CervoMed Announces Oral Presentation at CTAD 2023 Which Highlighted Learnings from Phase 2a That Optimized the Design of the Phase 2b Clinical Study of Neflamapimod in Dementia with Lewy Bodies

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With incorporation of key learnings, Phase 2b has >95% (approaching 100%) statistical power to meet its primary endpoint: change in Clinical Dementia Rating Sum-of-Boxes (CDR-SB) vs. placebo

New data included in the presentation show that in patients without Alzheimer's-related co-pathology, neflamapimod treatment demonstrates significant reduction vs. placebo of a potential blood biomarker of dementia with Lewy bodies

BOSTON, Oct. 25, 2023 /PRNewswire/ -- CervoMed Inc. (NASDAQ: CRVO), a clinical-stage company focused on developing treatments for degenerative diseases of the brain, announced an oral presentation today by Dr. Niels Prins, Chief Executive Officer of the Brain Research Center in the Netherlands, at the 16th Clinical Trials in Alzheimer's Disease (CTAD) conference highlighted the neflamapimod clinical development program, including the RewinD-LB Phase 2b study design and the supportive Phase 2a clinical data, for the treatment of patients with dementia with Lewy bodies (DLB).

"We are pleased to have had the opportunity at this year's CTAD conference to comprehensively present the findings in Phase 2a and discuss the analyses that went into optimizing the Phase 2b study design for the treatment of patients with DLB," said John Alam, MD, Chief Executive Officer of CervoMed. "Our Phase 2b DLB study, with its optimized design, has substantial statistical power to detect an effect on the Clinical Dementia Rating Sum-of-boxes, and is currently actively enrolling patients in the US, the UK, and the Netherlands. We look forward to completing enrollment during the first half of 2024 and then reporting initial results from the placebo-controlled portion of the study during the second half of 2024."

Based on the learnings, the distinctions from Phase 2a in the RewinD-LB study include, (1) the use of one dosing regimen of neflamapimod (40mg capsules three-times-a-day, TID), based on the dose-response analysis of the study, and on observations in AD studies; (2) the choice of Clinical Dementia Rating Sum of Boxes (CDR-SB) as the primary endpoint; and (3) the exclusion of patients with Alzheimer's related co-pathology, as evaluated by plasma levels of tau phosphorylated at position 181 (ptau181; to enrich for such patients, the global CDR score at entry will be limited to 0.5 or 1.0). With these modifications to the design from Phase 2a, sample size calculations (see below) indicate that the RewinD-LB Phase 2b study has greater than 95% statistical power (approaching 100%) to meet its primary objective of demonstrating improvement relative to placebo on change in CDR-SB over the course of the study.

Highlights of the presentation include the following:

- The Phase 2a inclusion criteria for the diagnosis of DLB was able to identify and support enrollment of a robust DLB patient population with significant attentional deficits, with >1.5 Standard Deviation (SD) deficits vs. age-adjusted norm in the cognitive tests of attention and/or working memory at baseline. Patients enrolled in the study had lesser decline in executive function, with ≤1 SD deficit in cognitive tests designed to evaluate executive function; consistent with the literature for mild DLB.
- Clinical endpoints that can detect effects on both cognitive and motor function (specifically, CDR-SB and the Timed Up and Go test, TUG) performed better in the Phase 2a study with respect to detecting improvement over placebo than endpoints that are purely focused on evaluating cognition. The underperformance in Phase 2a of a six cognitive test Neuropsychological Test Battery (NTB) evaluating attention and executive function can be attributed to ceiling effects due to (1) the modest deficits in executive function at baseline and (2) patients in Phase 2a all receiving cholinesterase inhibitors.
- Sample size for the potential endpoints in Phase 2b were evaluated through clinical trial simulations that utilized individual patient data in Phase 2a for the placebo and neflamapimod 40mg TID recipients. Based on the simulation of 100 clinical trials with 80 patients per treatment group, and assuming a 10% dropout rate, there is ~85% power with the NTB, 95% power with the TUG, and >95% power with CDR-SB (approaching 100%) to detect a treatment effect at an alpha level of 0.05.
- Electroencephalography (EEG) evaluations in Phase 2a showed that while there were no differences between neflamapimod and placebo in spectral analysis, neflamapimod treatment led to a significant dose-dependent increase vs. placebo in the beta band seen in functional connectivity analysis. These results were previously presented at the International Conference on Alzheimer's and Parkinson's Diseases 2022 meeting in Barcelona, Spain (video of presentation available here).
- In the Phase 2a study, in patients without Alzheimer's related co-pathology (assessed by plasma ptau181) at study entry, neflamapimod treatment led to significant improvement compared to placebo in the change in plasma levels of glial fibrillary acidic protein (GFAP): from baseline to week-16, GFAP was decreased by mean 10.6 pg/mL in neflamapimod-recipients and increased by mean 14.1 pg/mL in placebo-recipients (p=0.04 for neflamapimod vs. placebo). These data have not been previously presented and a full presentation of the GFAP data is planned for a future scientific conference. Plasma GFAP was recently reported as a potential biomarker for DLB (Hamilton et al, *Psychological Medicine*, 2023).

A copy of the CTAD presentation is available on the Presentations and Publications section of CervoMed's website.

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

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 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. Clinical sites are located in the US, the UK, and the Netherlands. Patients with Alzheimer's disease-related co-pathology, assessed by a blood biomarker (plasma ptau181), will be excluded. CervoMed expects to complete enrollment in RewinD-LB during the first half of 2024 and then report

initial results from the placebo-controlled portion of the study during the second half of 2024. 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 biotechnology company advancing CNS-focused therapeutics to benefit patients with a range of degenerative diseases of the brain. 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. CervoMed was formed in August 2023 with completion of the merger of EIP Pharma Inc. with Diffusion Pharmaceuticals Inc.

For more information, please visit www.cervomed.com or engage with us on Twitter and LinkedIn.

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 CervoMed Inc. (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 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 Exhibit 99.2 to the Company's Current Report on Form 8-K/A filed with the U.S. Securities and Exchange Commission (SEC) on September 29, 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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