CervoMed Publishes Positive Results from AscenD-LB Phase 2a Trial in Peer-Reviewed Journal that Supports the Therapeutic Potential of Neflamapimod in Dementia with Lewy Bodies

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-Integrated summary of all previously published Phase 2a clinical results, together with the first peer reviewed publication of EEG and MRI results, substantially derisk the ongoing RewinD-LB Phase 2b trial of neflamapimod in dementia with Lewy bodies -

-RewinD-LB trial remains on track to complete enrollment in the first half of 2024 and report primary efficacy results in the second half of 2024-

BOSTON, Feb. 12, 2024 (GLOBE NEWSWIRE) -- CervoMed Inc. (NASDAQ: CRVO), a clinical stage company focused on developing treatments for degenerative diseases of the brain, announced that data from the AscenD-LB Phase 2a trial evaluating treatment with neflamapimod in patients with dementia with Lewy bodies (DLB) were published online in *the Journal of Prevention of Alzheimer's Disease* (JPAD). The published manuscript titled "Phase 2a learnings incorporated into RewinD-LB, a Phase 2b clinical trial of neflamapimod in dementia with Lewy bodies," is available online.

"The publication of the EEG and MRI results round out the Phase 2a data that supports the advancement of neflamapimod into late-stage development as a treatment for DLB," said John Alam, MD, Chief Executive Officer of CervoMed. "While there are currently no approved treatment options for patients with DLB, we are encouraged by the positive data generated to date and look forward to building on the Phase 2a results with our ongoing RewinD-LB Phase 2b trial, which is expected to provide a clear path to market in this high value indication. Our RewinD-LB trial, which we believe is derisked through the incorporation of learnings outlined in the publication, is highly powered and designed to stratify patients most likely to benefit from neflamapimod. RewinD-LB remains on track to complete enrollment in the first half of 2024 and we expect to report primary efficacy results in the second half of 2024."

Results published for the first time in the JPAD manuscript are as follows:

- An integrated summary of the effects of neflamapimod 40mg three-times-a-day (TID) compared to placebo in the AscenD-LB Phase 2a clinical trial across all endpoints in (1) the overall patient population that contains a mixed population of patients with DLB with evidence of AD (i.e., with pre-treatment plasma ptau181 level above the pre-defined cutoff for AD co-pathology) and patients with pure DLB (i.e., with pre-treatment plasma ptau181 below cutoff); and (2) in the pure DLB patient population alone. As evident in the table, compared to the response in the overall patient population, the magnitude of the neflamapimod treatment effect vs. placebo is substantially higher in the pure DLB patient population. In addition, the pure DLB patients show significant improvement on working memory, assessed by the International Shopping List Test (ISLT) recognition, that is not evident in the overall patient population.

	Overall Study Population				**Patients With Pure DLB (Plasma ptau181 < cutoff)**			
	N= NFMD TID, Placebo	Difference[1] (95% CI)	*p*-value	Cohen's *d* Effect size	*N*= NFMD TID, Placebo	Difference[1] (95% CI)	*p*-value	Cohen's *d* Effect size
NTB	19,37	+0.17 (0.00,0.35)	0.049	0.47	11,19	+0.21 (-0.07,0.49)	0.13	0.56
Attention	19,36	+0.28 (0.04,0.51)	0.023	0.41	11,18	+0.42 (0.07,0.78)	0.023	0.78
CDR-SB	20,38	-0.56 (-0.96, -0.16)	0.007	0.31	11,22	-0.60 (-1.04, -0.06)	0.031	0.74
TUG	20,38	-1.4 (-2.6, -0.2)	0.024	0.50	11,20	-3.1 (-4.7, -1.6)	<0.001	0.74
ISLT	20,42	+0.32 (-0.48,1.12)	NS	0.15	11,22	+2.1 (0.0,4.2)	0.053	0.55
ISLT- RECOGNITION	19,39	+0.47 (-0.17,1.11)	0.15	0.17	10,21	+1.4 (0.02,2.5)	0.024	1.0

Table: AscenD-LB Results in Neflamapimod 40mg TID, in Overall Patient Population and in Pure DLB Patients

[1] Difference between neflamapimod 40mg TID and placebo from mixed model for repeated measures (MMRM) analysis. Improvement reflected by negative sign for CDR-SB and TUG and positive sign for other measures. Abbreviations: NFMD – neflamapimod; NTB — Neuropsychological Test Battery; CDR-SB — Clinical Dementia Rating Sum of Boxes; TUG — Time Up and Go test; ISLT — International Shopping List Test; RECOG —Recognition

- EEG results from the AscenD-LB Phase 2a trial, which demonstrated that neflamapimod 40mg TID treatment led to improvement (p=0.01 vs. placebo TID) in beta functional connectivity assessed by EEG. Deficits in beta band functional connectivity may be a key differentiator between DLB and Alzheimer's disease (AD).
- In a prior Phase 2a study in AD, neflamapimod treatment led to an increased volume and functional connectivity of the basal forebrain by MRI. Specifically, the analysis demonstrated that the volume of the nucleus basalis of meynert (NbM, the major cholinergic neuronal cluster in the basal forebrain) was higher at the end of 12 weeks neflamapimod treatment (EOT, mean 3.1% higher vs. baseline, p=0.03). Treatment with neflamapimod was also associated with higher functional dynamic connectivity between the NbM and deep grey matter (DGM) at EOT (mean 11% higher vs. baseline, p=0.04).

Key learnings from AscenD-LB have been incorporated into the ongoing RewinD-LB Phase 2b trial of neflamapimod, including the use of a single dose regimen of neflamapimod 40mg TID, enrolling patients with pure DLB and selecting CDR-SB as the primary endpoint. To further evaluate potential effects on the underlying disease process, structural and functional MRI will be evaluated in a 40-patient subgroup to assess treatment effects on atrophy of the basal forebrain, as well its functional connectivity.

About the RewinD-LB Phase 2b Study in Dementia with Lewy Bodies
The Phase 2b study, named RewinD-LB, is a randomized, 16-week double-blind, placebo-controlled clinical trial evaluating oral neflamapimod (40mg three times per day) in up to 160 patients with prodromal dementia with Lewy bodies (DLB) or mild dementia due to DLB. Patients with Alzheimer's disease-related co-pathology, assessed by a blood biomarker (plasma ptau181), will be excluded. Patients completing the 16-week placebo-controlled study period will be able to continue in the study while receiving open label neflamapimod treatment for an additional 32 weeks. The primary endpoint in the study is change in CDR-SB, and secondary endpoints include the TUG test, a cognitive test battery, and the Clinician's Global Impression of Change (CGIC). The study includes 41 sites (30 in the United States, 8 in the United Kingdom, 3 in the Netherlands), all of which have been initiated. The RewinD-LB study is funded by a $21 million grant from the National Institutes of Health's National Institute on Aging (NIA), which will be disbursed over the course of the study as costs are incurred. More information, including information on active clinical trial sites, on the RewinD-LB study is available at clinicaltrials.gov.

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 p38MAP kinase alpha (p38a). Neflamapimod has the potential to treat synaptic dysfunction, the reversible aspect of the underlying neurodegenerative processes that cause disease in dementia with Lewy bodies (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 therapeutic potential of neflamapimod and anticipated timing of clinical milestones. Terms such as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately," "potential" or other words that convey uncertainty of future events or outcomes 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; 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 Quarterly Report on Form 10-Q for the three-month period ended September 30, 2023 filed with the U.S. Securities and Exchange Commission (SEC) on November 13, 2023, 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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