June 5, 2023

Dear Rett Community,

Today, Taysha announced that the first patient was dosed with the investigational gene therapy, TSHA-102, in the REVEAL Adult Study, a clinical trial for females 18 years and older living with Rett syndrome.

We would like to thank the entire Rett community and the Rett patient advocacy groups for their partnership that supported this milestone. We would also like to acknowledge the family and individual who are participating in the trial for being the first to contribute to this important research in order to better understand the potential of gene therapy for Rett syndrome.

It is too early to make any conclusions about the potential safety or efficacy of TSHA-102. We will share additional information once data is collected and made public. Please see below for a list of frequently asked questions.

What is the REVEAL Adult Study?

- The REVEAL Adult Study is a multi-center Phase 1/2 open-label dose-escalation clinical trial designed to evaluate the potential safety, tolerability, and preliminary efficacy of a single administration of the investigational gene therapy, TSHA-102, in adult females 18 years and older with Rett syndrome
- The study is designed to evaluate two different dose levels to determine the optimal amount (highest dose without harmful side effects) of TSHA-102
- During the dose finding part, study participants may receive one of two dose levels via a single intrathecal administration of TSHA-102 via lumbar puncture (spinal tap)

When will the second patient be dosed in the REVEAL Adult Study?

- Taysha confers with an Independent Data Monitoring Committee (IDMC) to make decisions related to key clinical activities, such as proceeding with dosing a second participant
- The IDMC is an independent group of experts who monitor patient safety, potential efficacy and study conduct while a clinical trial is ongoing
- IDMC members are selected based on their deep expertise, understanding of clinical trial methodology and ability to make sensible recommendations in a rational and consensus-driven manner based on data and medical judgment
- The IDMC will review initial data from the first participant before recommending to proceed with dosing a second participant; there will be an interval of at least six weeks

Where is the REVEAL Adult Study clinical trial being conducted?

- The study is being conducted at CHU Sainte-Justine, the Université de Montréal mother and child university hospital centre in Montreal, Canada

Who do I contact for more information about the REVEAL Adult Study?

- If you are interested in learning more about the study, please contact medinfo@tayshagtx.com

What are Taysha's plans for a clinical trial for females with Rett syndrome in the United Kingdom (UK)?

- Taysha plans to submit a Clinical Trial Application (CTA) to the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK by mid-year 2023 for the investigation of TSHA-102 in pediatric females with Rett syndrome; we do not yet have details on the specific age range

What are Taysha's plans for a clinical trial for females with Rett syndrome in the United States (U.S.)?

- Taysha plans to submit an Investigational New Drug (IND) application to the U.S. Food & Drug Administration (FDA) in the second half of 2023; we do not yet have details on the age range

About Taysha's investigational gene therapy for Rett syndrome (TSHA-102):

- What is the underlying cause of Rett syndrome?
  - Rett syndrome is caused by a mutation in *MECP2*, which is a gene that makes a protein called Methyl-CpG-binding protein 2 (MeCP2)
  - This protein plays an important part in the development of the brain throughout childhood by maintaining normal brain function and communicating between nerve cells
  - In Rett patients with a *MECP2* gene mutation, the body does not make enough MeCP2 or produces abnormal MeCP2
- What is Taysha's investigational approach to gene therapy for Rett syndrome?
  - TSHA-102 is made up of a miniature form of the *MECP2* gene (*miniMECP2*) that is paired with a regulatory element, or control, called miRNA-Responsive Auto-Regulatory Element (miRARE)
  - The *miniMECP2* gene is inserted into a delivery vehicle, or vector, which is then injected intrathecally, into the spinal fluid in the lower back (lumbar region)
  - The miRARE technology was developed by Dr. Sarah Sinnet and Dr. Steven Gray of UT Southwestern Medical Center and is designed to regulate or control the amount of MeCP2 protein that is made to avoid overexpression
  - Taysha's clinical trials will determine whether the functioning *miniMECP2* gene can be packaged with miRARE technology to safely regulate the level of MeCP2 protein expression

If you have any additional questions or would like to connect with a member of our team, please contact medinfo@tayshagtx.com.

We are extremely grateful for the continued support of the Rett syndrome community and the Rett patient advocacy organizations. Your continued input helps to shape the work that we do to develop a treatment for Rett syndrome.

We look forward to providing further updates as new information becomes publicly available.

Sincerely,
The Taysha Patient Affairs Team