



March 4, 2024

Dear Rett Syndrome Community,

We are writing to share recent updates to Neurogene's Rett Syndrome clinical trial, ***A Phase 1/2, Open-Label Clinical Study to Evaluate Safety, Tolerability, and Efficacy of NGN-401 in Pediatric Subjects with Rett Syndrome***, which were announced in our March 4th press release which may be found at this [LINK](#).

NGN-401 is an investigational gene therapy being developed as a one-time treatment for Rett syndrome. It is designed to deliver functional copies of the full-length human *MECP2* gene directly to the central nervous system, where there are non-functional copies of the *MECP2* gene that cause Rett Syndrome. NGN-401 uses Neurogene's EXACT technology, which is designed to control *MECP2* transgene expression and avoid overexpression. In our March 4<sup>th</sup> update, we announced that we implemented a series of previously planned changes to expand the study. These changes were made to generate a more robust set of data to inform the design of a future registrational study, or a study that is required before an agency like the FDA can decide on whether a drug is approved for use outside of a clinical trial.

A summary of the updates we announced are outlined here:

- **We expanded the size of the trial** to include a total of 16 participants, and we have added a high dose to be evaluated. Eight participants will be enrolled in the first dosing group (low dose), and eight participants will be enrolled in the second dosing group (high dose).
  - It is typical to evaluate more than one dose in Phase 1 or Phase 1/2 gene therapy trials, and both doses demonstrated safety and efficacy in preclinical animal models.
- **We dosed the third participant in the trial** (low dose group), **and we are pleased to report that NGN-401 has been generally well-tolerated** with no treatment-emergent or procedure-related serious adverse events or signs of overexpression of *MECP2* or *MeCP2*-related toxicity. We continue to plan to share more detailed data from this group, including efficacy data, at the end of the year (Oct – Dec).
- Based on this initial safety and tolerability data, **we can dose the remaining five participants in the first dosing group without a dosing stagger**, or a delay between dosing each participant.

**Additional details about the clinical trial and the site contact information are at the end of this letter and at:**

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

### ***Why did Neurogene decide to add a higher dose in the trial?***

- Dose escalation, or evaluating a higher dose, has always been part of our clinical development strategy for this program. It is typical for Phase 1 or Phase 1/2 gene therapy trials to evaluate more than one dose level since gene therapy is designed to be a one-time treatment. Both the low and high doses were demonstrated to be safe and efficacious in preclinical animal models, and we are enrolling participants in both doses at the same time in the trial.
- The high dose group will use a targeted immunosuppression regimen designed to aid in avoiding immune responses that have been observed in this dose range with other AAV based treatments, while shortening the course of corticosteroids to limit side effects.

### ***Neurogene previously announced that the MHRA approved the clinical trial authorization in the UK; what does that mean for families?***

- The MHRA approval to initiate a clinical trial in the UK will allow eligible UK patients to participate in the clinical trial and would be included in the number of patients in the trial globally (16 participants).
- The next steps are to establish the first clinical trial site in the UK, which may take several months.
- Further communications will be shared at the time the clinical trial site is open and ready for families to contact them.

### *Which clinical trial sites are currently open?*

- **US:** Interested families should contact a clinical trial site that is currently enrolling to express interest.
  - Texas Children’s Hospital: [NeurogeneRettStudy@BCM.edu](mailto:NeurogeneRettStudy@BCM.edu)
  - Boston Children’s Hospital: [rettresearch@childrens.harvard.edu](mailto:rettresearch@childrens.harvard.edu)
  - Colorado Children’s Hospital: [NeurogeneRettStudy@childrenscolorado.org](mailto:NeurogeneRettStudy@childrenscolorado.org)

### *Can families living outside of the United States or the UK enroll in the clinical trial?*

- Since the number of participants expected to enroll is still relatively small, it is expected that families enrolling at this time will be residents of the United States or UK.

### *How can Neurogene be contacted? Is Neurogene on social media?*

Neurogene contact information is:

- By phone: +1-877-237-5020
- Patients and families can reach us at: [patientinfo@neurogene.com](mailto:patientinfo@neurogene.com)
- Healthcare providers can reach us at: [medicalinfo@neurogene.com](mailto:medicalinfo@neurogene.com)
- Our website is: [www.neurogene.com](http://www.neurogene.com)

We are on social media at the following channels:

- Neurogene Inc. Facebook page: <https://www.facebook.com/NeurogeneInc/>
- Neurogene Inc. X (formerly Twitter) handle: <https://twitter.com/NeurogeneInc/>
- Neurogene Inc. LinkedIn profile: <https://www.linkedin.com/company/NeurogeneInc>

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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