November 11, 2024

Dear Rett Syndrome Community,

Today we are sharing an update regarding Neurogene's ongoing Phase 1/2 open-label clinical trial evaluating the investigational gene therapy, NGN-401, in pediatric female participants (ages 4-10 years old) for Rett syndrome. This update includes:

- **Interim safety and efficacy data**
- **The addition of a pilot adolescent/adult dosing group to enroll 3 participants**
- **Additional clinical trial site locations in the U.S., U.K. and Australia**

First and foremost, we extend our sincere appreciation to the families who are participating in the clinical trial. Medical advancements in Rett syndrome would not be possible without their participation, and we are grateful that they have chosen to participate in the NGN-401 trial. We also thank the patient advocacy organizations and the Rett syndrome community for their ongoing partnership. They have provided critical information and insights which helped us design our gene therapy clinical trial, keeping the needs of patients and families at the forefront.

Background on NGN-401

NGN-401 is an investigational gene therapy that Neurogene is developing as a potential one-time treatment for Rett syndrome. Rett syndrome is caused by mutations in the *MECP2* gene and NGN-401 is designed to deliver functional copies of the full-length human *MECP2* gene (also known as a transgene). NGN-401 is delivered by a common neurosurgical procedure called intracerebroventricular (ICV) administration, which has been shown in preclinical studies to deliver gene therapy to the key areas of the brain and nervous system underlying Rett syndrome. NGN-401 uses Neurogene's EXACT™ technology, which is designed to control *MECP2* transgene expression to avoid overexpression toxicity. Two dose levels of NGN-401 (a low dose and a high dose) are being evaluated in the ongoing clinical trial.

Key Information from Today's Update

A safety update and interim efficacy data of the Phase 1/2 clinical trial of NGN-401 were announced. These data are reported as of the data cut-off date of October 17, 2024.*

- The safety data update includes the first five participants in the low-dose group (Cohort 1, 1E15 vg) and the first two participants in the high-dose group (Cohort 2, 3E15 vg).
    - NGN-401 was well-tolerated in the first seven participants.
    - There were no serious adverse events related to NGN-401.
    - There were no adverse events related to the ICV route of administration.
    - Most treatment-related adverse events are known potential risks of adeno-associated virus (AAV) gene therapy, and are resolved or resolving.

  *Today, Neurogene became aware of an emerging treatment-related serious adverse event (SAE) consistent with known risks of AAV gene therapy in the third high-dose participant who was recently dosed.
- Interim efficacy data includes the first four pediatric participants in the low-dose group (Cohort 1) with follow-up of up to 15, 12, 9 and 3 months post-dosing with NGN-401; we plan to share additional interim clinical data in the second half of next year.
    - All four participants showed consistent, concordant and durable improvements across multiple Rett syndrome assessments. All participants acquired skills and/or developmental milestones in one or more core clinical domains of Rett syndrome - hand function/fine motor, language/communication and ambulation/gross motor. New skills and milestones have increased and deepened over time.
    - Enrollment in the low-dose pediatric group (Cohort 1) is expected to be complete by the end of 2024.

A new study group (Cohort 3) in adolescents/adults with Rett syndrome has been added to the clinical trial.

- Cohort 3 will enroll three adolescents/adults with Rett syndrome aged 16 or older.
- This group is designed to enroll 3 participants at the high-dose of NGN-401.
- This pilot cohort is expected to provide initial information on the potential of NGN-401 to treat a broader patient population.

For more information about these updates, please visit www.neurogene.com.

New Clinical Trial Site Locations

Neurogene has opened additional clinical trial sites in the U.S., U.K. and Australia. Please see the current list of enrolling sites below:

- **U.S.**
  - Children's Hospital Colorado: NeurogeneRettStudy@childrenscolorado.org
  - Rush University Medical Center: Giulia_DiMarco@rush.edu
  - Boston Children's Hospital: rettresearch@childrens.harvard.edu
  - Montefiore Medical Center: ADJUKIC@montefiore.org
  - Texas Children's Hospital: NeurogeneRettStudy@BCM.edu
- **U.K.**
  - Royal Hospital for Children and Young People: Loth.RTT200@nhs.scot
  - Manchester University NHS Foundation Trust: genetics.research@mft.nhs.uk
- **Australia**
  - The Children's Hospital at Westmead: schn-chw-rettsyndrome@health.nsw.gov.au

If additional sites are added, site contact information will be found at: https://clinicaltrials.gov/ct2/show/NCT05898620.

Frequently Asked Questions

How can families express their interest in the clinical trial?

- Interested families should directly contact a clinical trial site that is currently enrolling.
- The contact information for all the clinical trial sites is available at: https://clinicaltrials.gov/ct2/show/NCT05898620.

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

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

Neurogene is on social media at the following channels:

- Neurogene Inc. Facebook page: https://www.facebook.com/NeurogeneInc/
- Neurogene Inc. X handle: https://x.com/NeurogeneInc/
- Neurogene Inc. LinkedIn profile: https://www.linkedin.com/company/NeurogeneInc

Sincerely,

Kimberly Trant, RN, MBA
Executive Director, Patient Advocacy and Engagement

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