Investigators to Present Clinical Trial Results Showing Neflamapimod Slows Clinical Progression in Dementia with Lewy Bodies in Oral Presentation at AD/PD™ 2025

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During the first 16 weeks of the Extension phase of the RewinD-LB clinical study neflamapimod slowed clinical progression compared to controls, as assessed by Clinical Dementia Rating Sum of Boxes (CDR-SB) and Clinical Global Impression of Change (CGIC)

Neflamapimod was associated with a reduced incidence of falls in the Extension phase of the study and new data to be presented at AD/PD™ 2025 demonstrates improvements on endpoints measuring cognitive fluctuations and working memory

The results demonstrate proof-of-concept for neflamapimod as a treatment for dementia with Lewy bodies (DLB)

BOSTON, April 02, 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 that investigators plan to present results, including new results, from the Extension phase of the Phase 2b RewinD-LB study that show neflamapimod demonstrated a clinically meaningful effect on slowing clinical progression in patients with DLB in an oral presentation during the 19th International Conference on Alzheimer's and Parkinson's Disease and Related Neurologic Disorders (AP/PD™) on Saturday, April 5, 2025.

"The RewinD-LB Extension phase results for neflamapimod are highly encouraging. We are seeing a clear and meaningful effect on clinical worsening over time in patients with DLB, as assessed by CDR-SB and CGIC, which is further supported by positive data across several additional clinical endpoints," stated Stephen Gomperts, MD, PhD, Associate Professor of Neurology at Harvard Medical School, Director, Lewy Body Dementia Unit at the Massachusetts General Hospital and site Principal Investigator for the RewinD-LB study. "Importantly, these results validate and replicate prior clinical trial results and are consistent with the scientific hypothesis that neflamapimod can provide clinical benefit by arresting the loss of cholinergic neuron function in the basal forebrain."

"The presentation of the Extension phase data at AD/PD™ 2025 is an opportunity to share our findings and engage deeply with the DLB medical community as we plan for pivotal development and work to bring neflamapimod to patients as rapidly as possible," said John Alam, MD, Co-Principal Investigator of the RewinD-LB study and CEO of CervoMed. "The positive findings across the primary outcome measure and multiple additional clinically important endpoints evaluated in the first 16 weeks of the Extension phase strengthen our belief that neflamapimod has the potential to be a transformative therapy for patients with DLB."

16-Week Results from the Extension Phase of the Phase 2b RewinD-LB Study[1]

Overview

Of the 159 participants randomized in the initial 16-week double-blind, placebo-controlled phase (Initial phase) of the study, 152 completed the Initial phase and 149 entered the extension phase (Extension phase), during which all participants received neflamapimod. As previously announced, during the Extension phase, 55 participants continued to receive the same batch of capsules (Old Capsules) utilized in the Initial phase of the study, while 94 participants received a new batch of capsules (New Capsules) for at least 8 weeks during the Extension phase, approximately half of which received only the New Capsules. In the Initial phase of the study, there were no discernible differences in clinical outcome between the neflamapimod (administered in Old Capsules) and placebo, which was hypothesized to be the result of sub-therapeutic plasma drug concentrations observed with the Old Capsules.

The New Capsules achieved target plasma drug concentrations, which has allowed CervoMed and clinical investigators to compare clinical outcomes between participants receiving the New Capsules (representing an active drug arm) and the Old Capsules (representing a control arm), as well as analyses that compared New Capsules administered during the Extension phase to placebo during the Initial phase of the study. For the comparison to placebo, the Old Capsules served as an important negative control. Participants and site personnel were blinded as to whether New or Old Capsules were being dispensed during the first 16 weeks of the Extension.

Positive effects seen with the New Capsules of neflamapimod compared to controls on multiple clinical endpoints:

- Improvement on primary outcome measures, change in CDR-SB, with the New Capsules both vs. Old Capsules ($p<0.001$) during first 16 weeks of the Extension phase and vs. placebo ($p=0.003$) utilizing all data in the study through to week 32 (includes Initial phase and first 16 weeks of the Extension phase).[1]
- The magnitude of the effect on the CDR-SB was for all participants a mean improvement of 0.73 points with the New Capsules compared to the Old Capsules, and a mean 0.81 points in participants whose screening plasma ptau181 was less than 2.2 pg/mL (indicating absence of Alzheimer's disease (AD) co-pathology); both exceeding the 0.5-point treatment group difference considered to be clinically meaningful (Tarawneh and Pankratz, *Alzheimers Res Ther* 2024;16:3).
- The percentage of participants who had clinically meaningful worsening (i.e. increased greater than or equal to 1.5 points on the CDR-SB) during the first 16 weeks of the Extension phase was 40% lower on a relative basis (26.8% vs. 45.1%) in New Capsule recipients compared to Old Capsule recipients; and 62% lower (17.7% vs. 45.8%) in participants whose screening plasma ptau181 was less than 2.2 pg/mL.
- Improvement on Alzheimer's Disease Cooperative Study (ADCS)-CGIC in participants administered New Capsules both in comparison to Old Capsules ($p=0.035$) during the Extension phase and in a within-participant comparison to placebo treatment during the Initial phase ($p=0.039$). The improvement compared to placebo in the within-participant analysis was not seen with the Old Capsules.
- Based on evaluation of 95% confidence intervals, improvement with New Capsules *versus* Old Capsules seen on Dementia Cognitive Fluctuation Scale and International Shopping List Test-Recognition (measuring working memory); and positive trends were seen on 12-item Neuropsychiatric Inventory (NPI-12), Timed Up and Go (TUG) and Unified Parkinson's Disease Rating Scale Part III (Motor). These new analyses support the positive findings previously reported for the CDR-SB and the ADCS-CGIC.

Old and New Capsules have similar overall safety and tolerability profile:

- Both Old and New Capsules demonstrated comparable tolerability profiles and no new safety signals were identified during the Extension phase.
- Lower incidence of falls with the New Capsules (4% vs.15.2% with Old Capsules during the Extension phase, p=0.025, and 19.7% with placebo in the Initial phase, p=0.007) in participants with screening ptau181 < 2.2 pg/mL.

About the RewinD-LB Phase 2b Study in Dementia with Lewy Bodies and Next Steps
The RewinD-LB clinical study is a randomized, 16-week, double-blind, placebo-controlled clinical study evaluating oral neflamapimod (40mg TID), with a 32-week neflamapimod only treatment Extension phase, in 159 patients with DLB. Patients with AD co-pathology, as assessed by plasma ptau181 levels, were excluded from the study. 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 outcome measure in the study is change in the CDR-SB, and secondary endpoints include Alzheimer's Disease Cooperative Study - CGIC, the TUG test, and a cognitive test battery. The RewinD-LB study is funded primarily by a $21.3 million grant from the National Institutes of Health's National Institute on Aging, which is expected to be disbursed over the course of the study as costs are incurred. The study includes 43 sites across in the United States, the United Kingdom, and the Netherlands). Participants completing the 16-week Initial phase of the study were able to continue in the study while receiving neflamapimod treatment for an additional 32-week Extension phase, within which the same efficacy assessments were conducted during the first 16 weeks as were obtained during the Initial phase.

CervoMed expects to complete the full 32-weeks of the Extension phase of the RewinD-LB study and engage with regulatory authorities to discuss finalizing Phase 3 plans for neflamapimod after these additional data become available later in 2025.

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 causes clinical disease expression in DLB and certain other major neurological disorders. Neflamapimod is currently being evaluated in a Phase 2b study 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 Company's financial position and cash runway, the therapeutic potential of neflamapimod, the anticipated timing and achievement of clinical and development milestones, including the completion the RewinD-LB Phase 2b clinical study and the Company's announcement of additional data therefrom, any other expected or implied benefits or results, including that any initial clinical results observed with respect to neflamapimod in the AscenD-LB study or RewinD-LB study 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 U.S. Food and Drug Administration; 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] Though all analyses reported are exploratory in nature, along with 95% confidence intervals which are reported for all endpoints, p-values are reported for the CDR-SB and CGIC to provide a measure of the probability that any differences identified between the treatment groups are due to chance.

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Source: CervoMed Inc.