Neumora Therapeutics Reports Data from KOASTAL-1 Study of Navacaprant in Major Depressive Disorder

January 2, 2025 12:00 PM EST

Study did not demonstrate statistically significant improvement on primary endpoint of reduction in depressive symptoms as measured by MADRS total score compared to placebo

Navacaprant showed an efficacy signal in female participants; Company plans to further analyze results

Navacaprant generally well-tolerated with safety profile comparable to placebo

Neumora expects to share additional updates on navacaprant development program at J.P. Morgan Healthcare Conference; podium presentation Tuesday, January 14 at 8:15am PT

WATERTOWN, Mass., Jan. 02, 2025 (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 results from the Phase 3 KOASTAL-1 Study of navacaprant for the treatment of major depressive disorder (MDD). The KOASTAL-1 Study is the first of three replicate Phase 3 studies that comprise the pivotal KOASTAL program. The study did not demonstrate a statistically significant improvement on the primary endpoint of change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at Week 6 or the key secondary endpoint of a change from baseline in the Snaith-Hamilton Pleasure Scale (SHAPS) scale.

"We are disappointed by the results from KOASTAL-1 as they were not consistent with the body of evidence supporting this mechanism in MDD. There is a lot to investigate from this study, in particular the contrast in drug and placebo responses in depressed mood and anhedonia in female participants compared to male participants," said Rob Lenz, executive vice president, head of research and development, Neumora.

"We will not waver on our mission to make a difference for people living with brain diseases, which our broad pipeline of novel programs has the potential to address. The outcome of KOASTAL-1 is not what we expected, but there are encouraging trends in the data that we are analyzing," said Henry Gosebruch, president and chief executive officer, Neumora. "Our strong financial foundation and cash balance of $342 million as of the end of the third quarter provides runway into mid-2026, and we look forward to providing additional updates on the navacaprant development program and our pipeline at the J.P. Morgan Healthcare Conference. We'd like to express our appreciation to the patients, families, and investigators who participated in this trial."

KOASTAL-1 Study Summary Results
The KOASTAL-1 study enrolled 383 adult patients with MDD. Topline efficacy results for navacaprant compared to placebo are outlined in the following table:

	MADRS Total Score			SHAPS Total Score		
Outcome	**Navacaprant 80 mg**	**Placebo**	**LSMD**	**Navacaprant 80 mg**	**Placebo**	**LSMD**
ITT population CFB at Week 6 (Primary Endpoint)	-12.5 (n = 191)	-12.5 (n = 192)	0.0 (p = 0.993)	-5.8 (n = 191)	-5.5 (n = 192)	-0.3 (p = 0.648)
Female population CFB at Week 6	-14.0 (n = 105)	-11.4 (n = 106)	-2.7 (p = 0.072)	-7.2 (n = 105)	-4.9 (n = 106)	-2.3 (p = 0.015)
Male population CFB at Week 6	-10.6 (n = 86)	-13.8 (n = 86)	3.2 --	-4.3 (n = 86)	-6.3 (n = 86)	2.0 --

CFB = change from baseline; LSMD = difference in LS mean change from baseline between navacaprant and placebo groups generated from mixed-effects model for repeated measures. Subgroup analysis for male or female are pre-specified.

Navacaprant was shown to be safe and generally well-tolerated with no serious adverse events reported. There was no signal for increased suicidal ideation or suicidal behavior compared to placebo, as measured by Columbia Suicide Severity Rating Scale (C-SSRS).

Treatment Emergent Adverse Events (TEAEs) in Either Treatment Group (≥5%)	**Navacaprant 80 mg (n = 191)**	**Placebo (n = 192)**
Headache	13 (6.8%)	14 (7.3%)
Diarrhea	10 (5.2%)	4 (2.1%)

- Other notable TEAEs included pruritus (navacaprant 80 mg: 7 (3.7%), placebo: 4 (2.1%)).
- Rates of treatment discontinuation due to TEAEs were low (navacaprant 80 mg: 2.1%, placebo: 3.1%).
- A significant proportion (83.3%) of navacaprant 80 mg-treated patients who completed 6 weeks' treatment elected to enroll in KOASTAL-LT.

The Phase 3 KOASTAL-2, KOASTAL-3 and KOASTAL-LT studies are ongoing.

About the KOASTAL Program
The KOASTAL program includes three replicate Phase 3 randomized, placebo-controlled, double-blind studies, KOASTAL-1, KOASTAL-2, and KOASTAL-3, designed to evaluate the efficacy and safety of navacaprant monotherapy in adult patients with moderate-to-severe MDD who have a MADRS total score ≥ 25 at baseline. The KOASTAL-1 Study was conducted in the U.S. The KOASTAL-2 and -3 studies include sites in the U.S. and other regions. The primary endpoint of these studies is change from baseline in MADRS total score at Week 6. Key secondary endpoints include change from baseline on the SHAPS at Week 6, a measure of anhedonia.

The KOASTAL Program also includes an open-label extension study, KOASTAL-LT, designed to evaluate the long-term safety of navacaprant. As noted above, a significant portion of patients who received navacaprant 80 mg (83.3%) in the KOASTAL-1 study elected to enroll in KOASTAL-LT. Patients will also have the opportunity to enroll in the KOASTAL-LT study following participation in the KOASTAL-2 and KOASTAL-3 studies.

About Navacaprant
Navacaprant is a highly selective, novel kappa opioid receptor (KOR) antagonist being developed as a potential monotherapy treatment for MDD. 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 and other major neuropsychiatric disorders.

About Major Depressive Disorder (MDD)
MDD is a chronic psychiatric condition characterized by low mood and impairment in functioning, including episodes where an individual experiences a loss of interest or pleasure in daily activities and has symptoms such as problems with sleep, eating, energy, concentration or sense of self-worth. MDD is estimated to impact over 21 million adults in the United States, and women are nearly twice as likely as men to experience depression according to the National Alliance on Mental Illness. Nearly 70% of MDD patients fail to achieve remission with first-line treatment, which can be associated with negative side effects, including weight gain, sexual dysfunction, drowsiness, nausea and insomnia.

Anhedonia is a core feature of MDD impairing the capacity to experience or anticipate pleasure and is present in up to 70% of people with MDD. Anhedonia is associated with poor treatment outcomes and is frequently not resolved with currently approved therapies.

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 mission 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; analysis of the rich data set from the KOASTAL-1 study; the potential role of navacaprant in the MDD treatment landscape; the opportunity for patients to enroll in the KOASTAL-LT study following participation in the KOASTAL-2 and KOASTAL-3 studies; the timing, progress, and plans for Neumora's therapeutic development programs, including the Phase 3 KOASTAL-2, -3, and -LT studies; the Company's strong financial foundation; 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, including but not limited to its Quarterly Report on Form 10-Q for the quarter ended September 30, 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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