November 18, 2024

Dear Rett Syndrome Community,

Neurogene has issued a press release with an important update regarding Neurogene's ongoing Phase 1/2 open-label clinical trial evaluating the investigational gene therapy, NGN-401, for the treatment Rett syndrome. The press release may be found on our website at https://ir.neurogene.com/.

- Last week, we announced that we became aware of an emerging treatment-related serious adverse event (SAE) in a girl who received NGN-401 at the dose of 3E15 vg on November 5, 2024.
- She subsequently had signs of a systemic hyperinflammatory syndrome, a rare and life-threatening immune response that has been reported with systemic exposure to high doses of AAV gene therapies.
- She is in critical condition, and the case is continuing to evolve.

"We are deeply saddened for the family. While no words could possibly provide comfort to her family, we ask the Rett syndrome community to join us in sending heartfelt thoughts to her family, friends and the dedicated clinicians who are caring for her," said Rachel McMinn, Ph.D., Founder and Chief Executive Officer of Neurogene. "The safety of the participants in our clinical trial is and remains our foremost priority as we work to find solutions for this devastating disease."

What is the status of the clinical trial?

- Neurogene is planning to advance NGN-401 at the 1E15 vg dose.
    - In a commitment to full transparency with the U.S. Food and Drug Administration (FDA), Neurogene proactively engaged with the FDA under the START program.
    - The FDA completed a review of the safety data for NGN-401 and allowed Neurogene to proceed with the Phase 1/2 clinical trial using the 1E15 vg dose in the pediatric and the adolescent/adult groups.
    - Neurogene paused further use of the 3E15 vg dose upon initial notification of the SAE and does not plan to enroll any further participants at the 3E15 vg dose level.

Have there been other treatment-related serious adverse events in the clinical trial?

- To date, there have been no other treatment-related SAEs in the clinical trial, including in the five participants who received the 1E15 vg dose and in the first two participants who received the 3E15 vg dose of NGN-401. All treatment-related adverse events (AEs) in the 1E15 vg have been Grade 1 (mild). Most treatment-related AEs are known potential risks of AAV, have been responsive to steroids, and have resolved or are resolving. There have been no signs or symptoms indicative of MeCP2 overexpression toxicity. In addition, there have been no intracerebroventricular (ICV) procedure-related AEs.

Understandably, families will have questions at this time. This letter and the press release have the totality of what we have to share at this time based upon the current information. We remain committed to the Rett syndrome community and will provide updates as we are able.

Sincerely,

Rachel McMinn, Ph.D.
Founder and Chief Executive Officer

NGN-401 is not approved by any regulatory agency for use outside of the clinical trial.

Neurogene Inc.
535 W 24th St, 5th Floor
New York, NY 10011
www.neurogene.co