplanted donor cells in allogeneic transplant or, in the case of gene therapy, of autologous gene-modified cells. In addition, the MGTA-117 ADC was shown to be stable in blood over time in all participants, and no free payload was detectable in the blood of any participants at any time point.

- *Tolerability*. MGTA-117 was well-tolerated in all participants. No serious adverse events were deemed to be related to MGTA-117, and no dose-limiting toxicities were observed. Treatment-related adverse events deemed to be related to MGTA-117 were low-grade liver enzyme elevations, low-grade fever, and grade 3 and grade 4 leukopenia in two participants who had baseline grade 2 and grade 3 leukopenia, respectively. All instances of observed liver enzyme elevations were low-grade, transient and resolved without intervention, as expected.

- *Continued Trial Progress and Data Expectations*. The Phase 1/2 clinical trial is currently enrolling in Cohort 4 (0.13 mg/kg) and Magenta anticipates presenting aggregate clinical data from the clinical trial, including Cohort 4, at a scientific conference in Q1 2023.

MGTA-117 Regulatory Engagement and Clinical Development Next Steps in Transplant-Eligible AML/MDS and Autologous Gene Therapy
As previously disclosed, Magenta has initiated formal engagements with regulatory agencies to transition MGTA-117 into a transplant-eligible AML and MDS patient population. Magenta also plans to engage regulators in H1 2023 for the purposes of initiating a MGTA-117 clinical trial in autologous *ex vivo* gene therapy.

- *Transplant-Eligible AML and MDS*. Magenta anticipates that MGTA-117's pharmacokinetics (PK), pharmacodynamics (PD) and tolerability in Cohorts 1-3 will support alignment with regulatory authorities to study MGTA-117 in AML and MDS transplant-eligible patients. Importantly, the proposed study design in the transplant setting will allow for the measurement of depletion of CD117-expressing cells in the bone marrow after a single dose of MGTA-117 prior to reduced-intensity conditioning (RIC) and the ensuing allogeneic transplant. By depleting residual cancer blast cells prior to a standard RIC regimen, MGTA-117 has the potential to boost disease control prior to transplant and improve disease outcomes post-transplant. These potential positive outcomes could address the current significant unmet need associated with RIC-conditioning where AML and MDS patients relapse at a rate of 40%-50% within six months post-transplant[1]. Pending regulatory alignment, Magenta plans to share additional details of the proposed transplant-eligible MGTA-117 study design in Q1 2023.

- *Gene Therapy*. Magenta expects to use the clinical data package from the ongoing Phase 1/2 trial, together with supporting insights from PK/PD modeling, to engage with regulators on a potential MGTA-117 clinical trial in autologous *ex vivo* gene therapy. In a gene therapy clinical trial, Magenta anticipates dosing patients with MGTA-117 to deplete stem and progenitor cells before the patient receives an infusion of gene-modified stem cells, with a goal of replacing the current standard-of-care conditioning that relies on high doses of chemotherapeutic agents such as busulfan, which is known to be carcinogenic. Magenta anticipates sharing more details in 2023 as development plans progress in collaboration with gene therapy partners. Magenta has existing clinical collaborations with gene therapy companies and anticipates entering into additional collaborations as MGTA-117 development advances.

CD45-ADC IND-Enabling Plans
Magenta's CD45-ADC is a second targeted conditioning ADC, designed to selectively target and deplete both stem cells and immune cells, and is intended to replace the use of chemotherapy-based conditioning prior to stem cell transplant in patients with blood cancers and autoimmune diseases.

- As previously disclosed, Good Manufacturing Practice (GMP) manufacturing and other investigative new drug application (IND)-enabling activities are ongoing for the CD45-ADC program. A Good Laboratory Practice (GLP) toxicology study is expected to be completed in H2 2023.

- Magenta anticipates regulatory interactions prior to filing an IND and anticipates providing further details on the CD45-ADC program in 2023, including molecule design, key preclinical data, and timelines to IND.

MGTA-145 Phase 2 Progress
Magenta is developing MGTA-145, in combination with plerixafor, to improve the process by which stem cells are released out of the bone marrow and

into the bloodstream, known as stem cell mobilization. The mobilized cells are then collected and available for transplant. This is the first step for patients and is required for the majority of transplants and stem cell gene therapies.

- Magenta, in partnership with bluebird bio, is enrolling patients in a Phase 2 clinical trial evaluating the ability of MGTA-145 in combination with plerixafor to mobilize stem cells for collection in patients with sickle cell disease.

- Due to enrollment delays at the clinical sites that are unrelated to MGTA-145, Magenta anticipates disclosing clinical data in H1 2023.

Conference Call Information:
Magenta will host a conference call and webcast at 8:30 a.m. Eastern Time / 7:30 a.m. Central Time tomorrow, Tuesday, December 13, 2022 to review the MGTA-117 data presented at the 2022 ASH Annual Meeting.

To access the conference call, please register online at https://register.vevent.com/register/BI872661cff05d4191a7bb100830aae147. Upon registering, each participant will be provided with call details and a conference ID. The live webcast of the call and slide deck may be accessed at https://edge.media-server.com/mmc/p/hk2eojv2, or by visiting the Investors & Media section of the company's website at https://investor.magentatx.com. A replay of the webcast will be available shortly after the conclusion of the call and will be archived on the Events & Presentations page.

[1] Scott, Journal of Clinical Oncology 2017. https://pubmed.ncbi.nlm.nih.gov/28380315/

About Magenta Therapeutics
Magenta Therapeutics is a clinical-stage biotechnology company developing medicines designed to bring the curative power of stem cell transplant to more patients with blood cancers, genetic diseases and autoimmune diseases. Magenta is combining leadership in stem cell biology and biotherapeutics development with clinical and regulatory expertise to revolutionize blood and immune reset to allow more patients to take advantage of the curative potential of stem cell transplant and potentially improve eligibility for future gene therapies.

Magenta is based in Cambridge, Mass. For more information, please visit www.magentatx.com.

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Forward-Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, as amended. These statements include, without limitation, implied and express statements relating to: Magenta's future business expectations, plans and prospects; the potential of, and expectations for, Magenta's product candidate pipeline; proposed study designs; potential collaborations with other companies; the potential benefits and expected performance of Magenta's product candidates and programs; the development of product candidates and advancement of preclinical and clinical programs, including, without limitation, patient enrollment; expectations, plans and timing for preclinical activities, clinical trials and related results involving Magenta's product candidates; expectations, plans and timing for the generation, receipt and disclosure of preclinical and clinical trial data, toxicology results, and other results involving Magenta's product candidates; timing for the disclosure of developmental timelines, developmental plans and program updates regarding Magenta's product candidates; the completion of dose-limiting toxicity observation periods; regulatory interactions and alignment with regulators; the use of clinical data and supporting insights from PK/PD modeling in regulatory engagement and advancement into transplant eligible AML and MDS patients and gene therapy patients; that MGTA-117's pharmacokinetics (PK), pharmacodynamics (PD) and tolerability in Cohorts 1-3 will support alignment with regulatory authorities to study MGTA-117 in AML and MDS transplant-eligible patients; that clinical evidence of depletion in the AML and MDS patient population provides valuable support that MGTA-117 will robustly deplete target cells in the proposed next phase of development in (i) transplant-eligible AML and MDS patients who have significantly lower numbers of cancer blast cells and (ii) gene therapy patients who have no cancer blast cells, and Magenta's expectation that MGTA-117 will bind and deplete target cells in the bone marrow in these patient populations at the same or lower dose levels studied in R/R AML and MDS patients; the planned transition of the MGTA-117 Phase 1/2 clinical trial into transplant-eligible AML and MDS patients, as well as into patients who are receiving gene therapy; and the predictive value of Magenta's MGTA-117 preclinical modeling.

Words such as "anticipate," "believe," "continue," "could," "designed," "endeavor," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "seek," "should," "target," "preliminary," "will," "would" and similar expressions are intended 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: uncertainties inherent in preclinical and clinical trials and in the availability and timing of data from ongoing and planned clinical and preclinical trials; the ability to initiate, enroll, conduct or complete ongoing and planned preclinical and clinical trials; vulnerability and/or fragility of, and the presence of underlying disorders in, the patient population for the clinical trials of Magenta's product candidates, including the MGTA-117 Phase 1/2 clinical trial in patients with relapsed/refractory AML and MDS; that preliminary data from Magenta's clinical trials may change materially following a more comprehensive review of the data; the delay of any current or planned preclinical or clinical trials, or the delay in development of Magenta's product candidates; whether results from preclinical or earlier clinical trials will be predictive of the results of future trials; interactions with regulatory agencies such as the U.S. Food and Drug Administration; the expected timing of submissions for regulatory approval to conduct or continue trials or to market products; Magenta's ability to successfully demonstrate the safety and efficacy of its product candidates; whether Magenta's cash resources will be sufficient to fund Magenta's foreseeable and unforeseeable operating expenses and capital expenditure requirements; and risks, uncertainties and assumptions regarding the impact of the continuing COVID-19 pandemic on Magenta's business, operations, preclinical activities, clinical trials, strategy, goals and anticipated timelines. These and other risks are described in additional detail in Magenta's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 and its other filings made with the Securities and Exchange Commission from time to time. Any forward-looking statements contained in this press release represent Magenta's views only as of today and should not be relied upon as representing its views as of any subsequent date. Magenta explicitly disclaims any obligation to update any forward-looking statements, except to the extent required by law.

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