Neumora Therapeutics Announces Initiation of Phase 1b Study of NMRA-511 for Treatment of Alzheimer's Disease Agitation

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NMRA-511 is a highly potent and selective, best-in-class, antagonist of the vasopressin 1a receptor, which is known to play a role in regulation of aggression, stress and anxiety response

NMRA-511 was generally well-tolerated at all dose levels in Phase 1 single ascending dose / multiple ascending dose study, with no serious adverse events reported to date

Alzheimer's disease agitation is associated with increased morbidity and mortality and creates significant burden for patients and caregivers

WATERTOWN, Mass., June 20, 2024 (GLOBE NEWSWIRE) -- **Neumora Therapeutics, Inc.** (Neumora), a clinical-stage biopharmaceutical company with a therapeutics pipeline consisting of seven clinical and pre-clinical brain disease programs, today announced the initiation of a Phase 1b study evaluating NMRA-511 for the treatment of agitation associated with dementia due to Alzheimer's disease (AD). NMRA-511 is an oral, highly potent and selective antagonist of the vasopressin 1a receptor (V1aR) and is highly brain penetrant. Modulation of the V1aR is known to play a role in the regulation of aggression, stress and anxiety responses.

"We believe there is a strong rationale to evaluate the potential benefits of NMRA-511 for the treatment of agitation associated with dementia due to AD given the preclinical and clinical data supporting the role that the V1aR plays in regulating key agitation-related processes in the brain," said Robert Lenz, M.D., Ph.D., executive vice president and head of research and development, Neumora. "Millions of people in the U.S. are impacted by AD, and agitation is one of the most disruptive and burdensome symptoms for individuals and their families as it is associated with greater caregiver stress, increased morbidity and mortality, and earlier placement in long-term care facilities. Despite the significant impact of agitation in AD, there is currently only one approved product available, which carries a black-box warning for mortality in elderly people. We believe that patients deserve added treatment options and are eager to further elucidate the potential of NMRA-511 in this indication."

The Phase 1b study will investigate NMRA-511 initially in healthy elderly adult participants and then people with agitation associated with dementia due to AD. Part A of the Phase 1b study will be a randomized, double-blind, placebo-controlled cohort designed to evaluate the safety, tolerability and pharmacokinetics of NMRA-511 in approximately 8 healthy elderly participants. Part B of the Phase 1b study is a multicenter, randomized, double-blind, placebo-controlled, parallel-group cohort designed to evaluate the safety, tolerability, and efficacy of NMRA-511 20 mg twice-daily (BID) in approximately 88 people with agitation associated with dementia due to AD. The primary endpoint of this signal-seeking study is change from baseline to Week 8 on the Cohen-Mansfield Agitation Inventory total score. Neumora expects to report topline data from this Phase 1b study in the second half of 2025.

Several lines of evidence indicate that V1aR antagonists have therapeutic potential for reducing symptoms of agitation. Pre-clinically, multiple models have demonstrated that activating the vasopressin system with the endogenous agonist AVP modulates social-emotional, anxiety and threat-related behaviors across species. In rodents, the selective breeding of strains for aggressive or anxiety traits show dysregulated vasopressin release and hypothalamic-pituitary-adrenal axis functioning. Additionally, vasopressin-deficient rodents displayed impaired responses to threat stimuli, reduced anxiety and depressive-like behaviors, and impaired aggression toward intruders. Clinically, in healthy volunteers, exogenously administered vasopressin increased autonomic responsiveness to threat stimuli and increased anxiety. Conversely, V1aR antagonist administration suppressed anxiety induced by unpredictable threats. This finding is in line with data showing that concentrations of vasopressin in cerebrospinal fluid were positively correlated with levels of aggression in individuals with personality disorders. Together, these data support the development of a V1aR antagonist for the treatment of symptoms of agitation, aggression, and anxiety.

Neumora recently completed a Phase 1a Single Ascending Dose (SAD) / Multiple Ascending Dose (MAD) study that evaluated 5,10, 15, 20 and 40 mg doses of NMRA-511 in 92 healthy adult participants. NMRA-511 was generally well tolerated across doses in the study, with no serious adverse events observed at any dose level. The Company looks forward to sharing additional data from the SAD / MAD study with NMRA-511 at future medical meetings.

About NMRA-511
NMRA-511 is a highly potent and selective, best-in-class investigational antagonist of the vasopressin 1a receptor (V1aR) that exhibited greater than 3,000-fold selectivity over the V1b and V2 receptors and approximately 300-fold selectivity over the oxytocin receptor in preclinical studies. The V1aR is known to play a role in regulation of aggression, affiliation, stress and anxiety response and several lines of evidence indicate that V1aR antagonists have therapeutic potential for reducing symptoms of agitation. Based on data available to date, Neumora believes NMRA-511 has the potential to be a promising novel medication for multiple neuropsychiatric disorders and neurodegenerative diseases across the spectrum of anxiety, aggression and stress.

About Alzheimer's Disease Agitation
Alzheimer's disease is the most common cause of dementia, resulting in changes in memory, thinking and behavior. Approximately 7 million people in the United States currently live with Alzheimer's disease, and as the population ages, that number is expected to grow to more than 13 million by 2050. Behavioral symptoms including agitation and anxiety represent one of the most challenging aspects of managing Alzheimer's dementia. Literature suggests that approximately 70% of people with AD experience agitation at some point in their disease, which results in significant disability, contributes to institutionalization, and diminishes quality of life for both patients and their caregivers. Despite the substantial unmet medical need associated with agitation in Alzheimer's disease, only one medicine with a black box warning for increased mortality in elderly patients has been approved as a treatment in the United States. As a result, Neumora believes that an unmet medical need for treatments to address agitation in Alzheimer's disease remains.

About Neumora
Neumora Therapeutics, Inc. is a clinical-stage biopharmaceutical company founded to confront the global brain disease crisis by taking a

fundamentally different approach to the way treatments for brain diseases are developed. Our therapeutic pipeline currently consists of seven clinical and preclinical neuroscience programs that target novel mechanisms of action for a broad range of underserved neuropsychiatric disorders and neurodegenerative diseases. Our work is supported by an integrated suite of translational, clinical, and computational tools to generate insights that can enable precision medicine approaches. Neumora's mission is to redefine neuroscience drug development by bringing forward the next generation of novel therapies that offer improved treatment outcomes and quality of life for patients suffering from brain diseases.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements about Neumora Therapeutics, Inc. (the "Company," "we," "us," or "our") within the meaning of the federal securities laws, including statements related to: Neumora's intention to redefine neuroscience drug development by bringing forward the next generation of novel therapies that offer improved treatment outcomes and quality of life for patients suffering from brain diseases; the timing, progress and plans for its therapeutic development programs, including the timing of initiation and data read outs for its programs and studies including the Phase 1b study for NMRA-511, as well as its clinical trial and development plans; the potential for NMRA-511 to be a treatment for Alzheimer's disease agitation and other statements identified by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and the negatives of those terms. Other than statements of historical facts, all statements contained in this press release, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These statements are subject to risks and uncertainties that could cause the actual results or to be materially different from the information expressed or implied by these forward-looking statements, including, among others: the risks related to the inherent uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals; risks related to the timely initiation and enrollment in our clinical trials; risks related to our reliance on third parties, including CROs; risks related to serious or undesirable side effects of our therapeutic candidates; risks related to our ability to utilize and protect our intellectual property rights; and other matters that could affect sufficiency of capital resources to fund operations. For a detailed discussion of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Neumora's business in general, please refer to the risk factors identified in the Company's filings with the Securities and Exchange Commission (SEC), including but not limited to its Annual Report on Form 10-K for the year ended December 31, 2023 that was filed with the SEC on March 7, 2024. Forward-looking statements speak only as of the date hereof, and, except as required by law, Neumora undertakes no obligation to update or revise these forward-looking statements.

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