Neurogene Announces Business Update and 2024 Outlook

January 5, 2024

DSMB clears third pediatric patient for dosing in ongoing NGN-401 Phase 1/2 clinical trial for Rett syndrome; On track to dose third pediatric patient in early 1Q:24

CTA clearance obtained from UK MHRA for NGN-401

Ended 2023 in a strong financial position with approximately $200 million in cash and runway into 2H:26

NEW YORK--(BUSINESS WIRE)--Jan. 5, 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, announced today a business update and provided its outlook for 2024. Key milestones for the Company’s clinical-stage gene therapy product candidates remain on track for 2024, while the Company continues to advance its discovery-stage transgene regulation portfolio.

Anticipated 2024 Key Milestones

- Rett Syndrome – NGN-401
  - Expand ongoing Phase 1/2 clinical trial for NGN-401 for Rett syndrome in 1H:24 to enroll a larger cohort of patients
  - Report interim Phase 1/2 clinical data for NGN-401 for Rett syndrome in 4Q:24
- CLN5 Batten Disease – NGN-101
  - Report interim Phase 1/2 clinical data for NGN-101 in 2H:24
  - Engage in discussions with U.S. Food and Drug Administration (FDA) regarding a streamlined registrational pathway for NGN-101 in 2H:24

“2023 was a transformational year for Neurogene, with the clearance by the FDA of our Investigational New Drug application for NGN-401 in female pediatric patients with Rett syndrome, completing the manufacturing of clinical-grade NGN-401 in-house at our GMP viral vector manufacturing facility, dosing the first two patients in our Phase 1/2 clinical trial for Rett syndrome with no treatment-emergent or procedure-related serious adverse events, or signs of overexpression-related toxicity, and completing a reverse merger and private financing to capitalize Neurogene into the second half of 2026,” said Founder and Chief Executive Officer, Rachel McMinn, Ph.D. “We remain on track to deliver interim results for our potentially best-in-class Rett syndrome gene therapy program in the fourth quarter of 2024.”

Rett Syndrome Program Update

Neurogene announced that the Data Safety Monitoring Board (“DSMB”) for the ongoing Phase 1/2 clinical trial of NGN-401 in female pediatric patients with Rett syndrome has recommended that the trial continue, which enables dosing of the third patient. This recommendation was based on safety data collected to date, following dosing of the first patient in the third quarter of 2023 and the second patient in the fourth quarter of 2023.

Neurogene also announced that the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA) has approved the Company’s clinical trial application (CTA) for NGN-401, marking the second regulatory clearance for NGN-401 in pediatric patients with Rett syndrome. This clearance enables Neurogene to expand enrollment in the Phase 1/2 trial beyond the United States to include patients with Rett syndrome in the UK, and is part of Neurogene’s global development and trial expansion strategy.

The ongoing NGN-401 Phase 1/2 clinical trial specifies a cohort of five patients, each receiving a total dose of 1×10^{15} total vector genomes delivered via intracerebral ventricular administration, which Neurogene believes may show promising efficacy results based on the nonclinical data package generated for NGN-401. In the first half of 2024, Neurogene plans to expand the trial to include (1) more patients in Cohort 1 of the trial for the low dose, and (2) a higher dose cohort to maximize the efficacy potential while still maintaining a favorable safety profile, pending regulatory clearances. Importantly, based on a comprehensive nonclinical dataset, the EXACT transgene regulation technology embedded in NGN-401 mechanistically constrains *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.

Neurogene expects to report interim clinical data from Cohort 1 in the fourth quarter of 2024, which is expected to include extensive follow up data on the first number of patients dosed.

CLN5 Program Update

Neurogene has completed enrollment of Cohorts 1 and 2 in the ongoing Phase 1/2 clinical trial for CLN5 Batten disease, and interim clinical data are expected in the second half of 2024. Neurogene is currently enrolling a final higher dose cohort. In the fourth quarter of 2023, Neurogene completed a positive meeting with the FDA regarding the future potency assay. The FDA accepted Neurogene’s proposed potency assay strategy and provided alignment with the testing approach, which will allow release of all future NGN-101 batches.

To enable a go/no-go decision to advance the program into a registration study, Neurogene is collecting and analyzing natural history data for CLN5 Batten disease and planning to request a clinical/regulatory strategy meeting with the FDA in the second half of 2024. The focus of this meeting will be to align with the FDA on the expected clinical requirements to support a streamlined registration pathway, which will be necessary to move this program forward into a pivotal clinical trial.

Discovery Portfolio Update

Neurogene announced that it has extended its research collaboration with the University of Edinburgh by an additional three years. This extension

allows Neurogene to continue advancing multiple products for commercially attractive indications in its discovery-stage, transgene regulation gene therapy portfolio.

Neurogene plans to advance one product from its discovery-stage pipeline into the clinic in 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 NGN-101

NGN-101 is being developed as a one-time treatment for both ocular and neurological manifestations of CLN5 Batten disease using AAV9 to deliver the gene encoding CLN5, which is deficient in children with the disease.

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

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). 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," "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. 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 trials; 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 trials; statements regarding the potential expansion of Neurogene's Phase 1/2 clinical trial in Rett syndrome into the United Kingdom and/or the expansion of Cohort 1 to include additional patients; the timing of any regulatory interactions regarding Neurogene's programs, including NGN-101 and NGN-401; statements regarding Neurogene's projected cash runway; and 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; risks related to Neurogene's ability to correctly estimate its respective operating expenses, including its projected cash runway, and any unexpected costs, charges or expenses resulting from the merger with Neoleukin Therapeutics, Inc. ("Neoleukin"); 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; 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 Exhibit 99.1 to the Company's Current Report on Form 8-K filed with the SEC on December 19, 2023, 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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