



Neurogene Provides Update on NGN-401 Gene Therapy Clinical Trial for Rett Syndrome

November 18, 2024

NEW YORK--(BUSINESS WIRE)--Nov. 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 an update on its ongoing Phase 1/2 open-label clinical trial evaluating NGN-401 gene therapy for the treatment of Rett syndrome.

As previously disclosed, on November 11, 2024, Neurogene became aware of an emerging treatment-related serious adverse event (SAE) in a trial participant who received NGN-401 at a dose of 3E15 vg (high-dose cohort). This participant, who was dosed on November 5, subsequently experienced signs of a systemic hyperinflammatory syndrome, a rare and life-threatening immune response that has been reported with systemic exposure to high doses of AAV. Hyperinflammatory syndromes are associated with aberrant cytokine release and include hemophagocytic lymphohistiocytosis (HLH) and multisystem inflammatory syndrome. The participant is in critical condition, and the case is continuing to evolve.

"We are deeply saddened for the family. While no words could possibly provide comfort to her family, we ask the Rett syndrome community to join us in sending heartfelt thoughts to her family, friends and the dedicated clinicians who are caring for her," said Rachel McMinn, Ph.D., Founder and Chief Executive Officer of Neurogene. "The safety of the participants in our clinical trial is and remains our foremost priority as we work to find solutions for this devastating disease."

In a commitment to full transparency with the U.S. Food and Drug Administration (FDA), Neurogene proactively engaged with the FDA under the START program following the Company's notification of the SAE. The FDA completed a review of the safety data for NGN-401 and allowed Neurogene to proceed with the Phase 1/2 trial using the 1E15 vg dose (low-dose cohort). Neurogene paused further use of the 3E15 vg dose (high-dose cohorts) upon initial notification of the SAE and does not plan to enroll any further participants at the 3E15 vg dose level.

To date, there have been no other treatment-related SAEs in the clinical trial, including in the five participants who received the 1E15 vg dose (low-dose cohort) and in the first two participants who received the 3E15 vg dose (high-dose cohort) of NGN-401. All treatment-related AEs in the 1E15 vg cohort (low-dose cohort) have been Grade 1 (mild). Most treatment-related AEs are known potential risks of AAV, have been responsive to steroids, and have resolved or are resolving. There have been no signs or symptoms indicative of MeCP2 overexpression toxicity. In addition, there have been no intracerebroventricular (ICV) procedure-related AEs.

Neurogene no longer anticipates completing enrollment in the 1E15 vg cohort (low-dose cohort) of NGN-401 in the fourth quarter of 2024 as the Company updates the protocol to reflect the discontinuation of the 3E15 vg dose.

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 are made as of the date of this press release. Neurogene does not undertake any obligation to make any updates to these statements to reflect events that occur or circumstances that arise after the date of this press release, except as may be required under applicable U.S. securities law.

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 safety of NGN-401, including the safety of AAV as a component of NGN-401 and the safety of any specific cohort of the trial; the therapeutic potential and utility, efficacy and clinical benefits of NGN-401; Neurogene's ability to identify any potential indicators of predisposition to the serious adverse event (SAE) experienced by the third participant of the high-dose cohort; information relating to an understanding of the nature of the SAE that occurred in the high dose cohort of the NGN-401 trial for Rett syndrome; trial designs, clinical development plans and timing for NGN-401, including anticipated timing of additional dosing of participants in the Company's NGN-401 Phase 1/2 trial for Rett syndrome; the status of participants in our clinical trials, including those that have in the past and may in the future experience safety-related events; and expected future interactions with or positions of the FDA;. 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 our Phase 1/2 clinical trial of NGN-401 for the treatment of Rett syndrome, including the potential impact of the SAE on the decision by care givers on whether to enroll participants in the clinical trial; the expected timing and results of dosing of patients in our NGN-401 clinical trial; the potential for negative impacts to participants in the Phase 1/2 clinical trial of NGN-401 for the treatment of Rett syndrome; the risk that we may not be able to report our data on the predicted timeline; risks related to our ability to obtain regulatory approval for, and ultimately

commercialize, our product candidates, including NGN-401; our ability to accurately characterize safety events that may arise in the course of our clinical trials; 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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