August 14, 2023

Dear Rett Community,

We are writing to share a series of updates that Taysha provided in a press release earlier today. Please find a summary of these updates below, as well as a list of answers to some questions you may have.

- Taysha shared early, interim data from the first adult patient that was dosed with the investigational gene therapy, TSHA-102, in the REVEAL Adult Study
- The United States (U.S.) Food and Drug Administration (FDA) cleared an investigational new drug (IND) application for Taysha's investigational gene therapy, TSHA-102, in female children with Rett syndrome
- Taysha submitted a clinical trial application to the United Kingdom (U.K.) Medicines and Healthcare products Regulatory Agency (MHRA) to study TSHA-102 in female children with Rett syndrome
- Taysha has secured financing that will help fund important work such as Taysha's Rett syndrome program

What is the REVEAL Adult Study?

- The REVEAL Adult Study is a 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 tolerable dose) of TSHA-102
- The study is currently being conducted at CHU Sainte-Justine, the Université de Montréal mother and Child University Hospital Centre in Montreal, Canada

What are the early, interim findings from the first patient dosed with TSHA-102 in the REVEAL Adult Study?
It is important to note that we cannot make any conclusions on interim findings of a clinical trial until all enrolled subjects are dosed and evaluated for the duration of the study, and once all the data has been collected and analyzed. Making conclusions about interim data may not accurately predict the full risk/benefit profile of an investigational product.

In this investigational study:

- There have been no treatment-emergent serious adverse events (SAEs) related to TSHA-102 in the first patient dosed as of six weeks following administration of TSHA-102
- The first patient dosed has shown improvements based on data collected from the following assessments four weeks following administration of TSHA-102, including:
    - Clinical Global Impression-Improvement (CGI-I) Scale adapted to Rett syndrome – a scale used by doctors to assess improvement or worsening of Rett syndrome on a seven-point scale, starting from one, which means "very much improved," to seven, which means "very much worse"
        - The first patient dosed demonstrated a score of two indicating "much improved"
    - Clinical Global Impressions-Severity (CGI-S) scale – a scale used by doctors to assess overall severity of a patient's illness on a seven-point scale, starting from one, which means "normal, not at all ill," to seven, which means "among the most extremely ill patients"
        - The first patient dosed demonstrated a one-point improvement from the baseline score of six ("severely ill") to a score of five ("markedly ill")

    - Rett Syndrome Behavior Questionnaire (RSBQ) – a 45-item questionnaire used by caregivers to assess Rett syndrome characteristics, including breathing, hand movement, nighttime behavior, facial expression, eye gaze and more
        - The first patient dosed demonstrated a total score improvement of 23 points from the baseline score of 52 to a score of 29
- Caregivers reported no measurable seizure events in the seizure diary as of five weeks following administration of TSHA-102
- There were no marked changes observed as of four weeks post-treatment in the Revised Motor Behavior Assessment (R-MBA), an assessment used by doctors to measure disease behaviors of Rett syndrome

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

- The Independent Data Monitoring Committee (IDMC) reviewed the above initial data from the first participant and recommended to proceed with dosing a second participant; dosing is expected in the third quarter of 2023

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

- The first clinical trial in the U.S. is called the REVEAL Pediatric Study and will study TSHA-102 in female children 5-8 years old, with plans to expand to female children 3-8 years old in future parts of the study
- Additional details about the clinical trial, including inclusion and exclusion criteria, number of participants, study site locations, and timing will be shared as soon as available

If you or your healthcare provider have questions for a member of our Medical Affairs team, please contact medinfo@tayshagtx.com. If you would like to connect with someone from the Taysha Patient Affairs team, please contact patientaffairs@tayshagtx.com.

We would like to thank the entire Rett community and the Rett patient advocacy groups for your continued partnership that helped to support these important milestones. We would also like to acknowledge the individuals and families participating in the trial for contributing to this important research to better understand the potential of gene therapy for Rett syndrome.

We look forward to sharing more information as it is publicly available.

Sincerely,
The Taysha Patient Affairs Team

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