Beam Therapeutics Presents First In Vivo Proof of Concept Preclinical Data on Multiplex Base Edited ESCAPE Platform for Non-Genotoxic Conditioning Regimen for Patients with Sickle Cell Disease Ahead of Autologous Transplant

December 10, 2022

Data from ESCAPE-1 and ESCAPE-2 Approaches to Be Presented During Poster Sessions at the 64th ASH Annual Meeting and Exposition

CAMBRIDGE, Mass., Dec. 10, 2022 (GLOBE NEWSWIRE) -- Beam Therapeutics Inc. (Nasdaq: BEAM), a biotechnology company developing precision genetic medicines through base editing, today announced new preclinical data from its Engineered Stem Cell Antibody Paired Evasion (ESCAPE) conditioning approach aimed at overcoming toxicity challenges associated with currently available conditioning regimens. Beam is advancing ESCAPE as part of its long-term strategy to support broad accessibility of base editing treatments for patients with sickle cell disease (SCD) and other hematologic diseases. “Wave 2” of this strategy is focused on improving the safety and tolerability of conditioning regimens, a required pretreatment for patients receiving *ex vivo* gene editing treatment via autologous transplant that can be coupled with a treatment for SCD through multiplex base editing.

Beam is currently advancing two ESCAPE programs: “ESCAPE-1” and “ESCAPE-2.” In both strategies, hematopoietic stem cells (HSCs) are multiplex edited to generate point mutations in the *CD117* gene and a therapeutic edit for the treatment of SCD. The base edit to *CD117,* a well-categorized conditioning target, results in amino acid substitutions and is intended to allow these HSCs to evade elimination by the conditioning antibody. ESCAPE-1 has been designed to induce a therapeutic edit for SCD at the *HGB1/2* gene to enable upregulation of fetal hemoglobin, while ESCAPE-2 is designed to install the therapeutic HbG-Makassar edit. Beam’s ESCAPE strategy is intended to allow the conditioning antibody to selectively clear unedited host cells while allowing cells containing the *CD117* edit to engraft and proliferate in the presence of the antibody.

“We continue to make important progress with our ESCAPE strategy to improve conditioning regimens for patients ahead of autologous transplant, with a goal of expanding the number of patients who may be able to benefit from our novel therapeutic candidates,” said Giuseppe Ciaramella, Ph.D., president and chief scientific officer of Beam. “We’re excited to share the first *in vivo* data from ESCAPE, which provide further evidence of our approach’s potential to enable less toxic pre-transplant conditioning, while minimizing treatment-related toxicities that arise from current busulfan-based conditioning. The latest findings for both ESCAPE-1 and ESCAPE-2 support their continued advancement as treatment approaches for SCD and other hematologic conditions in the future.”

ESCAPE-1 Data Summary
ESCAPE-1 consists of multiplex base edited HSCs that include a therapeutic edit for SCD at the *HGB1/2* gene and an additional edit at *CD117*. Findings to be presented today include the first *in vivo* data for the program which build upon data shared earlier this year demonstrating that ESCAPE antibodies bound to wild-type CD117 and blocked binding of its ligand. In addition, the ESCAPE antibodies led to the depletion of unedited cells, while enriching for edited cells. Further, today’s data show:

- Beam’s CD117 variants functioned comparably to its wild-type form in proliferation, differentiation, viability, and phosphorylation assays *in vitro,* supporting the notion that the edit does not alter the biological function of *CD117*
- CD117 base-edited human CD34+ HSCs led to multilineage reconstitution in a mouse model comparable with unedited HSCs, consistent with the cells having retained their stem-like engraftment potential
- Fc-engineered mAb-7 (anti-CD117 monoclonal antibody) did not induce mast-cell degranulation *in vitro*
- Multiplexing CD117 sgRNA with therapeutic sgRNAs (e.g. *HBG1/2*) with a single adenine base editor achieved greater than 85% A to G editing at *CD117* in HSCs, which also contain the therapeutic edit
- Multiplex base edited HSCs evaded mAb-mediated effects and CD117-ligand blocking, allowing for escape from depletion *in vitro* and *in vivo*
- mAb-7 selectively depleted unedited cells from the bone marrow of mice transplanted with a 1:1 mixture of unedited and edited HSCs

Title: Engineered Stem Cell Antibody Paired Evasion 1 (ESCAPE-1): Paired HSC Epitope Engineering and Upregulation of Fetal Hemoglobin for Antibody-Mediated Autologous Hematopoietic Stem Cell Therapy Conditioning for the Treatment of Hemoglobinopathies (1955)
Session Name: 701. Experimental Transplantation: Basic and Translational: Poster I
Date & Time: Saturday, December 10, 2022, 5:30-7:30 p.m.
Location: Ernest N. Morial Convention Center, Hall D

ESCAPE-2 Data Summary
In ESCAPE-2, Beam scientists screened two adenine base editor sgRNAs that could install the therapeutic HbG-Makassar edit and an edit in *CD117* which was compatible with the conditioning mAb (“mAb-7”) previously developed for ESCAPE-1. In preclinical studies, Beam’s ESCAPE-2 strategy demonstrated highly efficient base editing of *CD117* of HSCs and favorable mAb properties *in vitro*. Further, findings showed that primary human HSCs harboring the engineered epitope could effectively evade depletion by blocking of the CD117 ligand binding by a highly specific and potent mAb *in vitro*. Early *in vitro* biological assessment of receptor function suggested that the engineered CD117 epitope is compatible with normal function. During the poster session, Beam will also present additional *in vivo* data on ESCAPE-2, supporting its continued advancement and evaluation.

Title: Engineered Stem Cell Antibody Paired Evasion-2 (ESCAPE-2): Paired HSC Epitope Engineering and Direct Editing of Sickle Allele for Antibody-Mediated Autologous Hematopoietic Stem Cell Therapy Conditioning for the Treatment of Sickle Cell Disease (4585)
Session Name: 701. Experimental Transplantation: Basic and Translational: Poster III
Date & Time: Monday, December 12, 2022, 6:00-8:00 p.m.
Location: Ernest N. Morial Convention Center, Hall D

About Beam Therapeutics
Beam Therapeutics (Nasdaq: BEAM) is a biotechnology company committed to establishing the leading, fully integrated platform for precision genetic medicines. To achieve this vision, Beam has assembled a platform that includes a suite of gene editing and delivery technologies and is in the process of building internal manufacturing capabilities. Beam's suite of gene editing technologies is anchored by base editing, a proprietary technology that is designed to enable precise, predictable and efficient single base changes, at targeted genomic sequences, without making double-stranded breaks in the DNA. This has the potential to enable a wide range of potential therapeutic editing strategies that Beam is using to advance a diversified portfolio of base editing programs. Beam is a values-driven organization committed to its people, cutting-edge science, and a vision of providing life-long cures to patients suffering from serious diseases.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Investors are cautioned not to place undue reliance on these forward-looking statements, including, but not limited to, statements related to: our upcoming presentations at the ASH Annual Meeting and Exposition; the therapeutic applications and potential of our technology, including with respect to SCD and our conditioning regimens; and our ability to develop life-long, curative, precision genetic medicines for patients through base editing. Each forward-looking statement is subject to important risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement, including, without limitation, risks and uncertainties related to: our ability to develop, obtain regulatory approval for, and commercialize our product candidates, which may take longer or cost more than planned; our ability to raise additional funding, which may not be available; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the potential impact of the COVID-19 pandemic, including its impact on the global supply chain; the uncertainty that our product candidates will receive regulatory approval necessary to initiate human clinical studies; that preclinical testing of our product candidates and preliminary or interim data from preclinical studies and clinical trials may not be predictive of the results or success of ongoing or later clinical trials; that enrollment and initiation of our clinical trials may take longer than expected; that our product candidates may experience manufacturing or supply interruptions or failures; risks related to competitive products; and the other risks and uncertainties identified under the headings "Risk Factors Summary" and "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, and in any subsequent filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release. Factors or events that could cause our actual results to differ may emerge from time to time, and it is not possible for us to predict all of them. We undertake no obligation to update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by applicable law.

This press release contains hyperlinks to information that is not deemed to be incorporated by reference in this press release.

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