



June 12, 2023

Dear Rett Syndrome Community,

The purpose of this letter is to provide information about Neurogene's Rett syndrome clinical trial and to communicate the first clinical trial site location.

This first-in-human investigational gene therapy clinical trial is titled: **A Phase 1/2, Open-Label Clinical Study to Evaluate Safety, Tolerability, and Efficacy of NGN-401 in Pediatric Subjects with Rett Syndrome**. This clinical trial will test NGN-401, an investigational adeno-associated virus (AAV) gene therapy that contains a full-length human *MECP2* gene and Neurogene's Expression Attenuation via Construct Tuning (EXACT) transgene regulation technology, in females with Rett syndrome. EXACT gene regulation is designed to express a controlled amount of MeCP2 protein.

The clinical trial is enrolling participants at Texas Children's Hospital.

More details about the clinical trial and the site contact information are available at:

<https://clinicaltrials.gov/ct2/show/NCT05898620>

- This link will be updated with clinical trial site information as additional site locations are opened in the future.

Since this is the first time the investigational gene therapy NGN-401 will be given to humans, the clinical trial will start with a small group of 5 participants. After safety assessments in this group are complete, we will make an informed decision about how to expand the clinical trial for additional participants to enroll.

About the Phase 1/2 Investigational Gene Therapy Clinical Trial for Rett Syndrome

- **This is a prospective, open-label clinical trial**, which means all participants will receive the investigational gene therapy, NGN-401, and will be followed for 5 years, with an additional long-term follow-up for 10 years.
- The investigational gene therapy, NGN-401, will be given as a single **intracerebroventricular (ICV) injection into a ventricle of the brain**.
- This clinical trial will study the investigational gene therapy, NGN-401, in **5 females aged 4-10 years old**, with a diagnosis of typical Rett syndrome with a documented disease-causing mutation in the *MECP2* gene.
 - Participants are similar in age and stage of disease progression to better understand the safety and clinical effects of the investigational gene therapy.
- Individuals with **normal hand function will be excluded** (e.g., holding a pen/pencil effectively and/or drawing a shape).
- Individuals who are **participating in another clinical trial for an investigational medicine** will not be eligible for enrollment.
- **Each participant will be followed for safety and efficacy for 5 years after dosing.**
 - For approximately the first **3 months after the investigational gene therapy is given, families will be required to live (or temporarily relocate) within a 2-hour drive of the clinical trial site**.
 - Living near the clinical trial site is important to monitor safety and for multiple in-person follow-up visits required during the first three months.
 - After the initial safety monitoring period, there will be telephone and in-person visits with the clinical trial site in decreasing frequency over the rest of the 5-year period.
 - After the 5-year period, **it is expected that participants will enroll in a separate long-term observational study that will continue to collect information on safety and effects of the investigational treatment for 10 additional years**.

- **There is a comprehensive travel and expense policy in place to cover trial-related costs and expenses for participating families.**
 - Trial-related costs and expenses are paid by Neurogene; more details on the specific policy can be provided by the clinical trial site.
- **As with any clinical trial, participants may or may not benefit from this research.** There are potential risks, and there is no guarantee that being in this study will help the participant.

Can families living outside of the United States enroll in the US clinical trial?

- Not at this time. We are early in the process of working with regulators on the opportunity to add clinical trial sites outside the US. We will provide further information once it becomes available.

Can families contact someone now to express their interest in being in the clinical trial?

- **Interested families should contact a clinical trial site that is currently enrolling to express their interest.**

Additional information about the clinical trial and trial site(s) may be found at this link:

<https://clinicaltrials.gov/ct2/show/NCT05898620>

Previous letters to the Rett syndrome community, including frequently asked questions from the community, can be viewed at: <https://www.neurogene.com/patients-and-families/>

Sincerely,

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