Neurogene Doses First Patients in Phase 1/2 Trial of NGN-401 for the Treatment of Female Pediatric Patients with Rett Syndrome

November 30, 2023

Two pediatric patients with Rett syndrome dosed in the United States with NGN-401, Neurogene's lead gene therapy product candidate leveraging its proprietary EXACT gene regulation technology

NGN-401 has been well-tolerated to date with no treatment-emergent or procedure-related serious adverse events (SAEs) or transgene-related overexpression toxicity

Third patient dosing anticipated in 1Q24, and interim efficacy data from multiple patients in the first cohort remains on track for 4Q24

NGN-401 design and delivery approach optimized to maximize efficacy and safety profile

New York, NY – November 30, 2023 – Neurogene Inc., a clinical-stage company founded to bring life-changing genetic medicines to patients and families affected by rare neurological diseases, announced today the dosing of the first two female pediatric patients with Rett syndrome in its ongoing Phase 1/2 trial of NGN-401. Rett syndrome is a debilitating, X-linked, neurodevelopmental disorder with significant unmet medical need. To date, NGN-401 has been well-tolerated with no treatment-emergent or procedure-related SAEs, and no signs of transgene-related overexpression toxicity.

NGN-401 is an investigational adeno-associated virus (AAV) gene therapy candidate for Rett syndrome purposefully designed and administered to maximize the therapeutic activity while averting transgene overexpression toxicities. NGN-401 delivers the full-length human methyl cytosine binding protein 2 (*MECP2*) gene, providing an optimal gene replacement approach. Moreover, NGN-401 leverages Neurogene's novel and proprietary Expression Attenuation via Construct Tuning (EXACT) gene regulation technology, which provides highly controlled and consistent MeCP2 expression on a cell-by-cell basis, thus avoiding the overexpression related toxicities associated with conventional gene therapy. In non-clinical studies with NGN-401 at clinically relevant doses, cardinal features of Rett syndrome were ameliorated, and no overexpression toxicity was observed. These data were part of the robust non-clinical package that supported the U.S. Food and Drug Administration's (FDA) decision to allow Neurogene to proceed directly into a pediatric population for its first-in-human study. NGN-401 has also been granted Orphan Drug Designation, Rare Pediatric Disease Designation, and Fast Track Designation by the FDA.

"While gene therapy has proven to be a powerful tool in the treatment armamentarium for a number of devastating genetic conditions, the highly variable transgene expression associated with conventional gene therapies has limited its application in many complex neurological disorders, especially in Rett syndrome, in which *MECP2* transgene overexpression is toxic," said Bernhard Suter, M.D., Principal Investigator of the Phase 1/2 clinical trial, and Associate Professor of Pediatrics and Neurology at Baylor College of Medicine and Texas Children's Hospital. "NGN-401 has been well tolerated to date in the first two patients dosed, consistent with the wide safety margins established in non-clinical studies conducted in disease models and in normal non-human primates."

Ongoing Phase 1/2 Trial Update

The first-in-human, open-label, single-arm, multi-center Phase 1/2 clinical trial (NCT05898620) is evaluating NGN-401 at a dose of 1×10^{15} total vector genomes to assess the safety and tolerability of NGN-401 in female pediatric patients ages 4-10 with Rett syndrome. NGN-401 is administered as a one-time treatment using intracerebroventricular (ICV) administration, which has been shown to maximize the delivery of the therapeutic *MECP2* gene to key areas of the brain underlying Rett syndrome pathobiology. Clinical-grade NGN-401 for this trial was manufactured at Neurogene's Good Manufacturing Practices (GMP) facility.

The first two patients were dosed sequentially in the third and fourth quarter of 2023 at Texas Children's Hospital, an internationally recognized pediatric research center affiliated with Baylor College of Medicine, and the first clinical trial site to be opened in the U.S. for this study. Dr. Daniel Curry, M.D., director, Functional Neurosurgery and Epilepsy Surgery at Texas Children's Hospital and professor, Neurosurgery and Surgery at Baylor College of Medicine, performed the procedure to administer the gene therapy.

NGN-401 has been well-tolerated to date, with no treatment-emergent or procedure-related SAEs, and no observations of

transgene-related overexpression. Pending successful completion of the trial's upcoming pre-planned independent Data and Safety Monitoring Board review, Neurogene expects to dose a third patient in the first quarter of 2024. The first cohort is expected to enroll a total of five female pediatric patients, with a planned expansion pending additional data and subject to review by health authorities.

"NGN-401 was purposefully designed to deliver a therapeutic benefit with the full length MECP2 gene, avoid toxicity associated with overexpression, and leverage the ICV route of delivery to maximize the biodistribution of the transgene to key areas of the brain underlying Rett syndrome. Based on published peer-reviewed non-clinical research, we know that Rett syndrome is caused by loss of function of *MECP2* in the brain and spinal cord, and therefore we believe delivering robust transgene expression in these areas is essential for enabling a clinically meaningful benefit," said Rachel McMinn, Ph.D., Founder and Chief Executive Officer of Neurogene. "We are encouraged by the tolerability profile observed in our first two pediatric patients, and look forward to collecting sufficient follow up data on a larger number of patients to inform the therapeutic potential of NGN-401, which we believe could serve as a best-in-class therapy. We remain on track to report preliminary clinical data from the first cohort of patients in this trial in the fourth quarter of 2024, with additional data from an expanded number of patients expected in the second half of 2025."

Dr. McMinn added, "On behalf of the entire Neurogene team, we extend our gratitude to all those making this study possible, with special appreciation for the patients and their families. Your resilience, courage, and support not only contribute to the progress of this research, but also inspire hope within the entire Rett syndrome community. Together, we have the potential to make a meaningful impact on improving the many lives affected by this devastating disease."

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

About Rett Syndrome

Rett syndrome is a rare genetic disorder that occurs almost exclusively in females, and leads to severe impairments that affect nearly every aspect of their lives. This includes their ability to speak, walk, eat, and breathe. The impact on patients and families is profound. Most females are nonverbal, lack motor skills, and require 24-hour care for all activities of daily living. Many females with Rett syndrome appear to understand the world around them, leaving many caregivers feeling that their daughters are intellectually and emotionally intact.

Rett syndrome is an X-linked, progressive, neurodevelopmental disorder. It has an estimated worldwide incidence of 1 out of every 10,000-15,000 live female births.

The incidence in males is currently unknown. Advances in genetic testing and phenotypic identification have revealed that *MECP2* mutations in males are responsible for a wide spectrum of neurological disorders, including Rett syndrome.

Rett syndrome is caused by mutations in the *MECP2* gene that lead to deficiency of the methyl cytosine binding protein 2, an important protein responsible for normal function in the brain and other parts of the nervous system.

Females with Rett syndrome typically have normal development until 6-18 months of age, followed by a progressive deterioration of acquired skills such as gross and fine motor skills, purposeful hand function and communication. They subsequently develop stereotypic hand movements such as hand-wringing.

Over time females may develop muscle contractures, rigidity, and debilitating scoliosis, along with periods of recurrent seizures, and burdensome gastrointestinal and breathing abnormalities.

Although there are treatments available for Rett syndrome, there is no treatment option that addresses the root cause of disease and a significant unmet need still exists for new treatment options.

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 gene 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.

Neurogene Contacts:

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

Media:
David Rosen
Argot Partners
david.rosen@argotpartners.com

Cautionary Note Regarding Forward-Looking Statements

This communication contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended (Securities Act). 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. 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," 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. Statements that are not historical facts are forward-looking statements. Forward-looking statements in this communication include, but are not limited to, statements regarding the expected enrollment of and timing of data from Neurogene's Phase 1/2 clinical trial; statements regarding the potential of, and expectations regarding, Neurogene's programs, including NGN-101, NGN-401 and its research stage opportunities; the expected dosing of additional patients in Neurogene's Phase 1/2 clinical trial; statements by Neurogene's Founder and Chief Executive Officer. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: Neurogene's limited operating history; the significant net losses incurred since inception of Neurogene; the ability to raise additional capital to finance operations; the ability to advance product candidates through non-clinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, Neurogene's product candidates; the outcome of non-clinical testing and early clinical trials for Neurogene's product candidates, including the ability of those trials to satisfy relevant governmental or regulatory requirements; Neurogene's limited experience in designing clinical trials and lack of experience in conducting clinical trials; the ability to identify and pivot to other programs, product candidates, or indications that may be more profitable or successful than Neurogene's current product candidates; expectations regarding the market and potential for Neurogene's current product candidates; the substantial competition Neurogene faces in discovering, developing, or commercializing products; expectations regarding the potential tolerability, safety or efficacy for Neurogene's current product candidates; the ability to attract, hire, and retain skilled executive officers and employees; the ability of Neurogene to protect its intellectual property and proprietary technologies; reliance on third parties, contract manufacturers, and contract research organizations; Neurogene's ability to consummate the proposed merger transactions with Neoleukin Therapeutics, Inc. (Neoleukin); the risk that the conditions to the closing of the proposed transactions are not satisfied, including the failure to obtain stockholder approval for the proposed transactions from Neoleukin's stockholders or to complete the transactions in a timely manner or at all; uncertainties as to the timing of the consummation of the proposed transactions; risks related to Neoleukin's continued listing on the Nasdaq Capital Market until closing of the proposed transactions; risks related to Neoleukin's and Neurogene's ability to correctly estimate their respective operating expenses and expenses associated with the proposed transactions, as well as uncertainties regarding the impact any delay in the closing would have on the anticipated cash resources of the combined company upon closing and other events and unanticipated spending and costs that could reduce the combined company's cash resources; the occurrence of any event, change or other circumstance or condition that could give rise to the termination of the merger agreement or Neurogene's financing transaction; competitive responses to the proposed transactions; unexpected costs, charges or expenses resulting from the proposed transactions; the outcome of any legal proceedings that may be instituted against Neoleukin, Neurogene or any of their respective directors or officers related to the merger, the financing transaction, or the proposed transactions contemplated thereby; the expected trading of the combined company's stock on Nasdaq Capital Market under the ticker symbol "NGNE" and the combined company's ability to remain listed following the proposed transactions; and legislative, regulatory, political and economic developments and general market conditions. The foregoing review of important factors that could cause actual events to differ from expectations should not be

construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors included in Neoleukin's most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the Securities and Exchange Commission (SEC), the registration statement on Form S-4 filed with the SEC by Neoleukin, as well as risk factors associated with companies, such as Neurogene, that operate in the biopharma industry. There can be no assurance that the conditions of the proposed transactions will be satisfied or that future developments affecting Neurogene, Neoleukin or the proposed transactions will be those that have been anticipated. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond Neurogene and Neoleukin's control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. 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.

This communication contains hyperlinks to information that is not deemed to be incorporated by reference into this communication.

Important Additional Information About the Proposed Transactions Has Been Filed with the SEC

This communication is not a substitute for the registration statement or for any other document that Neoleukin has filed with the SEC in connection with the proposed transactions. In connection with the proposed transactions, Neoleukin has filed a registration statement on Form S-4 that contains a proxy statement/prospectus of Neoleukin. NEOLEUKIN URGES INVESTORS AND STOCKHOLDERS TO READ THE REGISTRATION STATEMENT, PROXY STATEMENT/PROSPECTUS AND ANY OTHER RELEVANT DOCUMENTS THAT MAY BE FILED WITH THE SEC, AS WELL AS ANY AMENDMENTS OR SUPPLEMENTS TO THESE DOCUMENTS, CAREFULLY AND IN THEIR ENTIRETY BECAUSE THEY CONTAIN IMPORTANT INFORMATION ABOUT NEOLEUKIN, NEUROGENE, THE PROPOSED TRANSACTIONS AND RELATED MATTERS. Investors and stockholders can obtain free copies of the proxy statement/prospectus and other documents filed by Neoleukin with the SEC through the website maintained by the SEC at www.sec.gov. In addition, investors and stockholders should note that Neoleukin communicates with investors and the public using its website (www.neoleukin.com), the investor relations website (https://investors.neoleukin.com/) where anyone can obtain free copies of the proxy statement/prospectus and other documents filed by Neoleukin with the SEC and stockholders are urged to read the proxy statement/prospectus and the other relevant materials before making any voting or investment decision with respect to the proposed transactions.

Participants in the Solicitation

Neoleukin, Neurogene and their respective directors and executive officers may be considered participants in the solicitation of proxies in connection with the proposed transaction. Information about Neoleukin's directors and executive officers who may, under the rules of the SEC, be deemed participants in the solicitation of the stockholders of Neoleukin in connection with the proposed transaction, including a description of their direct or indirect interests, by security holdings or otherwise, is set forth in the proxy statement/prospectus included in the registration statement on Form S-4 initially filed by Neoleukin with the SEC on August 21, 2023, as subsequently amended on September 28, 2023, October 18, 2023 and November 8, 2023.