Neumora Therapeutics Announces Initiation of Phase 2 Study of Navacaprant in Bipolar Depression

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Potential to alleviate unmet need associated with depressed mood and anhedonia in bipolar depression; navacaprant has demonstrated the ability to improve these symptoms in MDD in a Phase 2 study

Navacaprant is also currently in Phase 3 development for the treatment of MDD with data from KOASTAL-1 anticipated in the fourth quarter of 2024

WATERTOWN, Mass., May 14, 2024 (GLOBE NEWSWIRE) -- **Neumora Therapeutics, Inc.** (Nasdaq: NMRA), 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 2 study evaluating the safety and efficacy of navacaprant in people with bipolar depression. Navacaprant is an oral 80 mg once-daily best-in-class kappa opioid receptor (KOR) antagonist, a novel mechanism of action in development for the treatment of major depressive disorder (MDD) and bipolar depression.

“Navacaprant’s novel mechanism of action has the potential for broad benefit across multiple neuropsychiatric disorders, and there is a strong rationale to evaluate its efficacy in bipolar depression. A growing body of research has characterized the pathophysiologic underpinnings of anhedonia in bipolar depression, a key feature that often remains unaddressed by standard of care. Given that in Phase 2 navacaprant demonstrated the ability to meaningfully improve depressed mood and anhedonia in other populations, we believe it may also be effective in treating these symptoms in bipolar depression,” said Robert Lenz, M.D. Ph.D., executive vice president and head of research and development, Neumora. “This is important because people with bipolar depression experience significant unmet need due to the atypical symptomology and resistance to current treatment options they often experience.”

“It’s clear that there’s an urgent unmet need for new approaches in the treatment of bipolar depression. With the current treatment paradigm, patients often cycle through multiple lines of therapy that do not sufficiently treat depressive symptoms, resulting in significant negative impact on patients’ quality of life and ability to function,” said Dan Iosifescu, M.D., Professor, Department of Psychiatry at NYU Grossman School of Medicine. “With this unmet need in mind, it is encouraging to see new mechanisms in development to address depressive symptoms in bipolar disorder that are supported by biological rationale. In fact, research suggests that KOR antagonism can play an important role in improving depressed mood and anhedonia – a hypothesis that has been reinforced by positive results from multiple clinical studies.”

The randomized, double-blind, placebo-controlled, Phase 2 clinical trial is designed to evaluate the safety and efficacy of navacaprant in people with depression associated with bipolar II disorder. The study will evaluate navacaprant 80 mg monotherapy in approximately 60 patients with a moderate-to-severe major depressive episode (Montgomery–Åsberg Depression Rating Scale (MADRS) ≥ 25). The primary endpoint of the study is change in MADRS at Week 6, and key secondary endpoints will evaluate the impact of navacaprant on anhedonia as well as other measures. Neumora expects to report topline data from this Phase 2 study in the second half of 2025. Results from this proof-of-concept study will inform further development of navacaprant in bipolar disorder, potentially including development in broader bipolar disorder populations.

About Navacaprant
Navacaprant (NMRA-140) is a highly selective, novel, best-in-class kappa opioid receptor (KOR) antagonist being developed as a potential monotherapy treatment for major depressive disorder (MDD) and bipolar depression. Navacaprant is an investigational once-daily oral 80 mg medication that is designed to modulate the dopamine and reward processing pathways, which play an important role in the regulation of mood, cognition, reward, and behavior. The KOR system is a well-characterized pathway known to mediate depressive-like states, and modulating this system represents a novel approach to treating MDD, bipolar depression, and other major neuropsychiatric disorders.

About Bipolar Disorder
Bipolar disorder may cause extreme shifts in a person’s mood, energy and activity levels. Bipolar and related disorders include bipolar I, bipolar II and cyclothymic disorders. People with bipolar I disorder experience episodes of both mania and depression, whereas those with bipolar II disorder experience depressive and hypomanic episodes, but never have a full manic episode. People with bipolar disorder are typically treated with mood stabilizers, antidepressants, atypical antipsychotics and anticonvulsants, but despite available medications, patients generally do not respond sufficiently to treatment. These patients often require multiple lines of therapy, which is associated with significant negative outcomes. People with bipolar II disorder are among those with the highest unmet need, due to the atypical symptomology and resistance to current treatment options they often experience.

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, as well as its clinical trial and development plans; the potential for navacaprant to be a treatment for major depressive disorder, bipolar disorder, and other neuropsychiatric disorders 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 that was filed with the SEC on May 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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