Neurogene Reports Positive Interim Data in Pediatric Cohort from NGN-401 Gene Therapy Trial for Rett Syndrome

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Multidomain, durable gains with continued skill acquisition over time

All 8 participants showed functional gains across spectrum of disease severity

35 total developmental milestones/skills acquired across 8 participants

NGN-401 at the registrational dose continues to be generally well-tolerated, with no evidence of HLH

Neurogene management to discuss results during Stifel 2025 Healthcare Conference webcast today at 4:40 p.m. ET

NEW YORK--(BUSINESS WIRE)--Nov. 12, 2025-- Neurogene Inc. (Nasdaq: NGNE), a clinical-stage company founded to bring life-changing genetic medicines to patients and families affected by rare neurological diseases, today announced positive, updated interim clinical data in the pediatric cohort (ages 4-10 cohort) from its ongoing Phase 1/2 trial evaluating NGN-401 gene therapy for the treatment of females with Rett syndrome.

“Updated interim data from our Phase 1/2 trial of NGN-401 show that all pediatric participants, regardless of baseline disease severity, have gained developmental milestones/skills or experienced functional gains, with durability and continued skill acquisition over time,” said Rachel McMinn, Ph.D., Founder and Chief Executive Officer of Neurogene. “These skill gains far exceed the bar for our Embolden registrational trial, and coupled with NGN-401’s tolerability profile at the 1E15 vg dose, create the potential for a best-in-class gene therapy for Rett syndrome. It is gratifying to see the benefits of our strategy to use local delivery to the brain coupled with the naturally occurring full-length human gene as a key to unlocking meaningful efficacy in this devastating disorder. Moreover, we are the only company evaluating a gene therapy in children with Rett syndrome as young as three years old in a single trial, which provides us an efficient path to market and first-in-class potential.”

“In gene therapy for Rett syndrome, caregivers value improvements across multiple domains – hand function, gross motor skills and communication – especially when new abilities are gained and sustained over time. The interim NGN-401 results are particularly encouraging, showing continued skill acquisition across these areas with durable gains observed up to 24 months post treatment,” said Bernhard Suter, M.D., Medical Director of the Blue Bird Circle Rett Center at Texas Children’s Hospital, Associate Professor of Pediatrics and Neurology at Baylor College of Medicine, and principal investigator in the NGN-401 Phase 1/2 clinical trial. “These gains also translate into meaningful improvements in daily function, reduced caregiver burden and greater ability to express needs and wants, while supporting more complex tasks that foster greater independence.”

Interim Phase 1/2 Clinical Data

Safety Data (N=10; as of data cutoff date of October 30, 2025)

- NGN-401 at the 1E15 vg dose has been generally well-tolerated with a favorable safety profile across the pediatric cohort and the adolescent/adult cohort (ages ≥ 11 cohort)
- All treatment-related adverse events have been mild (Grade 1) or moderate (Grade 2) in severity and the majority are known potential risks of AAV and have resolved or are resolving
- No evidence of hemophagocytic lymphohistiocytosis (HLH) has been observed in any participant

Efficacy Data (N=8 in the pediatric cohort; as of data cutoff date of October 30, 2025)

- All pediatric participants experienced functional gains across the spectrum of disease severity, with an aggregate 35 developmental milestones/skills gained across core clinical domains of Rett syndrome – hand function/fine motor, language/communication and ambulation/gross motor
    - All developmental milestones/skills gained have been durable, with multidomain improvements observed in key domains
    - Participants with longer term follow-up continued to gain developmental milestones/skills, with notable gains in executive function and motor planning for those with the longest follow-up
    - Developmental milestones/skills have been gained by participants recently dosed with six months of follow-up, consistent with previously dosed participants
- Previously reported improvements in the Clinical Global Impression-Improvement (CGI-I) have been durable

- Additional clinical data will be reported in 2026

Neurogene management will discuss these results and the Embolden™ registrational trial at the Stifel 2025 Healthcare Conference today at 4:40 p.m. ET. A live webcast presentation will be accessible from the Investor Relations section of Neurogene's website under events, where a replay of the event will also be available for a limited time.

About Neurogene

The mission of Neurogene is to treat devastating neurological diseases to improve the lives of patients and families impacted by these rare diseases. Neurogene is developing novel approaches and treatments to address the limitations of conventional gene therapy in central nervous system disorders. This includes selecting a delivery approach to maximize distribution to target tissues and designing products to maximize potency and purity for an optimized efficacy and safety profile. The Company's novel and proprietary EXACT™ transgene regulation platform technology allows for the delivery of therapeutic levels while limiting transgene toxicity associated with conventional gene therapy. Neurogene has constructed a state-of-the-art gene therapy manufacturing facility in Houston, Texas. CGMP production of NGN-401 was conducted in this facility and will support pivotal clinical development activities. For more information, visit www.neurogene.com.

About NGN-401

NGN-401 is an investigational AAV9 gene therapy being developed as a one-time treatment for Rett syndrome. It is the first clinical candidate to deliver the full-length human *MECP2* gene under the control of Neurogene's EXACT™ transgene regulation technology. EXACT technology is an important advancement in gene therapy for Rett syndrome, specifically because the disorder requires a treatment approach that enables targeted levels of *MECP2* transgene expression without causing overexpression-related toxic effects associated with conventional gene therapy.

NGN-401 was selected by the U.S. Food and Drug Administration (FDA) for its START Pilot Program and has also received Regenerative Medicine Advance Therapy (RMAT) designation, orphan drug designation, Fast Track designation and rare pediatric designation from the FDA. Neurogene was previously granted an INTERACT meeting with the FDA regarding the EXACT technology. NGN-401 also received Priority Medicines (PRIME) designation, orphan designation and advanced therapy medicinal product designation from the European Medicines Agency (EMA) and the Innovative Licensing and Application Pathway (ILAP) designation from the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA).

Cautionary Note Regarding Forward-Looking Statements

Statements in this press release 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 therapeutic potential and utility, efficacy and clinical benefits of NGN-401; the safety and tolerability profile of NGN-401; the applicability of reported interim results from the NGN-401 Phase 1/2 clinical trial to other participants or potential participants, including adolescent or adult participants; the potential for NGN-401 to be a best-in-class gene therapy for Rett syndrome; trial designs and clinical development plans for our Embolden™ registrational clinical trial of NGN-401 for Rett Syndrome, including timing of anticipated enrollment and completion of the enrollment in our clinical trial; the response rate, expected durability and deepening of clinical data results from our NGN-401 clinical trials; expected timing for release of additional data from our Phase 1/2 clinical trial of NGN-401; the potential superiority of ICV administration; patient and KOL sentiment relating to priorities on selecting potential gene therapy treatments; the potential for success of the Embolden registrational clinical trial of NGN-401 for Rett Syndrome; and expected future interactions with or positions of the FDA or foreign regulatory authorities. 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 June 30, 2025, filed with the SEC on August 11, 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.

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