CervoMed Announces Publication in Neurology® Results Showing a Blood Test at Study Entry Identified Patients Who Demonstrated Substantial Response to Neflamapimod in Dementia with Lewy Bodies

September 6, 2023 11:00 AM EDT

Additional protocol-specified analyses of the AscenD-LB Phase 2a results show that patients without elevated plasma ptau181 levels are more responsive than those with such elevation and have substantial treatment benefits to neflamapimod.

BOSTON, MA – Sept 6, 2023 – CervoMed Inc., a clinical stage company focused on developing treatments for degenerative diseases of the brain, today announced the publication online on September 1, 2023, in *Neurology*®, the medical journal of the American Academy of Neurology, of additional pre-specified analyses of the AscenD-LB Phase 2a clinical trial showing an association between plasma phosphorylated tau at position 181 (ptau181) levels at study entry and patient's response to neflamapimod in the treatment of dementia with Lewy Bodies (DLB).

"The overall results of the AscenD-LB study, which were published last year, demonstrated that treatment with oral neflamapimod at a dose of 40mg three-times-per-day was associated with significant improvements in outcomes compared to placebo on measures of dementia severity, mobility and attention. After the study was completed, multiple reports were published that showed that the blood-based biomarker plasma ptau181 can identify patients with DLB who harbor Alzheimer's disease related co-pathology, which is associated with a greater degree of brain atrophy and associated neuronal loss. Consequently, as pre-specified in the protocol, we further analyzed the effects of neflamapimod 40mg three-times-per-day in the AscenD-LB dataset after stratifying the samples according to pre-treatment levels of plasma ptau181. These new results show that when the analysis is restricted to patients with normal plasma ptau181 at study entry, in addition to the previously reported effects, significant improvement compared to placebo was observed on a measure of recognition memory, an effect not seen in the overall patient population. Moreover, the magnitude of the neflamapimod treatment effect in patients with normal plasma ptau181 at study entry is greater than that seen in the overall study population and substantial, with an effect size relative to placebo of at least 0.7 for each of the measures of dementia severity, attention, recognition memory, and functional mobility," said Stephen Gomperts, MD, PhD, a senior author on the publication, and Director of the Lewy Body Dementia (LBD) Unit at the Massachusetts General Hospital in Boston.

"The results support our long-standing thesis that the key to treating chronic neurodegenerative disease is to intervene early in the disease process, ahead of the patient having extensive neuronal loss in the brain," said John Alam, MD, Chief Executive Officer of CervoMed and first author of the publication. He added, "In the near term, we believe the exclusion of patients with abnormal levels of plasma ptau181 in our ongoing Phase 2b clinical trial of neflamapimod in patients with DLB will substantively increase the probability of success in that clinical trial. In the long-term, blood-based biomarkers such as plasma ptau181 hold the potential to implement a personalized medicine approach to treating the major neurodegenerative diseases to enhance the value delivered to patients."

A water-marked version of the manuscript, entitled "Association of plasma phosphorylated tau with the response to neflamapimod treatment in patients with dementia with Lewy bodies", is available on the *Neurology* website and the full publication, both online and a short version in print, will be published later in the fall. The online publication can be accessed here.

The AscenD-LB Phase 2a Study Results and Analyses as Published in *Neurology*

The AscenD-LB clinical trial was a Phase 2a double-blind, placebo-controlled, 16-week treatment study of neflamapimod in 91 patients with mild-to-moderate DLB (NCT04001517). The main results, which were published in September 2022 in the journal *Nature Communications*, demonstrated that neflamapimod significantly improved dementia severity compared to placebo and also showed significant improvement on motor function compared to placebo; at the highest dose evaluated, neflamapimod also improved cognition, particularly with respect to attention. For the *Neurology* publication, as pre-specified in the protocol, after the study was completed (*i.e.*, *post-hoc*), with the availability of information regarding the utility of the assay to identify patients with Alzheimer disease (AD) co-pathology in patients with DLB, pre-treatment plasma ptau181 levels were determined in patients who had at least one on-study efficacy measure and participants were grouped based on a cut-off for AD pathology of 2.2 pg/mL (established in a separate cohort to identify AD from healthy controls). Clinical outcomes for the comparison of placebo with neflamapimod 40mg three-times-daily (TID), the higher and more clinically active of two doses studied, were analyzed utilizing Mixed Models for Repeated Measures within each sub-group (baseline plasma ptau181 < and ≥2.2 pg/mL). The results, as reported in the current publication, showed 45 participants were below, and 40 above, the 2.2 pg/mL cut-off at baseline. Moreover, during the 16-week treatment period, in the comparison of placebo with neflamapimod 40mg TID, for all endpoints evaluated, improvements with neflamapimod treatment were greater in participants below the cut-off, compared with that in those above the cut-off. In addition, participants below the ptau181 cut-off at baseline showed significant improvement over placebo in an Attention Composite measure (+0.42, 95%CI: 0.07–0.78, p=0.023, Cohen's d effect size=0.78), the Clinical Dementia Rating Scale Sum of Boxes (-0.60, 95%CI:-1.04,-0.06, p=0.031, d=0.74), the Timed Up and Go test (-3.1 sec, 95%CI:-4.7,-1.6, p<0.001, d=0.74), and International Shopping List Test-Recognition (+1.4, 95% CI: 0.2–2.5, p=0.024, d=1.00).

About Neflamapimod

Neflamapimod is an investigational drug that is an orally administered small molecule brain penetrant that inhibits p38MAP kinase alpha (p38a). P38a, which is expressed in neurons under conditions of stress and disease, plays a major role in inflammation-induced synaptic toxicity, leading to synaptic dysfunction. Neflamapimod is currently being developed for the treatment of dementia with Lewy bodies (DLB) and is the first treatment with the potential to have a positive impact on cognition, function, and mobility.

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 300 participants, neflamapimod has been shown to be generally well tolerated. Results from the AscenD-LB Phase 2a clinical study demonstrated that neflamapimod significantly improved dementia severity compared to placebo and also showed significant improvement on motor function compared to placebo. At the highest dose evaluated, neflamapimod also improved cognition. The combined preclinical and clinical data are consistent with neflamapimod treating the underlying DLB

disease process and suggest that neflamapimod has the potential to be the first disease-modifying treatment for DLB. Neflamapimod was granted Fast Track status by the U.S. Food and Drug Administration for the treatment of DLB, and EIP Pharma Inc. (a wholly owned subsidiary of CervoMed) in January 2023 was awarded a $21 million grant from the National Institutes of Health's National Institute on Aging (NIA) to evaluate neflamapimod in a Phase 2b clinical study in DLB. The NIA grant funds will be disbursed over the course of the ongoing phase 2b study as the costs are incurred.

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 after the merger of EIP Pharma Inc with Diffusion Pharmaceuticals Inc. For more information, please visit www.cervomed.com, or follow 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; anticipated milestones related to the development of the Company's clinical programs, including timelines for trial enrollment and reporting of data; the potential results of our ongoing Phase 2b clinical trial of neflamapimod in patients with DLB; and the potential commercial opportunity of neflamapimod, if approved. Terms such as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately," 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 Company's ability to maintain its listing on the Nasdaq Capital Market, as well as comply with applicable Nasdaq rules and regulations; the market price of the Company's securities, which may be volatile due to a variety of factors, including changes in the competitive and highly regulated industry in which the Company operates; variations in operating performance across competitors; changes in laws and regulations affecting the Company's business; 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 most recent Annual Report on Form 10-K, in the proxy statement/prospectus/information statement that is included in the Company's registration statement on Form S-4 (File No. 333-271823) that was filed with the SEC, and other filings that the Company may file from time to time with the SEC. Any forward-looking statements in this release speak to the date hereof (or such earlier date as may be identified). New factors emerge from time to time, and it is not possible for the Company to predict all such factors, nor can we assess the impact of each such factor on the Company's business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. The Company does not undertake any obligation to update such forward-looking statements to reflect events or circumstances after the date of this release, except to the extent required by law.

Contacts
CervoMed Investors & Media:
Argot Partners
212.600.1902
CervoMed@argotpartners.com