11 Hurley Street
Cambridge, MA 02141
P 617-401-9000
F 617-494-0985

Editas Medicine Announces Strategic Transition to a *in vivo* Gene Editing Company with Intent to Develop a Transformative *in vivo* Medicine for the Treatment of Sickle Cell Disease and Beta Thalassemia

What is the news?

Editas Medicine, Inc., a pioneering gene editing company, announced its transition to a fully *in vivo* company with the intent to develop an *in vivo* treatment for Sickle Cell disease (*Editas Press Release*). As part of this strategic transition, Editas is ending development of the investigational *ex vivo* cell therapy, renizgamglogene autogedtemcel (reni-cel).

What is reni-cel?

Reni-cel is an investigational medicine made by collecting and editing a patient's own blood-forming stem cells. It is designed to be a one-time treatment that changes a part of a person's DNA with the goal of increasing fetal hemoglobin.

Some people are born with a change in their HBG1/HBG2 genes that allows them to keep creating fetal hemoglobin into adulthood. Reni-cel is designed to mimic that naturally occurring change.

Reni-cel uses CRISPR/AsCas12a to find and reactivate the gamma-globin genes, HBG1/HBG2, in blood-forming stem cells.

What is the reason?

Given the challenges associated with development and commercialization of an *ex* vivo gene therapy, and Editas' preclinical progress on *in vivo* editing, Editas actively sought to partner or out-license reni-cel to most effectively advance reni-cel towards potential commercial access and enable Editas to focus on *in vivo* drug development. Editas worked diligently to identify a path that would allow for the continued development and ultimate commercialization of reni-cel for sickle cell disease and transfusion-dependent beta-thalassemia, but after an extensive search, the company was not successful in securing a commercial partner.

Editas plans to combine its established CRISPR-based gene editing capabilities and clinically validated target and enzyme (based on experience with reni-cel), with novel *in vivo* delivery approaches, to develop an *in vivo* medicine for the treatment of sickle cell disease.

What does this mean for clinical trials with reni-cel?

Enrollment for both trials is complete, including adult and adolescent cohorts for RUBY and an adult cohort for EdiTHAL. Editas is in ongoing consultations with the clinical trial sites, FDA, and other parties to determine a path forward for each participant in the clinical trials. We are in regular contact with the clinical trial sites and will provide an update once there is a final resolution. Currently, the clinical trials, RUBY, EdiTHAL, and the LTFU (long-term follow up), are continuing according to protocol.

What can you tell me about the Editas *in vivo* hematopoietic stem cell (HSC) editing strategy?

The patient journey for *ex vivo* gene-edited cell therapies, which entails editing a patient's own cells outside of the body and then re-infusion of the edited cells through a hematopoietic stem cell transplant, requires the burdensome process of mobilization and collection of a patient's stem cells, as well as toxic chemotherapy conditioning, with associated complications, including infertility, thereby limiting patient access. In contrast, an *in vivo*–based gene editing approach offers the potential to significantly decrease the patient burden, without the need for stem cell collection or chemotherapy regimens, as well as provide an opportunity for global access.

In alignment with Editas' long-term vision to be a leader in *in vivo* CRISPR-based gene editing medicines, the company is focusing on use of the clinically validated *HBG1/2* promoter–targeted gene editing strategy and targeted delivery to HSCs to develop an *in vivo* therapy for the treatment of SCD, with the potential to minimize the burden to patients and the healthcare system, as well as increase patient access. To this end, Editas has recently announced pre-clinical progress on *in vivo* gene editing of HSCs:

Hematopoietic Stem Cells (HSCs):

- Editas achieved ~40% editing of the *HBG1/2* promoter site after using a novel, Editas-proprietary targeted lipid nanoparticle (tLNP) for extrahepatic tissue delivery to deliver a single dose of its clinically validated Cas12a editing machinery directly to human hematopoietic stem cells (HSCs) in mice engrafted with human HSCs. Furthermore, Editas achieved high efficiency delivery and *HBG1/2* editing with a single dose in non-human primates.

- *HBG1/2* biology has been validated and derisked in patients with reni-cel in the RUBY trial.

- The editing in HSCs with the Company's proprietary delivery mechanism resulted in a meaningful functional outcome of fetal hemoglobin induction, indicated by the presence of fetal hemoglobin expressing human red blood cells (on average 20%) that populate in the host by one month.

- We are excited about this early preclinical data and look forward to continuing to advance this program towards initiating clinical trials to fully evaluate the efficacy and safety of this potential therapeutic in humans.

Editas is committed to developing transformative *in vivo* gene edited medicines for people living with serious genetic diseases around the world. In addition to HSC, Editas achieved *in vivo* pre-clinical proof of concept of high efficiency editing in the liver and in other non-liver cell types with the potential to address multiple diseases.

How and when will I be able to get more information?

Editas intends to share additional *in vivo* pre-clinical editing data, including in HSCs, in 2025**.**

Editas is committed to collaborating with patients, advocacy groups, and healthcare providers. Editas believes in engaging regularly and transparently with the sickle cell disease and beta thalassemia community; should you have any questions you may email patients@editasmed.com or info@editasmed.com.