Beam Therapeutics Announces First Patient Dosed in the Phase 1/2 Study of BEAM-302 in Alpha-1 Antitrypsin Deficiency (AATD)

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CAMBRIDGE, Mass., June 26, 2024 (GLOBE NEWSWIRE) -- Beam Therapeutics Inc. (Nasdaq: BEAM), a biotechnology company developing precision genetic medicines through base editing, today announced the first patient was treated with BEAM-302, an investigational *in vivo* base editing medicine designed to precisely correct the underlying cause of severe alpha-1 antitrypsin deficiency (AATD), that is currently being evaluated in a Phase 1/2 clinical trial.

“Treating the first patient with BEAM-302 is an important milestone for Beam and the AATD patient community, who are in need of novel and more effective treatment options that can address the full spectrum of disease manifestations,” said John Evans, chief executive officer at Beam. “Using the power and precision of base editing technology, BEAM-302 is the first clinical program in the gene editing field designed to directly correct a genetic disease-causal mutation back to a normal functional gene sequence with a one-time *in vivo* therapy. We believe BEAM-302 has the potential to be a best-in-class treatment of both AATD-associated lung and liver disease through the correction of the PiZ allele, the most common gene variant associated with severe AATD. Advancing this Phase 1/2 study is a top priority for Beam, and we look forward to continued site activation, patient enrollment and dosing.”

BEAM-302 is being evaluated in an open-label, dose-escalation Phase 1/2 clinical trial that will investigate the safety, pharmacodynamics, pharmacokinetics and efficacy of BEAM-302. The study design includes a dose exploration portion followed by a dose expansion portion to identify the optimal dose to take forward in a pivotal study.

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 and increase circulating levels of corrected and functional AAT protein, thus 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 evidence.

About Alpha-1 Antitrypsin Deficiency (AATD)
AATD is an inherited genetic disorder that can cause early onset emphysema, liver disease and panniculitis. A severe form of AATD arises when a patient has the p.Glu366Lys (also referred to as E342K) point mutation in both copies of the SERPINA1 gene. This results in the expression of the pathogenic PiZ variant of alpha-1 antitrypsin (Z-AAT) that misfolds and aggregates inside liver cells causing liver damage, rather than being secreted. The Z-AAT that is made in the liver is approximately two-fold less effective in inhibiting neutrophil elastase and poorly secreted into circulation, leading to circulating levels of AAT that are 10-15% of normal in homozygous individuals. As a consequence, the lung is left unprotected from neutrophil elastase and other damaging proteases that can cause progressive, destructive changes in the lung, such as emphysema, and lead to severe lung disease and the need for lung transplantation. The accumulation of Z-AAT protein in the liver can cause liver inflammation, hepatocyte injury and cirrhosis, which can result in liver failure or cancer and, in some patients, require liver transplantation. In addition, circulating Z polymers have increasingly been recognized as a factor contributing to disease severity in the lungs.

It is estimated that approximately 100,000 individuals in the United States (U.S.) have two copies of the Z allele, known as the PiZZ genotype, although only 10-15% 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 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: the therapeutic applications and potential of our technology, including with respect to AATD; our plans, and anticipated timing, to advance our BEAM-302 program; 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; 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 initiation and enrollment of, and anticipated timing to advance, 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, 2023, our Quarterly Report on Form 10-Q for the quarter ended March 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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