Beam Therapeutics Announces Positive Initial Data for BEAM-302 in the Phase 1/2 Trial in Alpha-1 Antitrypsin Deficiency (AATD), Demonstrating First Ever Clinical Genetic Correction of a Disease-causing Mutation

March 10, 2025

Single Dose of BEAM-302 Led to Durable, Dose-dependent Increases in Total and Functional Alpha-1 Antitrypsin (AAT), Production of Corrected M-AAT, and Decreases in Mutant Z-AAT in Circulation Across Initial Three Dose Levels

Third Dose Level of BEAM-302 (60 mg, N=3) Achieved Mean Total AAT of 12.4μM at Day 28, Exceeding Protective Therapeutic Threshold, and Reduced Mutant Z-AAT up to 78%

Initial Safety Findings Demonstrated BEAM-302 was Well Tolerated at All Dose Levels with No Serious Adverse Events or Dose-Limiting Toxicities Observed

Clinical Profile Supports Continued Dose Escalation, with Updated Data from Part A of the Phase 1/2 Trial Expected to be Presented at Medical Conference in Second Half of 2025

Company to Host Conference Call Today, March 10, 2025, at 8 a.m. ET

CAMBRIDGE, Mass., March 10, 2025 (GLOBE NEWSWIRE) -- Beam Therapeutics Inc. (Nasdaq: BEAM), a biotechnology company developing precision genetic medicines through base editing, today announced initial safety and efficacy data from its Phase 1/2 trial of BEAM-302, establishing clinical proof-of-concept as a potential treatment for alpha-1 antitrypsin deficiency (AATD) and for *in vivo* base editing. Preliminary results from the first three single-ascending dose cohorts demonstrated that BEAM-302 was well tolerated, with single doses of BEAM-302 leading to durable dose-dependent correction of the disease-causing mutation.

AATD is an inherited genetic disorder that affects the lungs and/or liver, leading to early onset emphysema and liver disease, and for which there are no currently approved curative treatments. BEAM-302 is a liver-targeting lipid-nanoparticle (LNP) formulation of a guide RNA and an mRNA encoding a base editor designed to correct the disease-causing PiZ mutation. Patients homozygous for this mutation, known as the PiZZ genotype, have very low circulating levels of functional alpha-1 antitrypsin (AAT) protein, all of which is the mutant form, known as Z-AAT, which accumulates and causes liver toxicity. By correcting the PiZ mutation at the DNA level, BEAM-302 has the potential to be a one-time therapy that simultaneously reduces the amount of Z-AAT in circulation, generates therapeutic levels of corrected protein (M-AAT), and increases total and functional AAT in circulation above the 11μM protective threshold, thereby addressing the underlying pathophysiology of both the liver and lung disease. It is estimated that approximately 100,000 individuals in the U.S. have the PiZZ genotype.

“AATD is a serious genetic disorder that impacts the lungs and liver, often leading to emphysema and significant liver disease. Despite its severity, AATD remains underdiagnosed, and effective treatment options remain limited,” said Noel “Gerry” McElvaney, M.D., professor of medicine, Royal College of Surgeons, Dublin, Ireland. “The initial data for BEAM-302 demonstrate that the direct correction of the PiZ mutation both increased levels of functional AAT in the blood and reduced the harmful mutant protein which directly contributes to the liver and lung disease in this condition. These data represent a major breakthrough in the area of AATD, offering, for the first time ever, an opportunity to simultaneously treat the lung and liver disease associated with the condition by targeting the root cause and the potential for a cure from a single therapeutic administration, something which we have never seen before in a genetic lung disease.”

BEAM-302 is being evaluated in a Phase 1/2, open-label, dose exploration and dose expansion clinical trial to investigate its safety, tolerability, pharmacodynamics, pharmacokinetics and efficacy. Part A of the trial is designed to evaluate AATD patients with lung disease, and Part B will evaluate AATD patients with mild to moderate liver disease with or without lung disease. The dose expansion portions of the trial will identify the optimal dose to take forward in development. To date, single-ascending fixed doses of 15 mg (n=3), 30 mg (n=3) and 60 mg (n=3) of BEAM-302 have been administered via intravenous infusion in patients in Part A. Initial safety and efficacy data reported are from all nine patients as of a data cut-off date of February 26, 2025.

Treatment with BEAM-302 was well tolerated with an acceptable safety profile at all dose levels explored to date. All adverse events (AEs) were mild to moderate, with no serious AEs reported and no dose-limiting toxicities as of the data cutoff. Grade 1 asymptomatic alanine transaminase (ALT) and aspartate aminotransferase (AST) elevations and transient Grade 1 infusion-related reactions were observed in some patients and did not require treatment.

Following a single infusion of BEAM-302, rapid, durable, and dose-dependent increases in total AAT, new production of corrected M-AAT, and decreases in mutant Z-AAT were observed in circulation. Changes in total AAT were observed by turbidimetry assays as early as Day 7, plateaued around Day 21 and were maintained for the duration of follow-up (up to Month 6 in the 15 mg cohort, Month 2 in the 30 mg cohort, and Day 28 in the 60 mg cohort). Increased total AAT was functional as determined by both neutrophil elastase inhibition and neutrophil elastase binding assays.

Mean (Standard Error)			
Dose Cohorts	15mg (n=3)	30mg (n=3)	60mg (n=3)
Baseline total AAT* (μM)	4.4 (0.22)	5.3 (0.25)	4.4 (0.30)
Total AAT* at Day 28 (μM)	7.0 (0.66)	10.1 (1.42)	12.4 (1.03)

Fold change in total AAT* from baseline at Day 28	1.6x (0.08)	1.9x (0.21)	2.8x (0.06)
% change from baseline in circulating mutant Z-AAT** at Day 28	-11% (8.0)	-38% (15.5)	-78% (n=1)

Baseline defined as average of all assessments conducted within screening period prior to BEAM-302 infusion.
*As measured by turbidimetry
** As measured by liquid chromatography-mass spectrometry (LC-MS)

“This landmark result in medicine represents the first clinical evidence of precise correction of a disease-causing mutation by rewriting the genetic code. The correction of the PiZ mutation in AATD is a potentially optimal application of base editing to precisely and potently repair mutations in DNA,” said John Evans, chief executive officer of Beam. “With a simple intravenous infusion, promising safety profile, sustainable increase of total AAT above the therapeutic threshold, and rapid reduction in toxic mutant Z-AAT, we believe BEAM-302 has the potential to be a transformative therapy that could treat the entire spectrum of disease manifestations in severely deficient AATD patients. We look forward to continuing dose escalation and accelerating the development of BEAM-302 for patients with AATD who urgently need more effective therapeutic options. Importantly, these data are also a demonstration of Beam’s state-of-the-art LNP *in vivo* delivery capabilities and open the door for the further expansion of our liver genetic disease franchise.”

Beam plans to continue the dose-escalation portion of Part A of the ongoing Phase 1/2 trial, including enrolling and dosing a fourth dose cohort, and expects to report further data at a medical conference in the second half of 2025. In addition, the company plans to dose the first patient in Part B, which will include AATD patients with mild to moderate liver disease, in the second half of 2025.

Conference Call and Webcast Details
Beam will host a conference call and webcast to discuss these updates today, March 10, 2025, at 8 a.m. ET. A live webcast of the presentation will be available under "Events" in the Investors section of the company's website at www.beamtx.com. A replay of the webcast will be archived on the company’s website for 60 days following the presentation.

About BEAM-302
BEAM-302 is a liver-targeting lipid-nanoparticle (LNP) formulation of base editing reagents designed to correct the PiZ mutation. Patients homozygous for this mutation (PiZZ) represent the majority of patients living with severe AATD disease. A one-time A-to-G correction of the PiZ mutation with Beam’s adenine base editor has the potential to simultaneously reduce the aggregation of mutant, misfolded AAT protein that causes toxicity to the liver (Z-AAT), generate therapeutic levels of corrected protein (M-AAT), and increase total and functional AAT in circulation, thereby addressing the underlying pathophysiology of both the liver and lung disease. In addition, the reduction in circulating PiZ aggregates (i.e., polymers) has the potential to further minimize lung inflammation and dysfunction. Importantly, because the native AAT gene would be corrected in its normal genetic location, AAT levels are anticipated to increase physiologically in response to inflammation or infection. This is a critical aspect of AAT’s normal function to regulate the body’s inflammatory response, which does not occur with currently approved protein replacement therapies. Correction of the PiZ mutation is expected to be durable based on preclinical and clinical evidence.

About Alpha-1 Antitrypsin Deficiency (AATD)
AATD is an inherited genetic disorder that can cause early onset emphysema and liver disease. The most severe form of AATD arises when a patient has a point mutation in both copies of the SERPINA1 gene at amino acid 342 position (E342K, also known as the PiZ mutation or the “Z” allele). This point mutation causes alpha-1 antitrypsin, or AAT, to misfold, accumulating inside liver cells rather than being secreted, resulting in very low levels (10%-15%) of circulating AAT. In addition to resulting in lower levels, the PiZ AAT protein variant is also less enzymatically effective compared to wildtype AAT protein. As a consequence, the lung is left unprotected from neutrophil elastase, resulting in progressive, destructive changes in the lung, such as emphysema, which can result in the need for lung transplants. The mutant AAT protein also accumulates in the liver, causing liver inflammation and cirrhosis, which can ultimately cause liver failure or cancer requiring patients to undergo a liver transplant.

It is estimated that approximately 100,000 individuals in the U.S. have two copies of the Z allele, known as the PiZZ genotype, although only about 10% of all patients are thought to have been diagnosed. There are currently no curative treatments approved for patients with AATD, and the only approved therapy in the U.S., intravenous AAT protein replacement, has not been shown to prevent ongoing lung function decline and destruction in patients.

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 with integrated gene editing, delivery and 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: the therapeutic applications and potential of our technology, including our potential to develop life-long, curative, precision genetic medicines for patients through base editing; our plans, and anticipated timing, to advance our BEAM-302 program; and the clinical trial designs and expectations for BEAM-302. 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 uncertainty that our product candidates will receive regulatory approval necessary to initiate human clinical trials; 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 initiation and enrollment of, and anticipated timing to advance, our clinical trials may take longer than expected; that our product candidates or the delivery modalities we rely on to administer them may cause serious adverse events; 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, 2024, 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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