# Neurogene Announces Expansion and Plans for More Rapid Patient Enrollment of Rett Syndrome Gene Therapy Clinical Trial

March 4, 2024

*Ongoing Phase 1/2 clinical trial for NGN-401 to include additional patients in Cohort 1 and a dose-escalation cohort*

*Both previously planned updates are expected to provide a more robust dataset to inform future registrational trial design*

*Removal of staggered dosing in Cohort 1 expected to enable the anticipated completion of Cohort 1 dosing in the second half of 2024*

*Third patient dosed in Cohort 1*

NEW YORK--(BUSINESS WIRE)--Mar. 4, 2024-- Neurogene Inc. (NASDAQ: NGNE) ("Neurogene" or "the Company"), a clinical-stage company founded to bring life-changing genetic medicines to patients and families affected by rare neurological diseases, today announced the expansion of its ongoing Phase 1/2 gene therapy clinical trial for NGN-401 for female pediatric patients with Rett syndrome and updates to enable more rapid enrollment in the trial.

"We are excited to share that we have met our first 2024 program milestones, including dosing the third patient in the NGN-401 Phase 1/2 trial for Rett syndrome and expansion of the trial to include more patients in the current dosing cohort and the addition of a high dose cohort," said Founder and Chief Executive Officer, Rachel McMinn, Ph.D. "Our clinical development strategy has been to build flexibility and optionality early in the program with two concurrent dose cohorts designed to generate a more complete data package, which we expect will inform future registration discussions with global health authorities. We expect that expansion of the clinical trial and the removal of staggered dosing in Cohort 1 will enable us to treat more patients in a shorter period of time. Based on this update, we expect to complete enrollment of Cohort 1 in the second half of 2024."

**Rett Syndrome Program Update**

The U.S. Phase 1/2 clinical protocol for NGN-401 has been amended as follows:

- Cohort 1, which specifies a total dose of $1\times10^{15}$ total vector genomes delivered via intracerebroventricular (ICV) administration, was expanded from five patients to eight patients. The dosing stagger has been removed from Cohort 1, enabling the remaining patients to be dosed in parallel.
- Cohort 2, which specifies a total dose of $3\times10^{15}$ total vector genomes delivered via ICV administration, was added and is expected to include a total of eight patients.
- The first three patients in Cohort 2 will be dosed in a staggered manner, with first patient dosing expected in the second quarter of 2024; pending Data and Safety Monitoring Board review of the safety data for the first three patients, the protocol will allow parallel enrollment for the remaining patients in Cohort 2.
- In addition, the protocol includes a targeted immunosuppression regimen for Cohort 2, designed as a preventative measure to aid in avoiding potential adeno-associated virus (AAV)-related immune responses that have been observed with other AAV-based products in this dose range. The immunosuppression regimen includes the use of rituximab and sirolimus, along with a shortened course of corticosteroids. Cohort 1 immunosuppression remains unchanged with corticosteroids alone.

A similar protocol amendment was submitted to the UK regulatory authorities. These changes are consistent with the Company's guidance issued in January 2024. Importantly, in comprehensive nonclinical studies, the EXACT transgene regulation technology embedded in NGN-401 was shown to mechanistically constrain *MECP2* transgene expression levels, allowing for the potential to dose escalate and enhance biodistribution to the brain, without the commensurate increase in *MECP2* transgene expression observed with conventional gene therapy. Both doses in the updated protocol are below the "no observed adverse effect" level established in rodent and nonhuman primate models.

A third patient was dosed in the trial early in the first quarter. NGN-401 has been generally well-tolerated and there have been no treatment-emergent or procedure-related serious adverse events, or signs of overexpression-related toxicity observed in any patient.

Neurogene remains on track to report interim clinical data from Cohort 1 in the fourth quarter of 2024 and additional data, including from Cohort 2, in the second half of 2025.

**About EXACT**

Neurogene's novel and proprietary EXACT gene regulation platform technology is a self-contained transgene regulation platform that can be tuned to deliver a desired level of transgene expression within a narrow and therapeutically relevant range, with the goal of avoiding transgene-related toxicities associated with conventional gene therapy. EXACT is compatible with viral and non-viral delivery platforms.

**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. The robust

nonclinical data package for NGN-401 provides evidence of a potentially compelling efficacy and safety profile in Rett syndrome.

**About Neurogene**

Neurogene's mission 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 by 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. GMP production of NGN-401 was conducted in this facility and will support pivotal clinical development activities. For more information, visit www.neurogene.com.

**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, trial designs, clinical development plans and timing for NGN-401, including completion of Cohort 1 dosing, first patient dosing of Cohort 2 and anticipated clinical data results in NGN-401 Phase 1/2 trial for Rett syndrome and anticipated impact of expansion of Phase 1/2 trial and removal of staggered dosing in Cohort 1. 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 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 result 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 the timing and success of enrolling patients in the expanded cohort of our Phase 1/2 clinical trial of NGN-401 for the treatment of Rett syndrome, the expected timing and results of dosing of patients in our clinical trials, including NGN-401, the potential that we may not be able to expand our Phase 1/2 clinical trial of NGN-401 for the treatment of Rett syndrome into the UK based on a variety of factors, including but not limited to any decisions of regulatory authorities, costs of expanding the trial in the UK, the availability of suitable clinical test sites, the ability to enroll patients in the UK or other reasons, 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, the risk that we may not be able to report our data on the predicted timeline, our limited operating history; the risk that we may not be able to raise adequate additional capital to finance our operations, complete our clinical trials and commercialize our products, risks related to our ability to obtain regulatory approval for, and ultimately commercialize, our product candidates, including NGN-401; risks related to the outcome of non-clinical testing and early clinical trials for our product candidates, including the ability of those trials to satisfy relevant governmental or regulatory requirements; risks related to our limited experience in designing clinical trials and lack of experience in conducting clinical trials; expectations regarding the market and potential for Neurogene's current product candidates, including NGN-401; the substantial competition we face in discovering, developing, or commercializing products, including NGN-401; expectations regarding the potential tolerability, safety or efficacy for our current product candidates, including NGN-401; our ability to attract, hire, and retain skilled executive officers and employees; our ability to protect our intellectual property and proprietary technologies; risks related to our reliance on third parties, contract manufacturers, and contract research organizations and legislative, regulatory, political and economic developments and general market conditions. These and other risks and uncertainties are identified under the heading "Risk Factors" included in our periodic reports that we file with the Securities and Exchange Commission.

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, we do not undertake any 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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