CervoMed Announces New Data from Phase 2b Trial Demonstrating Neflamapimod's Potential as a Treatment for Dementia with Lewy Bodies

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Significant improvement relative to placebo on primary outcome measure, change in Clinical Dementia Rating Sum of Boxes (CDR-SB), demonstrated in a within-subject analysis in participants with low likelihood of having Alzheimer's disease (AD) co-pathology

Significant reduction in plasma levels of a well-established biomarker of neurodegeneration, plasma glial fibrillary acidic protein (GFAP), correlated to treatment response assessed by CDR-SB

CervoMed anticipates U.S. Food and Drug Administration (FDA) feedback on Phase 3 trial design in the fourth quarter of 2025

BOSTON, Oct. 08, 2025 (GLOBE NEWSWIRE) -- CervoMed Inc. (NASDAQ: CRVO), a clinical stage company focused on developing treatments for age-related neurologic disorders (CervoMed or the Company), today announced additional data from its Phase 2b RewinD-LB trial, further demonstrating neflamapimod's potential as a treatment for dementia with Lewy bodies (DLB).

"With October recognized as Lewy Body Dementia Awareness Month, we are especially proud to share these new data from our Phase 2b RewinD-LB trial," said John Alam, M.D., Chief Executive Officer of CervoMed and Co-Principal Investigator of the RewinD-LB trial. "The significant improvements compared to placebo in change in CDR-SB observed in the within-subject comparison, along with correlated reductions in a key biomarker of neurodegeneration further strengthen our confidence in neflamapimod's potential as a treatment for DLB. Together with other insights gained from Phase 2b, these results have enabled us to refine and optimize the design of our planned Phase 3 trial as we await FDA feedback later this quarter."

New Results from the Phase 2b RewinD-LB Trial[1]

The results announced today (presentation here) are based on the final analyses of the RewinD-LB trial, conducted after the August 2025 database lock for the full 48-week trial (16 weeks placebo-controlled (Initial Phase), followed by a 32-week neflamapimod-only extension (Extension Phase)). In addition to confirming previously reported findings, today's announcement also includes:

- A subgroup analysis of participants with a low likelihood of AD co-pathology, defined by the criteria the Company expects to use in its planned Phase 3 trial in patients with DLB; and
- Further analyses of the RewinD-LB trial's primary biomarker endpoint, plasma GFAP.

Results in Participants Whose Plasma ptau181 Levels Were Below 21 pg/mL at Screening, Indicating a Low Likelihood of AD Co-Pathology

To enrich enrollment for participants without AD co-pathology, only individuals with plasma ptau181 <27.2 pg/mL[2] were randomized in the RewinD-LB trial. Based on the limited data available at the time the trial was designed, this 27.2 pg/mL threshold was estimated to be an appropriate cut-off for distinguishing patients with AD co-pathology from those without.

Recently, however, the first large, international multicenter study (n=1298) of the diagnostic performance of plasma ptau181 along the continuum of AD and non-AD dementias[3] identified a lower threshold – 21 pg/mL – as the high-sensitivity cutoff for detecting AD pathology. Based on this progress in understanding of using ptau181 to detect AD pathology and the Company's belief that neflamapimod is most effective as a treatment for the roughly 50% of DLB patients who do not have AD co-pathology, the statistical analysis plan for the RewinD-LB trial was amended in February 2025 to include sensitivity analyses using the <21 pg/mL cutoff, which are now being reported.

In the subset of participants whose plasma ptau181 levels were below 21 pg/mL at screening, results include:

- *Initial Phase*: On the primary endpoint of change in CDR-SB over 16 weeks, there was a trend toward NFMD/A (Drug product batch that did not achieve targeted plasma drug concentrations, "old capsules") [4] relative to placebo (difference −0.53, p=0.10, linear mixed-effects model) during the Initial Phase of the trial.
- *Extension Phase (First 16 Weeks)*: NFMD/B (drug product batch that achieved plasma drug concentrations, "new capsules") [4] demonstrated significant improvement versus NFMD/A on CDR-SB (−0.58, p=0.024), as well on the ADCS-CGIC, Dementia-Cognitive Fluctuations Scale, and International Shopping List Test-Recognition, over the first 16 weeks of the Extension Phase.
- ***Within-Subject Comparison to Placebo*:** Participants who transitioned from placebo in the Initial Phase to NFMD/B in the Extension Phase showed significant improvement on change in CDR-SB (difference= -1.12, p=0.005) and on ADCS-CGIC (difference=–0.82, p=0.004) while they were on NFMD/B relative to when on placebo over the respective 16-week periods.
- ***Time-to-Progression Analysis*:** NFMD/B reduced the risk of clinically meaningful progression (≥1.5-point CDR-SB increase) by 67% versus NFMD/A over 32 weeks (p<0.001) and by 75% versus placebo over 16 weeks (p<0.001).

New Analyses of Neflamapimod's Effect on Plasma GFAP, a Well-Established Biomarker of Neurodegenerative Disease Progression

In August 2025, CervoMed reported that, during the Extension Phase, neflamapimod significantly reduced plasma GFAP levels, the primary biomarker endpoint, in participants who had received 12 or more weeks of NMFD/B. This effect was not observed in participants who only received NMFD/A.

The new plasma GFAP analyses in the subset of participants whose plasma ptau181 levels were below 21 pg/mL at screening are summarized below:

- ***Within-Subject Comparison to Placebo*:** Among participants who received placebo during the Initial Phase and then transitioned to NMFD/B in the Extension Phase, the change in plasma GFAP over 32 weeks of NMFD/B treatment was significantly lower than the change observed over 16 weeks of placebo treatment in the same individuals (−16.7 pg/mL with NMFD/B vs. +5.8 pg/mL with placebo; median difference −23.1 pg/mL, p=0.016, paired Wilcoxon test). This represents an estimated 50% reduction in disease-specific elevation in plasma GFAP levels[5].

- ***Correlation with Clinical Outcomes*:** During the Extension Phase, in participants with a low likelihood of AD co-pathology, plasma GFAP change significantly correlated with CDR-SB change (p=0.036). Specifically, reductions in plasma GFAP were associated with improvements in CDR-SB scores (lower dementia severity), whereas increases in plasma GFAP corresponded to worsening scores. These findings directly correlate the biomarker effect to a clinically meaningful treatment response.

About the RewinD-LB Phase 2b Trial in Dementia with Lewy Bodies
The initial phase of RewinD-LB was a randomized, 16-week, double-blind, placebo-controlled clinical trial evaluating oral neflamapimod (40mg TID) in 159 participants with DLB, followed by a 32-week neflamapimod-only treatment Extension phase. Patients with AD co-pathology, as assessed by plasma ptau181 levels, were excluded from the trial. Compared to patients with "pure" DLB – who may comprise up to 50% of the total diagnosed DLB patient population at any given time – DLB patients with AD co-pathology have significant, irreversible neuronal loss in the hippocampus that limits response to treatment. The primary endpoint in the trial is change in the CDR-SB, and secondary endpoints include the ADCS-CGIC, the Timed Up and Go test, and a cognitive test battery. The RewinD-LB trial was funded primarily by a $21.3 million grant from the National Institutes of Health's National Institute on Aging, disbursed over the course of the trial as costs were incurred. The trial included 43 sites across in the United States, the United Kingdom, and the Netherlands. The initial phase of the study did not effectively evaluate the clinical activity of 40mg TID neflamapimod compared to placebo because the batch of neflamapimod capsules utilized during the placebo-controlled phase of the study did not lead to the average plasma drug concentrations expected with such a dose. However, in the Extension phase, a portion of participants were administered a more recently manufactured batch of capsules that achieved targeted average plasma drug concentrations, allowing the effects of 40 mg TID neflamapimod treatment to be effectively evaluated during the Extension phase, with participants receiving the newer capsules serving as an active drug arm. Outcomes in these participants were compared with those in the subset of participants who continued to receive the older batch of capsules during the Extension phase, which served as a control arm.

About CervoMed
CervoMed is a clinical-stage company focused on developing treatments for age-related neurologic disorders. The Company is currently developing neflamapimod, an investigational, orally administered small molecule brain penetrant that inhibits p38 mitogen-activated protein kinase alpha. Neflamapimod has the potential to treat synaptic dysfunction, the reversible aspect of the underlying neurodegenerative processes that cause disease in DLB and certain other major neurological disorders. The Company's recently completed Phase 2b trial evaluated neflamapimod in patients with DLB.

Forward-Looking Statements
This press release includes express and implied forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, regarding the intentions, plans, beliefs, expectations or forecasts for the future of the Company, including, but not limited to: the therapeutic potential of neflamapimod, including the degree of sustainability of any therapeutic effects; the anticipated timing and achievement of clinical and development milestones, including the Company's announcement of additional data, if any, from the RewinD-LB Phase 2b clinical trial and any meeting or correspondence between the Company and the FDA; any other expected or implied benefits or results, including that any initial clinical results observed with respect to neflamapimod in the RewinD-LB trial will be replicated in later trials; and the timing of the initiation of any potential future trials or interactions with regulatory authorities, including the Company's need to acquire sufficient funding for any Phase 3 trial of neflamapimod in DLB. Terms such as "believes," "estimates," "anticipates," "expects," "plans," "aims," "seeks," "intends," "may," "might," "could," "might," "will," "should," "approximately," "potential," "target," "project," "contemplate," "predict," "forecast," "continue," or other words that convey uncertainty of future events or outcomes (including the negative of these terms) may identify these forward-looking statements. Although there is believed to be reasonable basis for each forward-looking statement contained herein, forward-looking statements by their nature involve risks and uncertainties, known and unknown, many of which are beyond the Company's control and, as a result, actual results could differ materially from those expressed or implied in any forward-looking statement. Particular risks and uncertainties include, among other things, those related to: the Company's available cash resources and the availability of additional funds on acceptable terms; the results of the Company's clinical trials, including RewinD-LB; the likelihood and timing of any regulatory approval of neflamapimod or the nature of any feedback the Company may receive from the FDA; the ability to implement business plans, forecasts, and other expectations in the future; general economic, political, business, industry, and market conditions, inflationary pressures, and geopolitical conflicts; and the other factors discussed under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2024 filed with the U.S. Securities and Exchange Commission (SEC) on March 17, 2025, and other filings that the Company may file from time to time with the SEC. Any forward-looking statements in this press release speak only as of the date hereof (or such earlier date as may be identified). The Company does not undertake any obligation to update such forward-looking statements to reflect events or circumstances after the date of this press release, except to the extent required by law.

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[1] All analyses reported are exploratory in nature.

[2] The Company has historically reported plasma ptau181 levels based on the scale associated with the Quanterix Simoa ptau181 Advantage v2.0 assay kit. In this press release and going forward, the Company will report plasma ptau181 levels based on the scale associated with the current Quanterix Simoa ptau181 Advantage v2.1 assay kit, which was utilized in the RewinD-LB trial. Quantitative values on the v2.1 scale are approximately ten-fold higher than the corresponding values on the v2.0 scale.

[3] *Alzheimer's & Dement.* 2025 Jun 23;21(6):e14573. doi: 10.1002/alz.14573

[4] In the RewinD-LB trial, two different batches of drug product were administered. One batch of capsules, utilized in placebo-controlled phase and initially during the extension – which we refer to as NFMD/A or the "Old Capsules" – did not achieve expected and targeted average plasma drug concentrations. The other batch of capsules, introduced during the extension – which we refer to as NFMD/B or the "New Capsules" – achieved the

targeted average plasma drug concentrations.
[5] Based on mean ~150 pg/mL in participants with DLB vs. ~100 pg/mL in healthy controls; Doecke et al., 2025.

Source: CervoMed Inc.