Neurogene Reports Positive Interim Efficacy Data from First Four Low-Dose Pediatric Participants in NGN-401 Gene Therapy Clinical Trial for Rett Syndrome

November 11, 2024

All participants experienced a 2-point improvement in the clinician-rated Clinical Global Impression-Improvement (CGI-I) scale from baseline

All participants improved in the caregiver-completed Rett Syndrome Behavior Questionnaire (RSBQ), ranging from 28 to 52 percent improvement from baseline

All participants with disruptions in sleep, constipation, and dysphagia at baseline demonstrated objective improvements

Gains in skill and developmental milestones were consistent, durable, deepened over time and demonstrated improvements not expected based on natural history data

Low-dose NGN-401 well-tolerated with favorable safety profile

Company plans to provide an update of registrational trial design in the first half of 2025

Company to host investor/analyst webcast today, November 11, 2024, at 4:30 p.m. ET

NEW YORK--(BUSINESS WIRE)--Nov. 11, 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 positive interim clinical data in the first four participants in the low-dose cohort of its ongoing Phase 1/2 open-label trial designed to evaluate NGN-401 gene therapy for the treatment of female pediatric patients with Rett syndrome. Low-dose NGN-401 has demonstrated a favorable safety profile.

"Today marks an important day for Neurogene and the Rett syndrome community as we share positive interim data for NGN-401 from our low-dose cohort that shows the first four participants demonstrated meaningful gains of skills and developmental milestones in core clinical domains of Rett syndrome, which are not expected to occur when compared to and contextualized against the natural history of Rett syndrome. Data were also concordant across multiple scales and show consistency of effect across patients, despite their unique clinical presentations at baseline," said Rachel McMinn, Ph.D., Founder and Chief Executive Officer of Neurogene. "We are incredibly thankful to the participants, caregivers and Rett syndrome trial sites who are participating in our study."

"Rett syndrome is a devastating neurodevelopmental disease that is incredibly challenging for patients and their caregivers given there are no treatment options available to address the underlying cause of the disease," said Aleksandra Jacobs, M.D., Ph.D., Professor of Pediatric Neurology, Albert Einstein College of Medicine and Director of the Center for Rett Syndrome in the Children's Hospital at Montefiore Medical Center. "The totality of the outcomes shared today with NGN-401 gene therapy have never been seen before in the treatment of Rett syndrome. Notably, these initial participants acquired developmental skills post-treatment during the period in which the natural history of Rett syndrome indicates girls would not. I look forward to the continued progress in this program and additional data to come."

Interim Clinical Data as of Data Cut-Off Date of October 17, 2024

Interim Safety Data (N=7)*

Low-dose (1E15 vg) and high-dose (3E15 vg) NGN-401 have been well-tolerated with a favorable safety profile in the first seven pediatric participants (N=5 low-dose; N=2 high-dose):

- No treatment-related serious adverse events (SAEs)
- No signs or symptoms indicative of MeCP2 overexpression toxicity
- Most treatment-related adverse events (AEs) are known potential risks of adeno-associated virus (AAV), have been responsive to steroids, and are resolved or are resolving
- No intracerebroventricular (ICV)-related AEs
- No seizures for any participants following NGN-401 treatment

*Today, Neurogene became aware of an emerging treatment-related SAE consistent with known risks of AAV gene therapy in the third high-dose participant who was recently dosed.

Low-Dose Interim Efficacy Data (N=4)

The first four participants (age range 4-7 years old, efficacy assessments at 15, 12, 9, and 3 months post-dosing) in low-dose Cohort 1 showed consistent, concordant and durable improvements across key Rett syndrome assessments:

- All participants achieved a rating of "much improved," or a score of 2, on the clinician-rated Clinical Global Impression Scale of Improvement (CGI-I) from baseline; a score of $\leq$ 3 is considered clinically meaningful
- All participants improved in the caregiver-completed Rett Syndrome Behavior Questionnaire (RSBQ), ranging from 28 to 52 percent improvement from baseline
- All participants acquired skills and/or developmental milestones in one or more core clinical domains of Rett syndrome - hand function/fine motor, language/communication and ambulation/gross motor

- These improvements include complex skills that are rarely learned in this population and skills that are rarely relearned after developmental regression when compared to the NIH-sponsored Rett syndrome natural history
- New skills and milestones have increased and deepened over time

Initiation of Adolescent/Adult Cohort in NGN-401 Clinical Trial

Neurogene announced today that it has initiated an adolescent/adult Cohort 3 to gain initial data on the potential of NGN-401 to treat a broader patient population. This cohort is designed to enroll three participants ages 16 and above at the high dose.

FDA Alignment on CMC Requirements to Initiate Future Registrational Trial and Support Potential Product Launch

Neurogene also announced today that it has gained alignment with the FDA on its potency assay strategy for NGN-401, which is necessary to have in place prior to initiating a registrational trial. In addition, the FDA is aligned with Neurogene's manufacturing scale-up plans for NGN-401, which is important to support a future commercial product launch.

Completed and Upcoming Milestones for the NGN-401 Program

- Expect to complete enrollment in the low-dose pediatric Cohort 1 (N=8) in the fourth quarter of 2024
- Plans to provide an update of registrational trial design in the first half of 2025
- Plans to announce additional interim Phase 1/2 clinical data in the second half of 2025

CLN5 Batten Disease Program Update

Neurogene announced today that the Company does not expect to move forward with the NGN-101 CLN5 Batten disease gene therapy program at this time. Given the rarity of the disease, continued investment in the program was predicated on alignment on a streamlined registrational pathway with FDA. To support a streamlined pathway, Neurogene submitted a Regenerative Medicine Advance Therapy (RMAT) application to the FDA. Despite the Company's belief that the application met the standard of preliminary clinical evidence required to obtain an RMAT designation, the RMAT application was denied. Neurogene is currently evaluating options for the program.

Investor/Analyst Webcast Details

Management will host a live webcast and conference call today, November 11, 2024, at 4:30 p.m. ET to review the interim data from the NGN-401 clinical trial. Access information is available in the Investor Relations section of Neurogene's website under Events, where the webcast replay will also be available for a limited time.

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 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).

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.

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 and efficacy results of NGN-401; anticipated future improvements for participants in the NGN-401 Phase 1/2 trial for the treatment of Rett syndrome trial designs, clinical development plans and timing for NGN-401, including anticipated timing of enrollment in and clinical trial results from the Company's NGN-401 Phase 1/2 trial for Rett syndrome and expansion of that clinical trial to a third cohort for adolescent/adult patients; expected benefits of RMAT designation and participation in the FDA's START pilot program for NGN-401, including future interactions with the FDA; the timing and success of Neurogene's plans for scale-up of commercial production of NGN-401; any potential alternatives for the future development of NGN-101; and our expected cash resources and liquidity. 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 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 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 potential for unexpected results or negative impacts to adolescent or adult patients in Cohort 3 of the Phase 1/2 clinical trial for NGN-401; the risk that we may not be able to report additional data on the predicted timeline; risks related to our ability to obtain regulatory approval for, and ultimately commercialize, our product candidates, including NGN-401; and other risks and

uncertainties identified under the heading "Risk Factors" included in our 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 our Quarterly Report on Form 10-Q for the quarter ended June 30, 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.

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

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