Beam Therapeutics Outlines Long-term Strategy for Base Editing Programs in Sickle Cell Disease and Provides Preclinical Data Updates at ASH

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CAMBRIDGE, Mass., Dec. 12, 2021 (GLOBE NEWSWIRE) -- Beam Therapeutics Inc. (Nasdaq: BEAM), a biotechnology company developing precision genetic medicines through base editing, today shared a three-stage, long-term development strategy for its base editing approach to treat sickle cell disease (SCD). The plan, and supportive data, are being presented during a Scientific Program Session oral presentation and two poster sessions at the 63rd American Society for Hematology (ASH) Annual Meeting & Exposition.

SCD is a severe, hereditary monogenic blood disorder that alters the structure and function of oxygen-carrying hemoglobin in red blood cells and is caused by a single letter spelling error in the beta globin gene. To fully address SCD and support broad accessibility, Beam is deploying a stepwise strategy that includes advancements of its *ex vivo* programs, BEAM-101 and BEAM-102, improvements in patient conditioning regimens, and enablement of *in vivo* base editing with delivery directly into patients via lipid nanoparticles (LNPs).

"Our goal is to make disease-altering, lifelong treatments with base editing broadly accessible to SCD patients around the globe, and, over time, improve on the delivery of these therapies so patients everywhere can opt for a potentially curative therapy," said John Evans, chief executive officer of Beam. "We have focused our initial SCD efforts on our *ex vivo* programs, BEAM-101 and BEAM-102, which leverage established clinical and regulatory strategies and have the potential to offer transformative therapeutic options for SCD patients. To further improve the therapeutic options for SCD patients, we also aim to develop lower-toxicity conditioning methods for improved transplant, as well as pursuing *in vivo* delivery of our base editors using our innovative LNP delivery capabilities. We believe this suite of technologies – base editing, improved conditioning and *in vivo* delivery for editing HSCs – can maximize the potential of our SCD programs as well as create a powerful platform for the treatment of many other severe genetic blood disorders."

During the presentations at ASH, Beam is highlighting its stepwise strategy for treating SCD and is presenting complementary data supporting several components of its approach:

Wave 1: *Ex Vivo* Base Editing via Autologous Transplant
Beam is advancing *ex vivo* base editing programs, in which cells are collected from a patient, edited and then infused back into the patient following a conditioning regimen, such as treatment with busulfan, the standard of care in hematopoietic stem cell (HSC) transplantation today. This approach is being deployed in the company's BEAM-101 and BEAM-102 base editing programs, and allows the company to pursue an efficient path for development using increasingly validated clinical endpoints and regulatory strategies.

BEAM-101 is an investigational, patient-specific, autologous HSC therapy which incorporates base edits that mimic single nucleotide polymorphisms seen in individuals with hereditary persistence of fetal hemoglobin to potentially alleviate the effects of mutations causing SCD or beta-thalassemia. The company recently received clearance of its Investigational New Drug application for this program and is working to initiate its Phase 1/2 BEACON-101 trial.

BEAM-102 aims to treat SCD by directly editing the causative HbS point mutation to recreate a naturally occurring normal human hemoglobin variant, HbG-Makassar. The Makassar variant has been reported to have the same function as the wild-type variant and does not cause SCD.

During ASH, Beam is presenting updated preclinical data further characterizing Makassar hemoglobin created by BEAM-102 and demonstrating biophysical and biochemical properties consistent with normal hemoglobin, as expected:

- Makassar globin did not polymerize *in vitro*
- Cells co-expressing Makassar globin and sickle globin had properties similar to sickle trait cells, which are cells with one normal globin gene and one sickle globin gene and which do not sickle
- Oxygen binding of Makassar globin was comparable to the most abundant normal adult hemoglobin (HbA)
- The crystal structures of the Makassar globin and of HbA were superimposable, suggesting no meaningful structural differences

Wave 2: Improved Conditioning
In parallel with Wave 1 development, Beam also aims to improve the transplant conditioning regimen for SCD patients, reducing toxicity challenges associated with standard of care. Conditioning is a critical component necessary to prepare a patient's body to receive the *ex vivo* edited cells that must engraft in the patient's bone marrow in order to be effective. Today's conditioning regimens rely on nonspecific chemotherapy or radiation, which are associated with significant toxicities. Beam has a collaboration with Magenta Therapeutics to evaluate the potential utility of MGTA-117, Magenta's novel antibody drug conjugate that is designed to precisely target only hematopoietic stem and progenitor cells, sparing immune cells. Importantly, improved conditioning regimens could potentially be paired with BEAM-101 and BEAM-102, as well as other base editing programs in hematology.

Wave 3: *In Vivo* Base Editing via HSC-targeted LNPs
Beam is also exploring the potential for *in vivo* base editing programs for SCD, in which base editors would be delivered to the patient through an infusion of LNPs targeted to HSCs, eliminating the need for transplantation altogether. This approach could provide a more accessible option for patients, particularly in regions where *ex vivo* treatment is challenging. Building on its acquisition of Guide Therapeutics, Beam has established a DNA-barcoded LNP screening technology to enable high-throughput *in vivo* identification of LNPs with novel biodistribution and selectivity for target

organs beyond the liver.

During ASH, Beam is presenting updated preclinical data using this technology to screen more than 1,000 LNPs for potential to deliver to HSCs and identified LNP-HSC1 as the most potent, with efficient transfection in both mice and non-human primates. Updated findings in the poster showed:

- LNP-HSC1 was validated *in vivo*, leading to durable, dose-dependent mRNA transfection in HSCs and resulting in fluorescent reporter expression in more than 40% of cells, now maintained out to 16 weeks post-delivery
- LNP-HSC1 efficiently transfected human CD34+ cells *in vitro*
- LNP-HSC1 efficiently transfected nearly 20% of CD34+ HSCs in humanized mice and non-human primates at a dose of 1.0 mg/kg.

Beam is continuing work to identify more potent LNPs for applications in *in vivo* base editing of HSCs. As with Wave 2, Beam can potentially leverage the same base editing payloads used in BEAM-101 and BEAM-102 for future *in vivo* programs, as well as expanding the use of the technology to other indications in hematology.

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 enables precise, predictable and efficient single base changes, at targeted genomic sequences, without making double-stranded breaks in the DNA. This enables 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 strategic initiatives for our base editing program targeting SCD; our planned base editing and LNP screening data presentations at an upcoming scientific conference; the therapeutic applications and potential of our technology, including with respect to SCD, conditioning and LNP screening; the planned initiation of our BEACON-101 trial; 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; 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 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, 2020, our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, 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.

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