Excision BioTherapeutics Announces *Gene Therapy* Publication of Pre-Clinical Data Supporting its First-in-Class CRISPR-Based Gene Therapy Candidate Designed to Functionally Cure HIV-1

- Results demonstrate safety, biodistribution, and on-target editing of simian immunodeficiency virus (SIV) in non-human primates
- Data are a key component of scientific rationale supporting the ongoing Phase 1/2 clinical evaluation of EBT-101, a potentially curative treatment for HIV
- Research builds on Excision's enduring commitment to finding cures for people with infectious diseases including HIV, a virus that impacts 38 million people worldwide, including 1.1 million in the United States

SAN FRANCISCO, August 17, 2023 -- Excision BioTherapeutics, Inc., a clinical-stage biotechnology company developing CRISPR-based therapies to cure viral infectious diseases, today announced the publication of data in the journal *Gene Therapy* showing that EBT-001 – a simian-specific analogue of EBT-101 – safely removes the simian form of HIV from the genomes of non-human primates. The data support the safety, biodistribution, and on-target editing of Excision's EBT-101 program targeting HIV, which is being evaluated in first-in-human Phase 1/2 clinical trials.

"We are very excited by the positive data generated in this study, which set the foundation for an important first-in-human clinical trial of our lead candidate, EBT-101" said Daniel Dornbusch, Chief Executive Officer of Excision. "A cure for HIV would address a significant unmet need and we are committed to advancing this breakthrough science to finally end the HIV pandemic."

Today, people with HIV must take life-long antiretroviral therapy (ART). ART effectively reduces viral loads and can reduce the risk of HIV transmission, but it does not eliminate latent HIV in the body, which can cause significant medical conditions. The newly published data supplement the efficacy data generated in previous pre-clinical studies of EBT-101, demonstrating excision of integrated proviral SIV DNA in vivo, without any detectable off-target effects. The studies were conducted by researchers at the Lewis Katz School of Medicine at Temple University, including SIV pioneer Tricia Burdo, PhD, CRISPR gene editing of HIV innovator and Excision Co-Founder Kamel Khalili, PhD, and Excision scientists including Thomas J. Cradick, PhD, Jennifer Gordon, PhD, and others.

"These newly published results demonstrate the tremendous potential of EBT-101 to shape the future of HIV therapeutics" said Dr. Khalili.

In the studies, researchers treated non-human primates with a single intravenous injection of EBT-001 at one of four different dose levels. Necropsy and tissue analyses were carried out at three or six months after the start of treatment. Data were collected on the biodistribution, histopathology, and gene editing of the EBT-001 in blood and tissues representing sites of viral

latency, including lymph node and spleen tissue, as well as other tissues, and on safety, which included off-target analyses at the different dose levels.

Analyses showed that EBT-001 was broadly distributed throughout the tissues analyzed in a dose-dependent manner and evidence of gene editing of SIV proviral DNA was observed in all significant viral reservoirs. EBT-001 was well-tolerated at all dose levels, with no evidence of toxicity in clinical examination of the animals or following histopathological investigation.

“These important findings support the safety and tolerability of a potential CRISPR-based cure for HIV - a prospect that could significantly improve the well-being of people living with HIV,” said Jennifer Gordon, PhD, Senior Vice President of Research and Development at Excision and a senior investigator on the study. “This is an important milestone for the HIV community and signals the promise of multiplex, in vivo gene editing therapies to cure other viral infectious diseases like herpes simplex virus and hepatitis B.” Dr. Gordon joined Excision from Lewis Katz School of Medicine at Temple University to continue her work on EBT-101 and advance the company’s pipeline programs.

To read the announcement by Lewis Katz School of Medicine at Temple University, click here.

About EBT-101

EBT-101 is a unique, *in vivo* CRISPR-based therapeutic designed to cure HIV infection after a single intravenous infusion. EBT-101 employs an adeno-associated virus (AAV) to deliver CRISPR-Cas9 and dual guide RNAs, enabling a multiplexed *in vivo* editing approach that simultaneously targets three distinct sites within the HIV genome. This allows for the excision of large portions of the HIV genome, thereby minimizing potential viral escape.

About the EBT-101 Clinical Program

The EBT-101 Phase 1/2 trial is an open-label, multi-center, single ascending dose study designed to evaluate the safety, tolerability, and preliminary efficacy of EBT-101 in approximately nine participants with HIV-1 who are suppressed on antiretroviral therapy. The primary objective of the trial is to assess the safety and tolerability of a single dose of EBT-101 in study participants with an undetectable viral load on antiretroviral therapy. Biodistribution, pharmacodynamic, and efficacy assessments will also be conducted. All participants will be assessed for eligibility for an analytical treatment interruption (ATI) of their background ART at Week 12 post EBT-101 administration. Following the initial 48-week follow up period, all participants will be enrolled into a long-term follow up protocol. For more information, see ClinicalTrials.gov identifiers NCT05144386 (Phase 1/2 trial) and NCT05143307 (long-term follow up protocol). The EBT-101 Phase 1/2 clinical trial is supported by a grant from the California Institute for Regenerative Medicine (CIRM). For more information on CIRM go to www.cirm.ca.gov.

About Excision BioTherapeutics, Inc.

Excision BioTherapeutics, Inc. is a clinical-stage biotechnology company developing CRISPR-based therapies as potential cures for viral infectious diseases. EBT-101, the Company’s lead program, is an *in vivo* CRISPR-based therapeutic designed to cure HIV infection after a

single intravenous infusion. Excision's pipeline unites next-generation CRISPR nucleases with a novel gene editing approach to develop curative therapies for Herpes Virus, JC Virus, which causes PML, and Hepatitis B Virus. Excision's foundational technologies were developed in the laboratories of Dr. Kamel Khalili at Temple University and Dr. Jennifer Doudna at the University of California, Berkeley. For more information, please visit www.excision.bio.

About the California Institute for Regenerative Medicine (CIRM)

At CIRM, we never forget that we were created by the people of California to accelerate stem cell treatments to patients with unmet medical needs, and act with a sense of urgency to succeed in that mission. To meet this challenge, our team of highly trained and experienced professionals actively partners with both academia and industry in a hands-on, entrepreneurial environment to fast track the development of today's most promising stem cell technologies.

With $5.5 billion in funding and more than 150 active stem cell programs in our portfolio, CIRM is one of the world's largest institutions dedicated to helping people by bringing the future of cellular medicine closer to reality. For more information go to www.cirm.ca.gov.

Editor's Note:

Kamel Khalili is Co-Founder and Chief Scientific Consultant and holds equity in Excision BioTherapeutics, which has licensed the viral gene-editing technology from Temple University. Kamel Khalili and Rafal Kaminski are named inventors on patents that cover the viral gene-editing technology. Tricia Burdo serves on Excision BioTherapeutics' Scientific Advisory Board and holds equity in Excision BioTherapeutics. These three named researchers are employed by Temple University and also conduct research activities sponsored by the company. Questions regarding their affiliations with Temple University may be directed to coisom@temple.edu.

Dr. Khalili has not received financial compensation from any other third parties for any aspects of this published work.

In addition to owning the viral gene-editing technology that Excision is licensing, Temple University also holds an equity interest in Excision. As a result of these interests, Temple University could ultimately potentially benefit financially from the outcome of this research. These interests have been reviewed and approved by Temple University in accordance with its Institutional Conflict of Interest policy. Questions about this can be directed to coitemple@temple.edu.

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