Beam Therapeutics Announces Clearance of Clinical Trial Authorisation Application for BEAM-302 for the Treatment of Alpha-1 Antitrypsin Deficiency (AATD)

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Initiation of Phase 1/2 Trial of BEAM-302 in AATD Expected in First Half of 2024

CAMBRIDGE, Mass., March 26, 2024 (GLOBE NEWSWIRE) -- Beam Therapeutics Inc. (Nasdaq: BEAM), a biotechnology company developing precision genetic medicines through base editing, today announced the clearance of its clinical trial authorisation (CTA) application by the United Kingdom (UK) Medicines and Healthcare Products Regulatory Agency for BEAM-302, an *in vivo* base editor, as a potential treatment for patients with alpha-1 antitrypsin deficiency (AATD).

"The clearance of our first CTA is an important step in the advancement of our global Phase 1/2 study of BEAM-302, a potentially best-in-class, liver-targeting *in vivo* base editor designed to correct the PiZ mutation, which is the most common gene variant associated with severe AATD," said Giuseppe Ciaramella, Ph.D., president of Beam. "AATD is an inherited genetic condition that can cause serious lung and liver disease, which can lead to significant debility and reduced life expectancy for patients. Preclinical data demonstrated the ability of BEAM-302 to significantly increase levels of corrected and functional alpha-1 antitrypsin (AAT) and reduce the mutant PiZ AAT protein in *in vivo* rodent disease models at clinically relevant doses. 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."

The Phase 1/2 clinical trial is an open-label, dose-escalation study that will evaluate the safety, pharmacodynamics, pharmacokinetics and efficacy of BEAM-302 initially in patients with AATD-associated lung disease. 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. The company expects to initiate the Phase 1/2 trial of BEAM-302 in the UK in the first half of 2024.

About BEAM-302
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 found in the majority of severe homozygous patients (PiZZ) living with AATD. 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. 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, a critical aspect of AAT's normal function to regulate the body's inflammatory response, which would not occur with currently approved protein replacement therapies. Correction of the PiZ mutation is expected to be durable based on preclinical evidence to date.

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; the clinical trial designs and expectations for 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 successfully achieve the benefits of our portfolio prioritization and strategic restructuring; 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, 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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