CervoMed Announces Late-Breaking Data at the 18th CTAD Conference Demonstrating Neflamapimod Significantly Slows Clinical Progression in Dementia with Lewy Bodies

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Phase 2b trial showed significant improvements on primary and key secondary outcomes measures, most prominently in patients without AD co-pathology

Significant reduction in key neurodegeneration biomarker correlated with treatment response, suggesting neflamapimod may act on underlying disease

CervoMed preparing to initiate Phase 3 registrational trial in patients with DLB in the second half of 2026

BOSTON, Dec. 04, 2025 (GLOBE NEWSWIRE) -- Today in a late-breaking oral session at the 18th Clinical Trials on Alzheimer's Disease (CTAD) Conference in San Diego, California, clinical investigators shared the full results of the Phase 2b RewinD-LB trial of neflamapimod, being developed by CervoMed Inc. (NASDAQ: CRVO) for the treatment of dementia with Lewy bodies (DLB). In the trial, neflamapimod, which targets the neuroinflammation and synaptic dysfunction that are known to drive DLB disease progression, demonstrated a significant and clinically meaningful effect on multiple outcomes in DLB patients, including on the primary outcome measure, change in CDR sum-of-boxes (CDR-SB). These positive clinical outcomes were correlated with observed reductions in glial fibrillary acidic protein (GFAP), a biomarker of neuronal damage, supporting neflamapimod's mode of action targeting the underlying mechanism of DLB.

"The magnitude of benefit and consistency of data across clinical measures in RewinD-LB provide great confidence that neflamapimod holds true potential to meaningfully slow clinical progression in DLB, a rapidly progressive disease with profound impact on patients and caregivers," said Dr. John-Paul Taylor, MBBS, MRCPsych, PhD, Professor of Translational Dementia Research at Newcastle University and the principal investigator of the RewinD-LB trial for the United Kingdom. "Importantly, the results build on a growing body of preclinical and clinical evidence supporting neflamapimod's potential and give us renewed confidence that we are moving closer to the first approved treatment for patients and their families."

"We're pleased to share for the first time with the academic dementia clinical research community the full results of the RewinD-LB trial. These results include new analyses that demonstrate neflamapimod treatment was associated with significant improvements in both clinical and biomarker measures, including CDR-SB, ADCS-CGIC, and plasma GFAP, in within-participant comparisons to placebo in patients with DLB without AD co-pathology," said Dr. John Alam, Chief Executive Officer of CervoMed. "These findings reinforce our conviction in neflamapimod's potential and boost our momentum as we prepare to initiate our pivotal Phase 3 trial next year."

Results from the Phase 2b RewinD-LB Trial

The RewinD-LB Phase 2b trial was comprised of an initial, randomized phase comparing neflamapimod to placebo, followed by an open-label, neflamapimod-only extension phase. In the initial phase, the participants did not achieve expected plasma drug concentration levels with the neflamapimod capsules used (DP Batch A), and neflamapimod did not demonstrate a statistically significant improvement on the trial's primary endpoint. The lower–than-expected bioavailability was subsequently determined to be related to the age of the capsules used during this phase of the trial.

In the extension phase, a group of participants received a new batch of capsules that enabled them to achieve target plasma concentration levels (DP Batch B). Several key analyses were performed that evaluated outcomes in participants who received DP Batch B compared with participants who continued to receive DP Batch A during the extension phase. DP Batch A served as a control arm, allowing both across patient and within patient comparisons. Additional pre-specified analyses of the extension phase data were performed based on a <21.0 pg/mL cutoff level of plasma ptau 181, which was externally validated as a high sensitivity cutoff for AD co-pathology earlier in 2025.

Key analyses of the extension phase of the RewinD-LB trial showed:

- A significant improvement on the primary endpoint, CDR-SB (Clinical Dementia Rating Sum of Boxes), at week 16 of the extension phase, with a mean change that was 52% lower with DP Batch B compared to DP Batch A in all participants and 82% lower in patients with a screening plasma ptau181 of <21.0 pg/mL (i.e., patients without AD co-pathology).
- The clinical effect in CDR-SB was durable to 32 weeks, with a 65% reduction in clinical worsening in all participants (mean increase=1.73 with DP Batch A vs. 0.53 with DP Batch B) and an 89% reduction in clinical worsening in the <21.0 pg/mL ptau181 subgroup (mean increase=1.44 with DP Batch A vs. 0.16 with DP Batch B).
- Compared to placebo, significant improvement was also seen with DP Batch B on change in CDR-SB and the Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (ADCS-CGIC). Specifically, among patients who transitioned from placebo in the initial phase to DP Batch B in the extension phase, there was improvement with DP Batch B compared to placebo over the respective 16-week treatment periods in change in CDR-SB (difference= 1.12 point improvement vs. placebo, p=0.005) and on the ADCS-CGIC (difference= 0.82 point improvement, p=0.004).
- In in the <21.0 pg/mL ptau181 subgroup, DP Batch B reduced the risk of clinical progression (≥ 1.5 point increase in CDR-SB) by 75% compared to placebo over 16 weeks of treatment and median time to clinical progression (MTP) increased from 16 weeks for placebo to an estimated 1.5 years with DP Batch B treatment (MTP for DP Batch B not reached and projected based on available data up to 32 weeks).
- During the 32-week extension phase, mean change in plasma glial fibrillary acidic protein (GFAP), a key biomarker of neurodegeneration, was markedly reduced with DP Batch B treatment (median -16.0, IQR: -35, +6.7; p<0.0001) and that reduction was correlated with clinical

treatment response. In a within-subject comparison in participants who received placebo during the initial phase and DP Batch B during the extension phase, change in plasma GFAP was significantly lower during treatment (difference = -23.5 pg/mL, p=0.016).

In addition, neflamapimod was well-tolerated with a low rate of treatment discontinuation over 48 weeks of treatment during the trial. During the initial, placebo-controlled phase of the study, 2.5% of neflamapimod recipients discontinued for liver enzyme elevation, and 1.3% of neflamapimod recipients discontinued for liver enzyme elevation during the extension phase. All events of liver enzyme elevation were reversible and none were associated with bilirubin elevation.

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 elevated plasma ptau181 levels at screening were excluded to enrich for patients without AD co-pathology. 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.

About Dementia with Lewy Bodies
DLB is the second most common progressive dementia after Alzheimer's disease, affecting millions worldwide yet there are no approved treatments in the United States (U.S.) or European Union. DLB typically progresses more rapidly than AD, with patients often requiring nursing-home care within two years of diagnosis as they experience a combination of decline in cognitive function, cognitive fluctuations, visual hallucinations, and sleep disorders, as well as motor symptoms similar to Parkinson's disease. Individuals without AD co-pathology, often referred to as "pure" DLB, represent up to half of the diagnosed patient population and the most significant clinical effects in CervoMed's Phase 2a and Phase 2b clinical trials were observed in this subgroup.

About CervoMed
CervoMed is a clinical-stage company developing treatments for age-related brain disorders. Its lead drug candidate, neflamapimod, is an oral, small molecule targeting critical disease processes underlying degenerative disorders of the brain by inhibiting a key enzyme involved in neuroinflammation and neurodegeneration. CervoMed's recently completed Phase 2b RewinD-LB trial evaluated neflamapimod in patients with DLB; patients with elevated plasma ptau181 levels at screening were excluded to enrich for patients without AD co-pathology. The Company plans to initiate a global, pivotal Phase 3 trial in substantially the same patient population in the second half of 2026.

About Neflamapimod
Neflamapimod is an investigational, orally administered small-molecule drug that readily crosses the blood–brain barrier and selectively inhibits the alpha isoform of p38 MAP kinase, a key driver of neuroinflammation and synaptic dysfunction. By targeting the critical disease processes underlying degenerative disorders of the brain, neflamapimod has the potential to reverse synaptic dysfunction, improve neuron health, and slow or prevent disease progression. Neflamapimod is currently in clinical development for the treatment of DLB, recovery after ischemic stroke, and frontotemporal dementia.

In non-clinical studies, neflamapimod restored synaptic function within the basal forebrain cholinergic system, the brain region most affected in DLB. Across Phase 1 and 2 clinical trials involving more than 800 participants, the drug has been generally well tolerated and demonstrated consistent signals of efficacy. In the 91-patient Phase 2a AscenD-LB trial, neflamapimod significantly improved dementia severity and functional mobility in patients with DLB. Results from the 159-patient Phase 2b RewinD-LB trial, a 16-week randomized, double-blind, placebo-controlled trial followed by a 32-week open-label extension, further supported neflamapimod's potential to deliver meaningful clinical benefit, improving both cognitive and functional outcomes and showing a positive effect on a key blood biomarker of neurodegeneration during the extension phase. Across both studies, the greatest benefits were observed in patients with "pure" DLB, those without AD co-pathology. Collectively, these findings underscore the therapeutic promise and scientific validity of neflamapimod as a potential treatment for DLB and other degenerative brain disorders.

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 and the meaningfulness of any correlation between any biomarker and clinical effects; the anticipated timing and achievement of clinical and development milestones, including the Company's announcement of additional data or any meeting or correspondence between the Company and the FDA or other regulatory bodies; 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, including the Company's planned Phase 3 clinical trial of neflamapimod in patients with DLB; the timing of the initiation of and the design and endpoints of, any potential future trials, including the Company's planned Phase 3 clinical trial of neflamapimod in patients with DLB; the Company's need to acquire sufficient funding for any Phase 3 clinical trial of neflamapimod in patients with DLB; expectations with respect to neflamapimod, including the timing of any regulatory submissions and potential approvals thereof, if any; and the potential market for any DLB treatment that may be approved in the future. 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, the availability of additional funds on acceptable terms, and the Company's ability to continue as a going concern; 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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