Beam Therapeutics Announces Preclinical Data Highlighting Potential of Base Editors to Target Disease Drivers of Chronic Hepatitis B Infection

September 27, 2021

Data to be Presented During an Oral Presentation at the 2021 International HBV Meeting

CAMBRIDGE, Mass., Sept. 27, 2021 (GLOBE NEWSWIRE) -- Beam Therapeutics Inc. (Nasdaq: BEAM), a biotechnology company developing precision genetic medicines through base editing, today announced preclinical data demonstrating the potential of Beam's cytosine base editors (CBEs) to reduce viral markers, including hepatitis B surface antigen (HBsAg) expression, and prevent viral rebound of hepatitis B virus (HBV) in *in vitro* models. These data will be presented today, September 27, 2021, in partnership with Fabien Zoulim's laboratory at the INSERM Cancer Research Center of Lyon, during an oral presentation titled, "cccDNA Inactivation Using Cytosine Base Editors," at the 2021 International HBV Meeting.

HBV causes serious liver infection that can become chronic, increasing the risk of developing life-threatening health issues like cirrhosis, liver failure or liver cancer. Chronic HBV infection is characterized by the persistence of covalently closed circular DNA (cccDNA), a unique DNA structure that forms in response to HBV infection in the nuclei of liver cells. Additionally, the HBV DNA integrates into the human genome becoming a source of HBsAg. While currently available treatments can manage HBV replication, they do not clear cccDNA from the infected liver cells. This inability to prevent HBV infection rebound from cccDNA is a key challenge to curing HBV.

Base editors are designed to enable direct and irreversible conversion of a specific DNA base into another without inducing double-stranded breaks. In HBV infected cells, CBEs can target the cccDNA minichromosome at multiple locations, introducing precise and permanent stop codons in the viral genome, which are intended to silence the viral genes without the risk of the chromosomal rearrangements.

"Hepatitis B is a major global health crisis, with more than 250 million people currently diagnosed with chronic disease worldwide. Despite current therapeutic approaches, a key challenge to finding a curative treatment to chronic HBV is being able to prevent infection rebound from cccDNA," said Giuseppe Ciaramella, Ph.D., president and chief scientific officer of Beam. "The data being presented today show that using our novel CBE, we can directly target and silence cccDNA to significantly reduce relevant HBV viral replicators, without the need to clear cccDNA from the cell. Furthermore, because HBV sequences are extensively integrated in the genome of infected cells, multiplex base editors are a natural fit for permanently silencing HBV genetic elements without creating double-stranded breaks or genetic rearrangements. These data underscore the advantages we believe base editing can offer in treating patients with HBV infection as well as a wide range of serious genetic diseases."

The results announced today are from a preclinical *in vitro* study designed to evaluate the potential of base editing to provide a new type of treatment for chronic hepatitis B disease. In the study, infected human hepatoma HepG2-NTCP cells, which are susceptible to HBV infection, and long-term primary human hepatocyte co-cultures, were multiplex edited with selected HBV-targeting gRNAs and mRNA-encoding CBEs. Edits included the introduction of stop codons to reduce HBsAg and HBeAg and silence the HBV gene and the cccDNA. Data findings show that:

- Multiplexing two gRNAs designed to introduce stop codons led to substantial, simultaneous reduction of relevant HBV viral markers (HBsAg, HBeAg, HBV DNA, 3.5kb RNA)
- Dual gRNA cccDNA-targeting CBE led to 30%-60% editing efficiency of the cccDNA, without reducing cccDNA levels;
- Combinatorial treatment of the base editing reagents with standard antiviral lamivudine resulted in 20% higher base editing efficiency leading to high antiviral efficacy; and
- Base editing prevented HBV rebound in long-term infected primary hepatocytes.

These results indicate that CBEs can introduce permanent mutations in cccDNA and prevent HBV rebound in relevant *in vitro* models. Based on these findings, Beam plans to evaluate its base editing approach in relevant *in vivo* proof of concept models.

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.

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: planned base editing data presentations at upcoming scientific conferences; and the therapeutic applications and potential of our technology, including the potential of base editing to provide a new type of treatment for chronic hepatitis B disease and our ability to develop life-long, curative, precision genetic medicines for patients through base editing. Each forward-looking statement is subject to 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 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 in any subsequent filings with the Securities and Exchange Commission. These forward-looking statements (except as otherwise noted) 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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