



CervoMed Announces Positive Results from the Extension Phase of its Phase 2b Clinical Study of Neflamapimod in Patients with Dementia with Lewy Bodies

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A new batch of neflamapimod capsules led to increased plasma drug concentrations and demonstrated improvement ($p < 0.001$ vs. old capsules; $p = 0.003$ vs. placebo) on the primary outcome measure, change from baseline in Clinical Dementia Rating Sum of Boxes (CDR-SB)

Improvement ($p = 0.035$ against either old capsules or placebo) also demonstrated on the Alzheimer's Disease Cooperative Study - Clinical Global Impression of Change (CGIC)

Compared to either old capsules or placebo, a lower incidence of falls was seen in participants receiving study drug from the new batch of capsules during the extension phase

Company to host investor webcast at 5:00 PM ET today to discuss results

BOSTON, March 10, 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 positive results from the first 16 weeks of the extension phase of the Phase 2b RewinD-LB study of neflamapimod in the treatment of dementia with Lewy bodies (DLB).

"This is a great day for patients and families impacted by DLB, as well as the DLB clinical community. The magnitude of the effect demonstrated on the CDR-SB and the CGIC, both clinically meaningful endpoints, as well as the apparent beneficial effect on the incidence of participant falls, suggests that neflamapimod has the potential to fundamentally change the disease course of DLB and our approach to treating the disease," said James E. Galvin, MD, MPH, Professor of Neurology at the Miller School of Medicine in Miami, Co-Principal Investigator of the RewinD-LB study and member of the Board at the Lewy Body Dementia Association (LBDA). Continued Dr. Galvin, "To date, there is not a single drug approved in the U.S. for the management of DLB. My colleagues in the DLB clinical community and I look forward to working with CervoMed and regulatory authorities to advance neflamapimod through phase 3 and the regulatory approval process."

"As presented at the recent International Lewy Body Dementia Conference, our working hypothesis for the failure of neflamapimod during the initial 16 weeks of the study is that the investigational drug capsules utilized in that phase of the trial delivered lower than expected plasma drug concentrations and effectively underdosed participants. Consistent with this hypothesis, the results announced today demonstrate the new batch of capsules led to both higher plasma drug concentration levels and improvements on the metrics used as the primary endpoint and a key secondary endpoint in the initial phase of the study. Further, the consistency and magnitude of the clinical effect of neflamapimod on the CDR-SB are similar to our Phase 2a study results and we believe demonstrate proof-of-concept for neflamapimod as a potential treatment for dementia with Lewy bodies," said John Alam, MD, Co-Principal Investigator of the RewinD-LB study and CEO of CervoMed. "We are excited to complete the full 32-weeks of the extension phase of the study and look forward to engaging with regulatory authorities to discuss finalizing our Phase 3 plans after these additional data are available later this year."

"The results from the extension phase of the RewinD-LB study are highly persuasive. It is rare in dementia clinical research to see results with the magnitude of effect and statistical strength as was seen on the CDR-SB. At the same time, the findings are similar to what was seen in the Phase 2a clinical study and I believe are the result of having utilized a targeted therapy such as neflamapimod as well as aligning the therapy with a DLB patient population that is well suited to respond to its mechanism of action," said John-Paul Taylor, MBBS(hons) MRCPsych PhD, Professor of Translational Dementia Research at Newcastle University, United Kingdom (UK) and the principal investigator for the UK.

16-Week Results from the Extension Phase of the Phase 2b RewinD-LB Study¹

Overview

Of the 159 participants randomized in the initial 16-week double-blind, placebo-controlled ("Initial") phase of the study, 152 completed the Initial phase and 149 entered the extension phase ("Extension"), during which all participants received neflamapimod. Though study participants and site personnel were aware that the treatment for all participants during the Extension phase was neflamapimod (i.e., treatment was "open label" neflamapimod), they were not aware of which batch of capsules was administered to any given participant during the first 16 weeks of the Extension. Of the 149 participants who entered the Extension, 55 received the same batch of capsules ("Old Capsules") utilized in the Initial phase throughout the first 16 weeks of the Extension and 94 received a new batch of capsules ("New Capsules") for all or a portion of those 16 weeks; 46 starting at day 1 of the Extension, 22 starting at week 4 of the Extension, and 26 starting at week 8 of the Extension).²

87.3% of Old Capsule recipients and 91.5% of New Capsule recipients who entered the Extension completed the first 16 weeks of treatment in this phase.

CDR-SB Results

As specified by the protocol and statistical analysis plan, linear Mixed-effects Model for Repeated Measures was utilized to analyze the change from baseline in CDR-SB, the metric used as the primary endpoint for the Initial phase of the study.

- From the end of the Initial phase of the study (i.e. Day 1 of the Extension) through to Week 16 of the Extension, the change in CDR-SB was lower in the New Capsule group compared to the Old Capsule group (difference=-0.73, 95% CI: -1.14, -0.32; $p < 0.001$).
- When analyzed from baseline of the study overall through to Week 16 of the Extension, (i.e., including all data from the first 32 weeks of the study, from Day 1 of the Initial phase through to Week 16 of the Extension), the New Capsules demonstrated a positive benefit compared to placebo (difference= -0.45, 95% CI: -0.78, -0.15; $p = 0.003$).

- The difference for both comparisons in the participants whose screening plasma ptau181 was < 2.2 pg/mL, the cut-off in the Phase 2a study for evidence of Alzheimer's disease related co-pathology, were more pronounced.

CGIC Results

- On CGIC, which was administered at Week 8 of the Extension, administration of the New Capsules led to an improved score (4.02 vs. 4.46 with Old Capsules, p=0.035), indicating less worsening with New Capsule administration. A greater magnitude difference was also observed in participants with screening plasma ptau181 < 2.2 pg/mL (3.90 with New Capsules vs. 4.45 with Old Capsules, p=0.011).
- In addition, in a within-subject analysis (i.e., comparing results in participants who received placebo in the Initial phase and New Capsules in the Extension), the CGIC score was reduced in participants administered the New Capsule compared to placebo (3.94 vs. 4.46, p=0.035).

Safety

- Both Old and New Capsules demonstrated comparable tolerability profiles and no new safety signals were identified during the Extension.
- The incidence of falls was lower in participants who received New Capsules compared to those who received Old Capsules during the Extension (7.4% vs. 14.5% for all participants; 4.0% vs. 15.4%, p=0.025, for participants with screening plasma ptau181 < 2.2 pg/mL).
- The incidence of falls measured during the Extension were also lower in participants who received New Capsules compared to those who received placebo during the Initial phase of the study (7.4% vs. 18.8% for all participants, p=0.04; 4.0% vs. 19.7%, p=0.007, for participants with screening plasma ptau181 < 2.2 pg/mL).

Pharmacokinetics

- As reported previously, in a within-subject comparison (N=13), the mean plasma drug trough concentration was significantly higher (5.1 vs. 4.0 ng/mL, p=0.03) with the New Capsules than in the Old Capsules. Analyses conducted to date suggest the lower-than-expected bioavailability with the Old Capsules is related to the age of the capsules and the development of inferior dissolution kinetics with extended aging, rather than chemical degradation.

Conference Call / Webcast Details

CervoMed will host a conference call and webcast to review and discuss the 16-week results from the Extension phase of the Phase 2b RewinD-LB study today, Monday, March 10, 2025, at 5:00 PM ET. Participants should dial 1-877-425-9470 (domestic) or 1-201-389-0878 (international) with the code 13752218.

To access the Call me™ feature, which avoids having to wait for an operator, click [here](#).

The live webcast and replay will be available under "Events & Presentations" in the Investor Relations section of the Company's website, <https://www.cervomed.com>

The results from the extension phase of the RewinD-LB study have been accepted as an oral presentation at the International Conference on Alzheimer's and Parkinson's Diseases and Related Neurologic Disorders in Vienna, April 1-5, 2025.

About Dementia with Lewy Bodies (DLB)

DLB is the third most common degenerative disease of the brain (after Alzheimer's disease (AD) and Parkinson's disease). Patients with this disease accumulate protein deposits, called Lewy bodies, in the brain's nerve cells. This negatively affects cognitive ability, including attention, judgement, and reasoning, along with motor function. Patients with DLB incur higher healthcare costs, have longer hospitalizations, report lower quality of life, and have caregivers with higher levels of distress when compared to patients with Alzheimer's disease. No treatments for DLB have been approved by the U.S. Food and Drug Administration (FDA) or European Medicines Agency, and there are few drugs in development. The current standard of care is cholinesterase inhibitor therapy, which is approved for use in AD, but in DLB patients typically improves cognition transiently, and does not impact the motor component of the disease.

About Neflamapimod

Neflamapimod is an investigational, orally administered small molecule brain penetrant drug that inhibits alpha isoform of the p38MAP kinase. In preclinical studies, neflamapimod reversed synaptic dysfunction, including and particularly within the part of the brain most impacted in DLB – the basal forebrain cholinergic system. In Phase 1 and Phase 2 clinical studies involving more than 400 participants, neflamapimod has been shown to be generally well tolerated. Results from the AscenD-LB Phase 2a clinical study demonstrated that neflamapimod improved dementia severity (assessed by CDR-SB) compared to placebo and improved functional mobility (assessed by TUG test) compared to placebo. At the highest dose evaluated, neflamapimod also improved results on a cognitive test battery. The treatment response in AscenD-LB in the participants who did not have AD co-pathology (as assessed by a blood biomarker, plasma ptau181) was substantial (effect size > 0.7) and greater than the overall study population.

About the RewinD-LB Phase 2b Study in Dementia with Lewy Bodies

The Initial phase of RewinD-LB is a randomized, 16-week, double-blind, placebo-controlled clinical study evaluating oral neflamapimod (40mg TID) 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. The primary endpoint in the study is change in the CDR-SB, and secondary endpoints include CGIC, the TUG test, and a cognitive test battery (NTB). The RewinD-LB study is funded 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, which includes a pre-specified data readout after the first 16 weeks.

About CervoMed

CervoMed Inc. 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 disease in DLB and certain other major neurological disorders. Neflamapimod is currently being evaluated in a Phase 2b study in patients with DLB.

National Institute on Aging Grant

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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; the anticipated timing and achievement of clinical and development milestones, potential discussions with regulatory authorities related to the Initial and Extension phases and clinical development of and approval process for neflamapimod; any other expected or implied benefits or results, including that any future clinical results observed with respect to neflamapimod in the Initial and Extension phases will be replicated in later studies; the timing of the initiation of any phase 3 study or other additional clinical trials evaluating neflamapimod in DLB, including as a result of the Company's need to acquire sufficient funding therefor. 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, 2023 filed with the U.S. Securities and Exchange Commission (SEC) on March 29, 2024, 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, p-values are reported to provide a measure of the probability that any differences identified between the samples are due to chance.

² Except as otherwise indicated, references to "New Capsule" data in this press release include these 94 participants as a single cohort.



Source: Cervomed Inc.