Beam Therapeutics Presents Preclinical Data Highlighting Utility of BEAM-302 to Correct an Alpha-1 Antitrypsin (AAT) Deficiency Disease-Causing Mutation

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First Preclinical Data for BEAM-302 Demonstrate Increased Levels of Corrected AAT and Reduced Mutant PiZ AAT in Multiple In Vivo Rodent Disease Models

CAMBRIDGE, Mass., Sept. 07, 2023 (GLOBE NEWSWIRE) -- Beam Therapeutics Inc. (Nasdaq: BEAM), a biotechnology company developing precision genetic medicines through base editing, today reported new preclinical data demonstrating the ability of its *in vivo* drug candidate, BEAM-302, to directly correct the PiZ mutation, the primary disease-causing mutation associated with severe alpha-1 antitrypsin deficiency (AATD). The data are featured in an oral presentation titled "BEAM-302: Targeting AATD Liver and Lung Disease with Base Editing" at the Alpha-1 Antitrypsin Deficiency 2023 Meeting in Naples, Italy.

"AATD, one of the most common genetic conditions, predominantly results in lung and liver disease, and we believe base editing is uniquely suited to address the underlying drivers of disease progression in both organs," said Giuseppe Ciaramella, Ph.D., president of Beam. "In today's presentation, we shared – for the first time – a full summary of preclinical *in vivo* data for BEAM-302, our lead candidate for the potential treatment of AATD. In two rodent models of AATD, one-time treatment at clinically relevant dose levels of BEAM-302 led to significant increases in circulating total corrected AAT and corresponding reductions in circulating mutant PiZ AAT. These data support the continued advancement of BEAM-302 as a potential treatment option for AATD-related lung and liver disease, and we remain focused on the planned submission of our regulatory application in the first quarter of next year."

AATD is caused by mutations in the *SERPINA1* gene, with >95% of severe clinical cases homozygous for the PiZ mutation (known as the PiZZ genotype). BEAM-302 is a liver-targeting lipid-nanoparticle (LNP) formulation of base editing reagents designed to precisely correct the PiZ mutation, a single-letter genetic error. 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 lung and liver disease. Correction is expected to be durable based on preclinical evidence to date. Importantly, because the native AAT gene would be corrected in its normal genetic location, AAT levels would be anticipated to increase in response to inflammation or infection, an important aspect of normal AAT function, which does not occur with currently approved protein replacement therapies.

BEAM-302 was evaluated in two preclinical species: an NSG-PiZ mouse model of AATD carrying multiple copies of the human PiZ allele and a novel humanized PiZ rat model developed by Beam scientists in which the normal rat AAT is replaced with human mutated PiZ AAT.

- Treatment with a single dose of BEAM-302 induced dose-dependent correction of the PiZ mutation. Clinically relevant doses up to 1mpk resulted in correction of up to 39% and 49% of liver DNA in rats and mice, respectively.
- Relative to pre-dose values, editing with BEAM-302 yielded two-times higher levels of total serum AAT and a 70% decrease in serum Z-AAT in rats. Editing with BEAM-302 yielded four-times higher levels of total serum AAT, and a 90% decrease in serum Z-AAT in mice.
- Relative to pre-dose values, editing with BEAM-302 yielded two- and three-times higher functional AAT in rats and mice, respectively, as indicated by the increased capacity of serum samples to inhibit human neutrophil elastase.
- Experiments with research-grade BEAM-302 demonstrated a reduction in toxic liver aggregates, also referred to as liver polymers.

These findings support the potential of BEAM-302 to efficiently correct the disease-causal PiZ mutation after a single dose and potentially address both the liver and lung disease associated with AATD.

Beam plans to submit a regulatory application for authorization to initiate clinical trials of BEAM-302 in the first quarter of 2024.

About Alpha-1 Antitrypsin Deficiency (AATD)
AATD is an inherited genetic disorder that causes early onset emphysema and liver disease. A severe form of AATD arises when a patient has the p.Glu366Lys point mutation in both copies of the *SERPINA1* gene, which 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 inability of liver cells to secrete Z-AAT results in roughly 10%-15% of the normal level of circulating AAT, which is a potent inhibitor of proteases such as neutrophil elastase. 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 Z-AAT protein that accumulates in the liver, causes liver inflammation and cirrhosis, which can ultimately result in liver failure or cancer requiring patients to undergo a liver transplant. In addition, circulating Z-AAT aggregates (called circulating Z polymers) have increasingly been recognized as a factor contributing to disease severity in both the lungs as well as the liver. It is estimated that approximately 60,000 individuals in the United States have two copies of the Z allele, known as the PiZZ genotype. There are currently no curative treatments approved for patients with AATD.

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 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 submit a regulatory application for authorization to initiate clinical trials of BEAM-302; 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 pandemics and other health emergencies, including their 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 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, 2022, our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, 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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