June 18, 2025

Dear Rett Syndrome Community,

We are pleased to share an overview of recent updates regarding Neurogene's ongoing Phase 1/2 open-label clinical trial evaluating the safety, tolerability and efficacy of the investigational gene therapy, NGN-401, in females with Rett syndrome.

Key Updates in 2025

- Expanded the eligibility age range in our Phase 1/2 clinical trial to include females aged 4 years and older
- Completed dosing of all participants in the trial in the 4-10 years group (n=8) and dosed 2 (of 3) participants in the 11 years and older group; anticipate the 3rd participant will be dosed in the near term which will complete dosing in the trial
- Announced there has been no evidence of HLH (hemophagocytic lymphohistiocytosis) in the recently dosed participants in the trial
    - Incorporated risk mitigation strategies and a monitoring and treatment protocol into the trial for HLH, a rare hyperinflammatory syndrome associated with higher doses of AAV gene therapy
    - HLH has been associated with doses ≥ 1E14 vector genomes/kilogram (vg/kg); the dose being used in the trial is 1E15 total vg, which translates to a lower systemic dose of ~E13 vg/kg
- Announced PRIME designation from the European Medicines Agency

Anticipated Updates:

- Expect to provide an update on plans for a registrational clinical trial with NGN-401 this month; a registrational trial is designed to gather a comprehensive set of efficacy and safety data for review by regulatory agencies with the goal of obtaining regulatory approval to market the product for patients outside of the clinical trial
- Expect to provide additional interim clinical data from the Phase 1/2 clinical trial in the second half of 2025

Background on HLH and Neurogene's Risk Mitigation Strategies

- As previously announced last year, we stopped dosing participants with the 3E15 vg total dose as HLH has only been reported at high doses of AAV (≥ 1E14 vg/kg). There has been no report of this syndrome at levels of AAV that correspond to the 1E15 vg total dose that we are using in the trial (which translates to ~E13 vg/kg).
- Research from other programs indicate that HLH can be reversed if treated early. Out of an abundance of caution, we have added increased monitoring for this rare syndrome and have an additional treatment plan in place should any early signs or symptoms of this condition occur.
- We presented this information at the American Society of Gene and Cell Therapy conference and the International Rett Syndrome Foundation (IRSF) Scientific Meeting, delivering on our promise to educate the community about this rare syndrome and how to monitor for and treat it.

Frequently Asked Questions

How can families find the most recent clinical trial information and status?

Families can find the most recent clinical trial information at https://clinicaltrials.gov/ct2/show/NCT05898620.

- The website has information such as inclusion criteria and clinical trial site contact information.

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
- 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

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.

Important Information

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

Cautionary Note Regarding Forward-Looking Statements

Statements in this communication which are not historical in nature are intended to be, and hereby are identified as, forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current expectations and beliefs of the management of Neurogene, as well as assumptions made by, and information currently available to, management of Neurogene, including, but not limited to, statements regarding: the safety, tolerability and efficacy of NGN-401; the effectiveness of the monitoring and treatment protocol for HLH in Neurogene's Phase 1/2 clinical trial of NGN-401; the ability to reverse cases of AAV-related HLH when following this protocol, the timing of completion of dosing of our adolescent/adult protocol in the NGN-401 Phase 1/2 clinical trial, the timing of announcements of material information regarding our clinical trial results; and our ability to align with regulators on our clinical design plans. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," "on track," and other similar expressions or the negative or plural of these words, or other similar expressions that are predictions or indicate future events or prospects, although not all forward-looking statements contain these words. Forward-looking statements are based on current beliefs and assumptions that are subject to risks, uncertainties and assumptions that are difficult to predict with regard to timing, extent, likelihood, and degree of occurrence, which could cause actual results to differ materially from anticipated results and many of which are outside of Neurogene's control. Such risks, uncertainties and assumptions include, among other things, the risks and uncertainties identified under the heading "Risk Factors" included in Neurogene's Annual Report on Form 10-K for the year ended December 31, 2024, filed with the Securities and Exchange Commission (SEC) on March 24, 2025, Neurogene's Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, filed with the SEC on May 9, 2025, and other filings that the Company has made and may make with the SEC in the future. Nothing in this communication should be regarded as a representation by any person that the forward-looking statements set forth herein will be achieved or that the contemplated results of any such forward-looking statements will be achieved. Forward-looking statements in this communication speak only as of the day they are made and are qualified in their entirety by reference to the cautionary statements herein. Except as required by applicable law, Neurogene undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.