CervoMed Announces Presentation of Biomarker Data from the AscenD-LB Phase 2a Trial and Preclinical Data Supporting Potential of Neflamapimod in Tau-Mediated Disease at AD/PD ™ 2024

March 05, 2024

- Neflamapimod led to significant reduction compared to placebo in plasma levels of glial fibrillary acidic protein (GFAP)

- Neflamapimod effects on GFAP correlated to clinical outcomes assessed by CDR Sum of Boxes (CDR-SB)

- Scientific collaborators from University College London (UCL) present data demonstrating neflamapimod improves axonal transport in a transgenic mouse model of frontotemporal dementia (FTD)

BOSTON, March 05, 2024 (GLOBE NEWSWIRE) -- CervoMed Inc. (NASDAQ: CRVO), a clinical stage company focused on developing treatments for degenerative diseases of the brain, today announced the presentation of biomarker data from the AscenD-LB Phase 2a trial of neflamapimod in patients with dementia with Lewy bodies (DLB), demonstrating that neflamapimod reduces plasma levels of glial fibrillary acidic protein (GFAP) compared placebo, and that the effects of neflamapimod on GFAP were inversely correlated to change in CDR-SB (reduction in GFAP associated with improvement in CDR-SB, and increase in GFAP associated with worsening in CDR-SB). These data will be featured in a poster presentation at the 18th International Conference on Alzheimer's and Parkinson's Diseases (AD/PD™) 2024, being held both virtually and in Lisbon, Portugal from March 5–9, 2024. In addition, academic researchers from UCL will be presenting data in a separate poster at the meeting demonstrating that p38MAPK inhibition, including with neflamapimod specifically, improves tau-induced axonal transport defects both *in vitro* and in a tauopathy mouse model.

"The effects on GFAP, particularly the association between GFAP response and clinical outcomes, further support that neflamapimod is clinically efficacious in patients with DLB," said John Alam, MD, Chief Executive Officer of CervoMed. "The exciting data from UCL are consistent with the mechanism of action of neflamapimod in the treatment of dementia with Lewy bodies, where axonal transport defects related to the microtubule-associated protein tau in basal forebrain cholinergic neurons are an important pathogenic driver. Moreover, their findings provide a strong scientific rationale for evaluating neflamapimod as a treatment for certain forms of frontotemporal dementia."

Full abstracts are accessible on the conference portal, and additional details are provided below. A PDF copy of the GFAP poster presentation will be available on the "Presentations and Publications" section of the CervoMed website.

Abstract #1095 (Neflamapimod reduces GFAP levels in patients with DLB):

- **Title**: EFFECT OF NEFLAMAPIMOD TREATMENT ON PLASMA GLIAL FIBRIALLARY ACIDIC PROTEIN (GFAP) LEVELS IN PATIENTS WITH DEMENTIA WITH LEWY BODIES (DLB)
- **Authors:** John Alam, Marleen Koel-Simmelink, Jennifer Conway, Amanda Gardner1, Kelly Blackburn, Inge Verberk, Charlotte Teunissen
- **Affiliations:** CervoMed Inc. (JA, JC, AG, KB); Amsterdam UMC location Vrije Universiteit Amsterdam (MK-S, IV, CT), Department of Laboratory Medicine, Neurochemistry Laboratory

Key Takeaways: The effects of neflamapimod on plasma GFAP were evaluated in both the overall and pure DLB patient population, and the treatment effects of GFAP correlated to clinical outcomes:

- In the overall population, there was a mean 3.7 pg/mL increase GFAP levels in placebo vs. mean 12.3 pg/mL reduction with neflamapimod (p=0.13 for difference).
- In pure DLB patients (i.e., patients with pre-treatment plasma ptau181 below the cutoff for AD-related co-pathology), there was a mean 14.1 pg/mL increase in placebo vs. mean 10.6 pg/mL reduction with neflamapimod (p=0.04 for the difference).
- In the pure DLB patient population, in participants treated with neflamapimod there was a significant correlation (r=0.542, p=0.036) between the effects of GFAP and clinical outcomes assessed by change from baseline to week 16 in CDR-SB, with increased GFAP being associated with worsening CDR-SB, while reduction in GFAP was associated with improvement on CDR-SB. The correlation was not seen in placebo-recipients (r=0.31, p=NS).

Abstract #2438 (Neflamapimod enhances axonal transport in tauopathy model)

- **Title**: IN VIVO IMAGING OF AXONAL TRANSPORT REVEALS EARLY PATHOLOGICAL CHANGES INDUCED BY TAU MUTATIONS AND THEIR REVERSIBILITY
- **Authors:** Edoardo Moretto, Chiara Panzi, Skye Stuart, Anna Masato, Samantha De La-Rocque, Emily Huff, Ian White, Jemima Burden, Giampietro Schiavo
- **Affiliations:** UCL, UK Dementia Research Institute (EM, CP, SS, AM, SDL-R, GS); CNR, Institute of Neuroscience (EM), Vedano al Lambro (MB), Italy; UCL, MRC Laboratory for Molecular Cell Biology (IW, JM); UCL, Queen Square Motor Neuron Disease Centre (GS)

Key Takeaways: The effects of p38 MAPK inhibition on FTD linked tau mutation induced axonal transport defects were evaluated both *in vitro* and *in vivo*:

- FTD-linked mutations, known to increase pathological phosphorylation and aggregation of tau, induces aberrant tau envelopes (clusters)

along axons, an effect that was reversed by inhibition of p38 MAPK (a kinase known to modulate tau hyperphosphorylation and the target of neflamapimod).

- By using a new assay based on two-photon microscopy on tauopathy mouse models, inhibition of p38 MAPK was able to partially rescue the defects in axonal transport both *in vitro* and *in vivo*.
- Neflamapimod, administered twice daily for 5 days at a dose of 3 mg/kg, was demonstrated to enhance axonal transport in the rTg450 transgenic mouse model of FTD that contains the P301L mutation in the tau gene.
- The authors conclude, “The evidence that reducing tau phosphorylation by inhibiting p38 MAPK potentiated axonal transport points towards inhibition of p38 MAPK as a promising therapeutic strategy in tauopathies”.

Additionally, John Alam, MD, Chief Executive Officer of CervoMed will participate in a panel discussion on recent developments that are advancing the therapeutic landscape, specifically on the development of biomarkers, imaging, and therapy of alpha-synuclein, LRKK2, and GBA pathologies. Additional details are provided below.

- Title: NEW INSIGHTS IN THE DEVELOPMENT OF BIOMARKERS, IMAGING, AND THERAPY OF ALPHA-SYNUCLEIN, LRKK2, AND GBA PATHOLOGIES
- Forum: 3
- Date and Time: Thursday, March 7, 2024, from 5:30-6:30pm CET
- Location: Auditorium I, Lisbon Congress Centre (Centro de Congressos de Lisboa)

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 p38MAP kinase alpha (p38a). Neflamapimod has the potential to treat synaptic dysfunction, the reversible aspect of the underlying neurodegenerative processes that cause disease 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 CervoMed (or 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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