August 12, 2024

Dear Rett Patient Advocacy Leaders,

We are writing to share a series of updates about Taysha's investigational gene therapy for Rett syndrome (TSHA-102) which were provided in a press release today. Please find a summary of these updates below.

- Interim safety data from the first participant in the REVEAL Adolescent & Adult Study who received the high dose level showed that TSHA-102 was generally well-tolerated with no serious adverse events (SAEs) or dose-limiting toxicities as of six weeks following administration.
- Following review of the initial safety data from the first adolescent/adult participant treated with the high dose of TSHA-102, the Independent Data Monitoring Committee (IDMC) approved dosing of a second participant in cohort two (high dose) in the REVEAL Adolescent & Adult Study and dosing of the first participant in cohort two (high dose) in the REVEAL Pediatric Study. These participants have been identified, enrolled and dosing is scheduled.

Taysha also announced today that Health Canada has authorized the clinical trial application (CTA) for TSHA-102 in pediatric patients with Rett syndrome, enabling expansion of the ongoing REVEAL Pediatric Study into Canada. We are grateful for our ongoing partnership with the Ontario Rett Syndrome Association (O.R.S.A.), an organization that provides unwavering advocacy for Rett syndrome families across Canada.

"Having gene therapy research happening right here in Canada is a beacon of hope for our Rett syndrome community. The expansion of the ongoing pediatric clinical trial into Canada represents not only scientific progress in the development of new treatment options for Rett syndrome, but it is also a testament to O.R.S.A.'s ongoing commitment to create the opportunity for families in Canada to potentially participate in the development of investigational treatments for Rett syndrome."

– Sabrina Millson, President, Ontario Rett Syndrome Association

Please find below a list of answers to some frequently asked questions.

What are the goals of the REVEAL Adolescent & Adult (age 12+) and the REVEAL Pediatric Phase 1/2 (ages 5-8) Studies?

- The goals of the REVEAL studies are to evaluate whether TSHA-102 is safe and tolerable, to determine whether it may have beneficial effects, and to assess two dose levels to find the highest tolerable dose.

How many participants have received TSHA-102 across the two REVEAL studies to date?

- A total of five (5) participants have received a one-time administration of TSHA-102.
- In the REVEAL Adolescent & Adult Study, three (3) participants have been dosed.
    - Two (2) participants received the low dose; One (1) participant received the high dose.
- In the REVEAL Pediatric Study, two (2) participants have been dosed.
    - Two (2) participants received the low dose.
- Cohort one (low dose) across both REVEAL studies is now considered complete. Going forward, participants in both REVEAL Phase 1/2 studies will receive high dose TSHA-102.

Where are the REVEAL Phase 1/2 studies being conducted?

- The REVEAL Adolescent and Adult Study is being conducted in the U.S. and Canada. For additional information and a list of clinical trial sites visit https://clinicaltrials.gov/study/NCT05606614.

- The REVEAL Pediatric Study is being conducted in the U.S., Canada, and the U.K. For additional information and a list of clinical trial sites visit https://clinicaltrials.gov/study/NCT06152237.

What are the interim findings from cohort one (low dose) of the REVEAL Studies that were shared in June at the 2024 International Rett Syndrome (IRSF) Scientific Meeting?
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 have been collected and analyzed. Making conclusions about interim data may not accurately predict the full risk/benefit profile of an investigational product.

- Interim data collected in the REVEAL Adolescent & Adult Study from the two participants in cohort one (low dose) showed:
    - No serious adverse events (SAEs) or dose-limiting toxicities related to TSHA-102 as of 52-weeks following administration (participant one) and as of 36-weeks following administration (participant two).
    - Sustained and new improvements across multiple clinician and caregiver-assessed efficacy measures and clinical observations, including motor skills, communication/socialization, autonomic function and seizure events, as of the 52-week (participant one) and 25-week (participant two) time points following administration of TSHA-102.
- Interim data collected in the REVEAL Pediatric Study from the two participants in cohort one (low dose) showed:
    - No SAEs or dose-limiting toxicities related to TSHA-102 as of 22-weeks following administration (participant one) and as of 11-weeks following administration (participant two).
    - Initial improvements across multiple clinician and caregiver-assessed efficacy measures and clinical observations, including motor skills, communication/socialization, autonomic function and seizure events, as of the 12-week (participant one) and 8-week (participant two) time points following administration of TSHA-102.

When will the next release of interim findings from the REVEAL Studies take place?

- Taysha plans to share clinical data from the high dose cohorts and an update on clinical data from the low dose cohorts in both REVEAL trials in the first half of 2025.

What does it mean that Taysha received RMAT designation from the FDA?

- Taysha received Regenerative Medicine Advanced Therapy (RMAT) designation for TSHA-102 following the FDA's review of clinical data supporting the potential of TSHA-102 to address the unmet medical need for patients with Rett syndrome. Receiving RMAT designation helps expedite the development of TSHA-102 by enabling increased dialogue with the FDA.

We would like to thank the entire Rett community and the Rett patient advocacy groups for your continued partnership. We would also like to acknowledge the individuals and families who choose to participate in research to help 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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