June 30, 2025

Dear Rett Syndrome Community,

Today Neurogene announced key elements of the design of our registrational clinical trial, named Embolden™, for the investigational gene therapy, NGN-401, for Rett syndrome. A registrational clinical 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 a clinical trial. The purpose of this letter is to provide an overview of our plans and address questions you may have.

Which elements of the registrational clinical trial have been agreed upon with the FDA?

- **The age range will be females aged 3 years and older with a Clinical Global Impression-Severity (CGI-S) score of 4–6.**
    - The age range in the registrational clinical trial has expanded from what we had in the Phase 1/2 clinical trial and now includes females age 3 years and older.
- **The dose used will be 1E15 vector genomes (vg) total dose.**
    - This is the same, and only, dose that is currently being used in the Phase 1/2 clinical trial.
- **This is an open-label, single-arm, baseline-controlled trial, meaning:**
    - All participants will receive the investigational gene therapy; there is no placebo group.
    - Each participant will serve as her own baseline (any changes in her status over the course of the trial will be compared to her status before receiving NGN-401).
- **The primary efficacy endpoint will have 2 components, 1) CGI-I, and 2) gain of developmental milestone/skill as determined based on analysis of video capture.**
    - The Clinical Global Impression-Improvement (CGI-I) scale with Rett syndrome anchors will be used by the study physician to determine improvement or worsening in the participant's overall functioning compared to the participant's status prior to receiving NGN-401.
    - Video recordings will be used to capture whether or not a participant has gained any one developmental milestone/skill (from a list of 28) in the 12 month period after receiving the investigational gene therapy. The 28 developmental milestones/skills in the clinical trial assessment include gross motor/ambulation, fine motor/hand function, and communication skills.
        - Neurogene's analysis of the NIH-sponsored, International Rett Syndrome Foundation (IRSF) Rett syndrome natural history study shows patients ages 3 and above rarely learn new skills/reach developmental milestones or relearn skills once lost.

We want to extend our sincere gratitude to the families who shared their time and insights while participating in our research survey and interviews.

- The families confirmed that the gain of any one of these 28 gross motor, fine motor, and communication skills would be considered meaningful to them.

Which elements of the registrational clinical trial are not yet finalized?

- We are working with the FDA to determine the total **number of participants** and the potential to include an endpoint **6 months** after dosing (in addition to the agreed upon 12-month endpoint).
    - Neurogene proposed 18 participants for the trial, which is subject to feedback from the FDA.
- We are still finalizing the **locations of the registrational clinical trial sites** that will enroll new patients.

What happens next?

- We will continue our activities to prepare for the registrational trial.
- We will provide an update when the registrational trial is open for enrollment and post updated information on www.clinicaltrials.gov at that time.
    - There is no mechanism for families to express their interest in registrational trial enrollment at this time, as this trial is not yet enrolling.

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: trial designs, clinical development plans and timing for NGN-401, including elements of the registrational clinical study trial design subject to final approval of the FDA, such as the proposed number of participants in the Embolden trial and the addition of a six month endpoint, and timing of the conversion of the NGN-401 Phase 1/2 clinical trial to a registrational clinical trial; expected future interactions with or positions of the FDA; the safety, tolerability and efficacy of NGN-401; the potential for success of the Embolden registrational clinical trial for NGN-401 for the treatment of Rett syndrome; expected timing for additional interim data from the Company's NGN-401 Phase 1/2 trial for Rett Syndrome; the effectiveness of the monitoring and treatment protocol for HLH in Neurogene's Phase 1/2 clinical trial of NGN-401; and the timing of announcements of material information regarding our clinical trial results. 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, uncertainties regarding interactions with and feedback received from the FDA staff responsible for approving the design of our registrational trial and 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.