Neurogene Announces First Patient Dosed in High-Dose Cohort of NGN-401 Gene Therapy Clinical Trial for Rett Syndrome

June 18, 2024

High-dose NGN-401 has been well-tolerated, and low-dose NGN-401 continues to show a favorable safety profile

Interim safety data presented at the International Rett Syndrome Foundation (IRSF) ASCEND Summit

NEW YORK--(BUSINESS WIRE)--Jun. 18, 2024-- 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 that the first patient in Cohort 2 received high-dose NGN-401 gene therapy in the Phase 1/2 trial for female pediatric patients with Rett syndrome, and high-dose NGN-401 has been well-tolerated following dosing in May 2024. The Company also provided an update on interim safety data on the first three patients in the low-dose cohort during the IRSF ASCEND 2024 Rett Syndrome National Summit, which shows that NGN-401 has continued to have a favorable safety profile with no new treatment-related adverse events (AEs).

“We have met an important program milestone of initiating dosing in the high-dose cohort of our Rett syndrome gene therapy trial, and we are pleased to share that high-dose NGN-401 has been well-tolerated thus far with an early favorable safety profile,” said Rachel McMinn, Ph.D., Founder and Chief Executive Officer of Neurogene. “We intentionally designed NGN-401 with the goal of creating a best-in-class treatment option by leveraging what we believe to be the optimal route of administration to deliver consistent and tightly controlled full-length *MECP2* expression to key areas of the brain and nervous system, and today’s safety update underscores NGN-401’s potential to deliver on that profile. We remain on track to share interim efficacy data from the low-dose cohort in the fourth quarter of 2024 and look forward to working with the FDA as part of its START Pilot Program to accelerate the development of NGN-401.”

During an oral and poster presentation, 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 clinical trial, will present an updated safety presentation on the first three low-dose patients. These data show:

- NGN-401 continues to have a favorable safety profile
- There have been no new treatment-related adverse events (AEs) since the last safety update during the American Society of Gene and Cell Therapy (ASGCT) Annual Meeting; all treatment-related AEs have been mild/Grade 1, and transient or resolving, and most AEs are known potential risks of AAV
- No signs or symptoms indicative of MeCP2 overexpression toxicity have been reported, including in the patient with a mild genetic variant predicted to result in residual MeCP2 expression
- No treatment-emergent or intracerebroventricular (ICV) procedure-related serious AEs

Dr. Suter will be joined at the podium by Neurogene’s Chief Scientific Officer, Stuart Cobb, Ph.D., who will present an overview of Neurogene’s EXACT™ transgene regulation technology.

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™ technology. The EXACT technology utilized in NGN-401 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 one of the Center for Biologics Evaluation and Research programs selected by the U.S. Food and Drug Administration (FDA) for its START Pilot Program. NGN-401 previously received 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 orphan designation and advanced therapy medicinal product designation from the European Medicines Agency and the Innovative Licensing and Application Pathway designation from the United Kingdom’s Medicines and Healthcare products Regulatory Agency.

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 is expected to support pivotal clinical development activities. For more information, visit www.neurogene.com.

Cautionary Note Regarding Forward-Looking Statements

Statements in this press release that 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; trial designs, clinical development plans and timing of the presentation of clinical trial data for NGN-401, and the anticipated benefits of participation in the FDA's START program. 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: risks related to the timing and success of enrolling patients in either or both of the cohorts of Neurogene's Phase 1/2 clinical trial of NGN-401 for the treatment of Rett syndrome; the expected timing and results of dosing of patients in Neurogene's NGN-401 clinical trial; the potential for negative impacts to patients resulting from using a higher dose of NGN-401 in Cohort 2 of the Phase 1/2 clinical trial for the treatment of Rett syndrome, including the risk of more significant or more severe adverse events; the risk that the Company may not be able to report its data on the predicted timeline; risks related to Neurogene's ability to obtain regulatory approval for, and ultimately commercialize, NGN-401;and other risks and uncertainties identified under the heading "Risk Factors" included in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, filed with the Securities and Exchange Commission ("SEC") on March 18, 2024, or its Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 filed with the SEC on May 10, 2024, 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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Company Contact:
Cara Mayfield
Vice President, Corporate Affairs
cara.mayfield@neurogene.com

Investor Contact:
Melissa Forst
Argot Partners
Neurogene@argotpartners.com

Source: Neurogene Inc.