UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

October 24, 2023
Date of Report (Date of earliest event reported)

CervoMed Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-24477**	**30-0645032**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

20 Park Plaza, Suite 424	
Boston, Massachusetts	**02216**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 744-4400

Not applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value	CRVO	NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Peer-Reviewed Journal Publications

On October 24, 2023, CervoMed Inc. (the "Company") issued a press release announcing the publication of two articles that support advancing neflamapimod as a potential disease-modifying treatment for Dementia with Lewy Bodies ("DLB") and Alzheimer's Disease, including (i) the final publication in *Neurology*® of an article previously announced by the Company on September 6, 2023 and (ii) a Research Highlight Article in *Molecular Neurodegeneration.* The press release is attached hereto as Exhibit 99.1.

CTAD Presentation

On October 25, 2023, the Company issued a press release announcing a presentation highlighting learnings from its Phase 2a clinical trial of neflamapimod in DLB at the 16th annual Clinical Trial in Alzheimer's Disease ("CTAD") conference, held October 24-27, 2023, in Boston, Massachusetts. A copy of the press release is attached hereto as Exhibit 99.2 and a copy of the presentation presented at the CTAD conference is attached hereto as Exhibit 99.3.

Corporate Presentation

Certain information concerning the business, clinical studies, development plans, financial position and related matters of the Company has been made available on our website, www.cervomed.com, under the heading, "Investors – Events and Presentations" and a copy of which is attached as Exhibit 99.4 hereto. Representatives of the Company may use this presentation, in whole or in part, and possibly with non-material modifications, periodically in connection with conferences, meetings, and presentations to investors, analysts and others.

The information contained in the presentation is summary information that is intended to be considered in the context of the Company's filings with the Securities and Exchange Commission ("SEC") and other public announcements that it may make, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in the presentation except as required by applicable law, although the Company may do so from time to time as its management believes is warranted. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases, or through other public disclosure.

The Company makes no admission or representation as to the materiality of any information in the presentations, in the press releases, or otherwise contained in this Current Report on Form 8-K. The information in this Current Report on Form 8-K and the exhibits thereto are furnished pursuant to Item 7.01 of Form 8-K and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of Section 18 of the Exchange Act, unless the Company specifically incorporates such information by reference in a document filed under the Exchange Act, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, except as previously set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The following exhibits relating to Item 7.01 are furnished and not filed:

Exhibit No.	Description
99.1	Press Release, issued October 24, 2023.
99.2	Press Release, issued October 25, 2023.
99.3	Presentation, dated October 25, 2023.
99.4	Corporate Presentation of CervoMed Inc. dated October 25, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: October 25, 2023

CervoMed Inc.
By: /s/ John J. Alam
Name: John J. Alam
Title: Chief Executive Officer

Exhibit 99.1

CervoMed Announces Publications in Major Peer-Reviewed Journals That Inform on Potential of Neflamapimod as a Disease-Modifying Therapy for the Major Dementias

Final publication in Neurology® of Phase 2a Results Stratified by Plasma Phosphorylated Tau Status at Baseline Strengthens the Case for Progressing Neflamapimod as a Disease-Modifying Treatment for Dementia with Lewy Bodies

Research Highlight Article in Molecular Neurodegeneration Comments That Through Acting on Cholinergic Degeneration Neflamapimod Has Potential to have Disease-modifying Effects in Both Dementia with Lewy Bodies and Alzheimer's Disease

BOSTON, MA – Oct. 24, 2023 – /PRNewsire/ -- CervoMed Inc. (NASDAQ: CRVO), a clinical stage company focused on developing treatments for degenerative diseases of the brain, today announced the publication of the following two articles that support advancing neflamapimod as a disease-modifying treatment for Dementia with Lewy Bodies (DLB) and Alzheimer's Disease (AD):

- Alam JJ, Maruff P, Doctrow S, Chu H-M, Conway J, Gomperts SN, Teunissen C.Association of plasma phosphorylated tau with the response to neflamapimod treatment in patients with dementia with Lewy bodies. Neurology, 2023, Volume 101, pages 1-10. The journal has released the final publication, including a Short Version in print, of the article that was the subject of a press release from CervoMed dated September 6th, 2023. The major finding is that the magnitude of the neflamapimod treatment effect in the DLB phase 2a study in the sub-group with normal plasma ptau181 at study entry (i.e., those with pure DLB, without biomarker evidence of AD related co-pathology) was greater than that seen in the overall study population and substantial, with a treatment effect size relative to placebo of at least 0.7 (indicative of a large effect) for each of the measures of dementia severity, attention, recognition memory, and functional mobility.

- Alam J and Nixon RA, Drug development targeting degeneration of the basal forebrain cholinergic system: its time has come. Molecular Neurodegeneration (2023) 18:74. This Research Highlight article reviews the preclinical and clinical data in the *Neurology*® publication and a prior publication in *Nature Communications* and concludes that the findings are "a major translational step forward" towards treating basal forebrain cholinergic degeneration, the primary pathology in DLB and considered to be a contributor to disease expression and/or progression in multiple other CNS disorders, including AD.

"As reported in Nature Communications last year, the primary analysis of the phase 2a study of DLB showed neflamapimod significantly improved dementia severity and motor function. As now published in the major clinical neurology journal, Neurology, there is consistency and greater magnitude of the clinical effect seen in patients without AD co-pathology, which further strengthens the conclusions regarding the clinical effect in DLB demonstrated in phase 2a," said John Alam, MD, Chief Executive Officer of CervoMed and first author of both publications announced today. He added, "The Molecular Neurodegeneration article provides a combined evaluation of the findings in the Neurology and Nature Communications articles that makes the case for advancing neflamapimod as a treatment for DLB. Further, the Molecular Neurodegeneration article also comments that the results viewed in the context of the broader scientific literature indicates that neflamapimod also has potential to impact disease progression in Alzheimer's disease, either as a standalone therapy or in combination with amyloid beta directed therapies."

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 (RewinD-LB Study). CervoMed was formed in August 2023 with completion of the merger of EIP Pharma Inc. with Diffusion Pharmaceuticals Inc.

For more information, please visit https://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.

Additional Reference:

Jiang, Y, Alam, JJ, Gomperts SN et al., "Preclinical and Randomized Clinical Evaluation of the p38α Kinase Inhibitor Neflamapimod for Basal Forebrain Cholinergic Degeneration," *Nature Communications*, 13, Article number: 5308 (2022).https://www.nature.com/articles/s41467-022-32944-3

Contacts

Investors & Media:
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cervomed@argotpartners.com

Exhibit 99.2

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

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 – **October 25, 2023** – 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 Presentationsand 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

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Contacts

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OC8 - A phase 2b clinical trial of neflamapimod in dementia with Lewy bodies designed to confirm the efficacy results from phase 2a

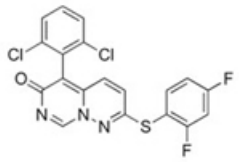
Niels D. Prins (1) Amanda Gardner (2), Hui-May Chu (3), Kelly Blackburn (2), James E. Galvin (4), John Alam (2)

(1) Brain Research Center - Amsterdam (Netherlands), (2) CervoMed (Formerly EIP Pharma) Inc - Boston (United States), (3) Anoixis Corporation - Natick (United States), (4) University of Miami Miller School of Medicine - Boca Raton (United States)

Disclosures

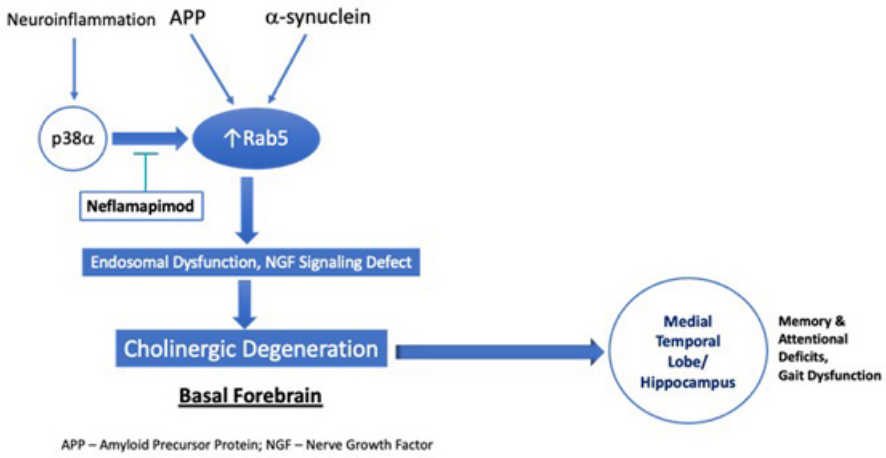
- Dr. Prins is CEO and co-owner of Brain Research Center, The Netherlands. He is also a consultant to Aribio, Eli-Lilly, and Janssen and received a speaker fee from Biogen.
- Dr. Alam is CEO of, Ms. Blackburn is a full-time employee of, and Ms. Gardner and Dr. Chu are consultants/contractors to CervoMed Inc. EIP Pharma, the corporate sponsor of the clinical trials of neflamapimod, is a wholly owned subsidiary of CervoMed.
- Dr. Galvin has no disclosures to report

Neflamapimod Background



- Oral small molecule highly selective inhibitor of the protein kinase p38α, a major activator of the cellular stress response
- In preclinical studies, reverses neurodegenerative process in basal forebrain
- Safety profile well defined, with clinical safety data in greater than 300 study participants
- Prior phase 2 studies in AD demonstrated blood-brain-barrier penetration and target engagement (reduction vs. placebo of CSF levels of p-tau and total tau)
- In dementia with Lewy bodies (DLB), in phase 2a neflamapimod improved versus placebo cognitive, functional and motor aspects of the disease

Neflamapimod Treatment Targets Basal Forebrain Cholinergic Degeneration



APP – Amyloid Precursor Protein; NGF – Nerve Growth Factor

Alam & Nixon, *Molecular Degeneration,* 2023

AscenD-LB demonstrated neflamapimod improved cognition and function in DLB

Outcome	Measure	40mg BID + 40mg TID		40mg TID	
		Mean vs. placebo (95% CI)	p-value	Mean vs. placebo (95% CI)	p-value
Dementia Severity	Clinical Dementia Rating Sum of Boxes (CDR-SB)	-0.45 (-0.83, -0.06)	0.023	-0.56 (-0.96, -0.16)	0.007
Cognition	Neuropsychological Test Battery (NTB) Composite z-score	0.04 (-0.11, 0.19)	>0.2	0.17 (0.00, 0.35)	0.049
	Attention Composite z-score	0.14 (-0.06, 0.35)	0.17	0.28 (0.04, 0.51)	0.023
Motor Function	Timed and Go Test (TUG)	-1.4 (-2.7, -0.1)	0.044	-1.4 (-2.6, -0.2)	0.024

On-study (all time-points) results; change from baseline analysis utilizing Mixed Model for Repeated Measures (MMRM)
Number of participants: 41 for placebo, 20 each for 40mg BID and 40mg TID

***Nature Communications*, 13, Article number: 5308 (2022). https://www.nature.com/articles/s41467-022-32944-3**

Objective of Presentation

Detail the major learnings from the Phase 2a AscenD-LB in DLB, as well MRI results from a prior phase 2a study in AD, that were incorporated into the final design of the ongoing Phase 2b RewinD-LB Study

AscenD-LB

- Phase 2a Exploratory Study
- Results Published:
  - Jiang et al, *Nature Communications*, 2022
  - Alam et al, *Neurology*, 2023

RewinD-LB

- Phase 2b study designed to confirm the phase 2a efficacy findings
- First patient dosing occurred August 2023
- Completion of enrollment planned for H1'24


Patient Population

AscenD-LB Inclusion Criteria Identified Robust DLB Patient Population

Inclusion criteria:

- Probable DLB by 2017 consensus criteria (dementia, with at least one core clinical feature of DLB)
- Demonstrated abnormality in dopamine uptake by DaTscan™ (Ioflupane I123 SPECT)]
- MMSE 16-28

Patients enrolled had attentional deficits, with >1.5 SD deficits vs. age-adjusted norm in One Back - accuracy, Identification and Detection tests

  - Lesser decline in executive function, with ≤1 SD deficit in Letter Fluency and Category Fluency; consistent with the literature for mild DLB

Baseline Disease Characteristics		Baseline z-score[1] on tests within NTB	
CDR 0.5/1.0/2.0	37%/52%/11%	Identification	-1.6 (1.6)
MMSE	23.0 (3.6)	Detection	-1.6 (1.6)
Fluctuating cognition	61%	One back (accuracy)	-2.6 (1.6)
Visual hallucinations	58%	One card learning	-1.1 (0.8)
REM sleep disorder	66%	Letter Fluency	-0.7 (1.0)
Parkinsonism	81%	Category Fluency	-1.0 (1.4)
≥2 features	85%		

[1] z-score relative to age adjusted norm; NTB — Neuropsychological Test Battery

AscenD-LB results stratified by presence of AD Co-Pathology (by plasma ptau181 levels)

- Efficacy results analyzed after stratification presence (46%) of patients in study) or absence (54%) of AD co-pathology at study entry, as assessed by prospectively defined cut-off for plasma ptau181
  - Analysis by presence/absence of AD co-pathology pre-specified in protocol
  - Ptau181 cut-off prospectively defined from an independent cohort in patients with AD

RESEARCH ARTICLE OPEN ACCESS

Association of Plasma Phosphorylated Tau With the Response to Neflamapimod Treatment in Patients With Dementia With Lewy Bodies

John J. Alam, MD, Paul Maruff, PhD, Susan R. Doctrow, PhD, Hui-May Chu, PhD, Jennifer Conway, BS, Stephen N. Gomperts, MD, PhD, and Charlotte Teunissen, PhD

Neurology® 2023;101:e1708-e1717. doi:10.1212/WNL.0000000000207755

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In print, Oct 24th, 2023

Patients in Phase 2a without AD Co-pathology show substantial response to neflamapimod

AscenD-LB

	Overall Study Population				Patients Without AD Co-pathology (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

[1] Difference between neflamapimod and placebo.

NTB: Neuropsychological Test Battery (6-test cognitive test battery); ISLT – International Shopping List Test. Improvement reflected by negative sign for CDR-SB and TUG and positive sign for other measures. By convention Cohen's d 0.2-0.4=small effect, 04-0.8=moderate, ≥0.8=large


Clinical Endpoints

Performance of Clinical Endpoints in AscenD-LB

- Clinical endpoints that can detect effects on both cognitive and motor function (specifically, CDR-SB and TUG) performed better in the trial with respect to detecting improvement over placebo than endpoints that are purely focused on evaluating cognition
- Underperformance of Neuropsychological Test Battery(NTB) attributable to:
  - Ceiling effects, as all patients receiving cholinesterase inhibitors, while the NTB was modeled after a cognitive test battery that showed responsiveness to treatment in a study of rivastigmine
  - Modest level of deficits of executive function at baseline, tests for which were a major component of the NTB

Clinical Trial Simulations to Estimate Statistical Power of Individual Endpoints

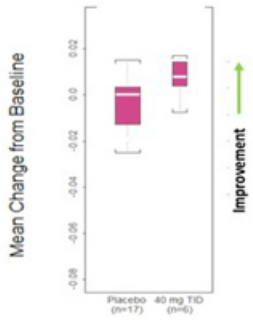
- Sample size for RewinD-LB was evaluated by power analysis via clinical trial simulations:
  - Data in AscenD-LB for the major clinical endpoints in the neflamapimod 40mg TID and placebo groups in patients *without* AD co-pathology was utilized to generate for each patient a change from baseline for each endpoint at individual visits over the course of each of the simulated clinical study
  - The result of each simulated clinical trial was analyzed by utilizing the linear mixed effects model for repeated measures (MMRM) that will be utilized to analyze RewinD-LB
- 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 TUG, and >95% power with CDR-SB (approaching 100%) to detect a treatment effect at an alpha level of 0.05


Biomarkers

EEG Effects in AscenD-LB Stud

- Baseline and end-of-treatment EEGs obtained in 29 patients (17 placebo, 6 neflamapimod 40mg BID, 6 neflamapimod 40mg TID)
  - Covid19 pandemic prevented obtaining EEGs in all patients
- No differences between neflamapimod and placebo in spectral analysis
  - Potentially confounded by all patients receiving cholinesterase inhibitors
- Significant dose-dependent increase vs,, placebo in beta band seen in functional connectivity analysis
  - Beta band power previously identified as strongest discriminator between DLB and AD (Dauwan, 2016, Mehraram, 2020)

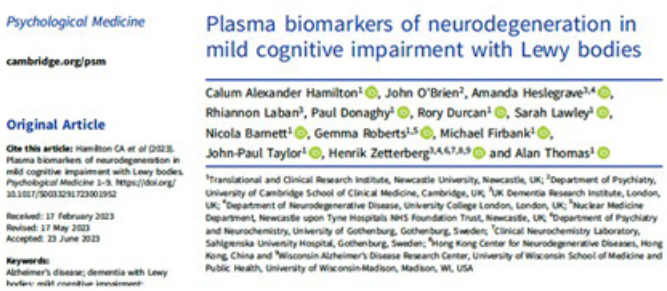
Increased Beta Functional Connectivity on EEG



Mean Functional Connectivity AECc in the **beta** band (13-30 Hz) significantly increased with neflamapimod TID (n=6) vs all placebo (n=17) (p=0.03) and vs placebo TID (n=6) (p=0.01).

CSF and Plasma Biomarkers in DLB

- No CSF or plasma biomarkers specific have been reported
- AD biomarkers (e.g., plasma ptau) may be elevated, but generally tracks with co-pathology
- Recent report (right) indicated that both glial fibrillary acidic protein (GFAP) and neurofilament light chain (NfL) can differentiate MCI due to Lewy bodies from healthy controls, with GFAP being more discriminant



Psychological Medicine

cambridge.org/psm

Original Article

Cite this article: Hamilton CA *et al* (2023). Plasma biomarkers of neurodegeneration in mild cognitive impairment with Lewy bodies. *Psychological Medicine* 1–9. https://doi.org/10.1017/S0033291723001952

Received: 17 February 2023
Revised: 17 May 2023
Accepted: 23 June 2023

Keywords:
Alzheimer's disease; dementia with Lewy bodies; mild cognitive impairment;

Plasma biomarkers of neurodegeneration in mild cognitive impairment with Lewy bodies

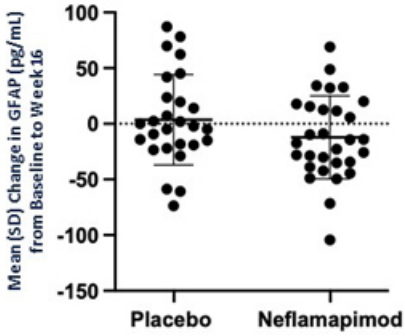
Calum Alexander Hamilton[1], John O'Brien[2], Amanda Heslegrave[3,4], Rhiannon Laban[3], Paul Donaghy[1], Rory Durcan[1], Sarah Lawley[1], Nicola Barnett[1], Gemma Roberts[1,5], Michael Firbank[1], John-Paul Taylor[1], Henrik Zetterberg[3,4,6,7,8,9] and Alan Thomas[1]

[1]Translational and Clinical Research Institute, Newcastle University, Newcastle, UK; [2]Department of Psychiatry, University of Cambridge School of Clinical Medicine, Cambridge, UK; [3]UK Dementia Research Institute, London, UK; [4]Department of Neurodegenerative Disease, University College London, London, UK; [5]Nuclear Medicine Department, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK; [6]Department of Psychiatry and Neurochemistry, University of Gothenburg, Gothenburg, Sweden; [7]Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Gothenburg, Sweden; [8]Hong Kong Center for Neurodegenerative Diseases, Hong Kong, China and [9]Wisconsin Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health, University of Wisconsin-Madison, Madison, WI, USA

Neflamapimod Reduced GFAP Levels vs. Placebo in Patients without AD Co-Pathology

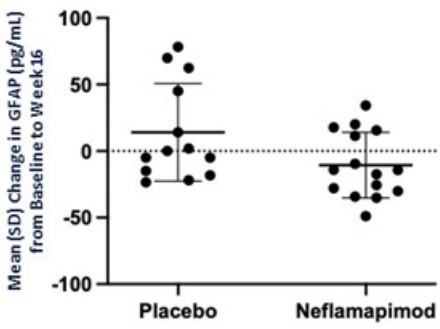
AscenD-LB

Overall Study Population



Mean 3.7 pg/mL increase in placebo vs. mean 12.3 pg/mL reduction with NFMD, p=0.13 for difference

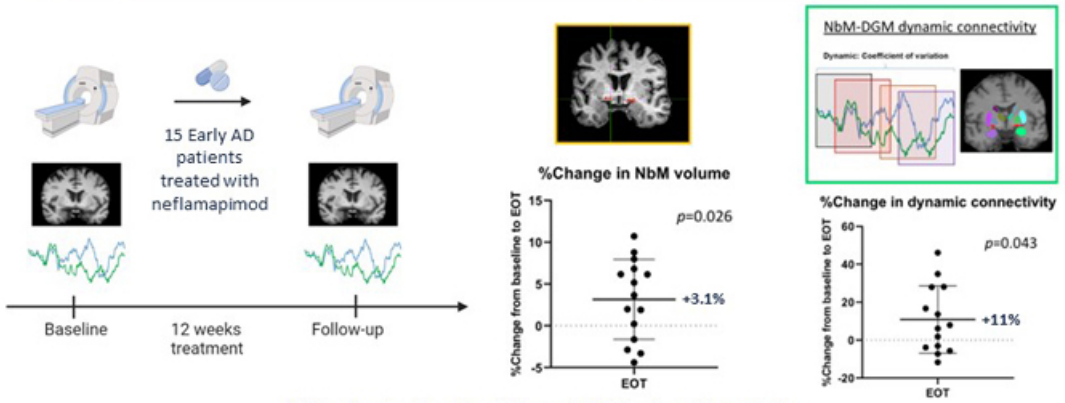
Patients < ptau181 cut-off for AD Co-Pathology



Mean 14.1 pg/mL increase in placebo vs. mean 10.6 pg/mL reduction with NFMD, p=0.04 for difference

Potential Effect on Basal Forebrain Atrophy in Prior Phase 2a Study in AD

Neflamapimod treatment is associated with increased basal forebrain volume and functional connectivity



NbM – Nucleus basalis of Meynert; DGM – Deep Grey Matter

Lin C-P, Noteboom S, Bet M, Alam J, Prins N, Barkhof F, Jonkman L, Schoonheim M, Oral Presentation at AD/PD™ 2023, Gothenburg, Sweden, 1 April 2023


Summary

Summary

- With incorporation of DaTscan, 2017 diagnostic criteria successfully identified a robust DLB patient population with prominent attentional deficits
  - Executive function deficits less prominent in early stage DLB
- CDR-SB is the optimal primary endpoint for phase 2b
- The exclusion of patients with AD co-pathology substantially increases the magnitude of the treatment effect vs. placebo
- Clinical trial simulations indicate that with CDR-SB as primary endpoint and the exclusion of patients AD co-pathology phase 2b study has > 95% statistical power (approaching 100%) to meet its primary endpoints
- Potential Biomarker Effects Identified:
  - Beta functional connectivity on EEG
  - Basal forebrain atrophy and functional connectivity by MRI
  - Plasma GFAP; additional plasma stored for analysis as additional biomarkers are developed

PARTICIPANTS

- DLB by consensus criteria, including abnormal DaTscan™
- Global CDR score of 0.5 or 1.0
- No AD co-pathology, assessed by plasma ptau181

RewinD-LB

INTERVENTION

- Randomized on a blinded basis 1:1 to neflamapimod 40mg capsules (n=80) or matching placebo capsules (n=80), TID for 16 weeks, followed by 32-week open-label neflamapimod extension treatment

OUTCOME MEASURES

- Primary: Clinical Dementia Rating Sum of Boxes (CDR-SB)
- Secondary: Timed Up and Go (TUG) test, Neuropsychological Test Battery (NTB), Clinical Global Impression of Change (CGIC)
- Tertiary: Cognitive fluctuation scale, 12-item Neuropsychiatric Inventory (NPI-12), Part 3 of MDS-Unified Parkinson's Disease Rating Scale (UPDRS)
- EEG: beta functional connectivity (primary), eyes-closed to eyes-open alpha reactivity
- MRI: atrophy of basal forebrain, and its functional connectivity

https://clinicaltrials.gov/study/NCT05869669

RewinD-LB Clinical Sites

Investigator Name	Site	Location
Liana Rosenthal, MD	Johns Hopkins University	Baltimore, MD
Matthew Barrett, MD	Virginia Commonwealth University	Richmond, VA
Andrea Bozoki, MD	University of North Carolina	Chapel Hill, NC
Irene Litvan, MD	UCSD	San Diego, CA
Daniel Huddleston, MD	Emory	Atlanta, GA
Paraunyou Julayanont, MD	Barrow Neurological Institute	Phoenix, AZ
Artin Minaeian, MD	SC3 Research Group	Pasadena, CA
Rajesh Pahwa, MD	KUMC	Kansas City, KS
Linda Pao, MD	JEM Research Institute	Lake Worth, FL
Kathryn Bradley, MD	Banner Alzheimer's Institute	Tucson, AZ
Bradley Boeve, MD	Mayo Clinic	Rochester, MN
Lawrence Honig, MD, PhD	Columbia	New York, NY
Stephen Gomperts, MD, PhD	Massachusetts General Hospital	Charlestown, MA
Babak Tousi, MD	Cleveland Clinic	Cleveland, OH
Douglas Scharre, MD	OSU	Columbus, OH
Jori Fleisher, MD	Rush University Medical Center	Chicago, IL
Sharon Sha, MD	Stanford	Palo Alta, CA
Samatha Holden, MD	University of Colorado	Aurora, CO

Investigator Name	Site	Location
Daniel Murman, MD	University of Nebraska Medical Center	Omaha, NE
Juan Toledo Atucha, MD	Houston Methodist Hospital	Houston, TX
Magdelena Tolea, PhD	University of Miami	Miami, FL
Charles Bernick, MD	Lou Ruvo Center for Brain Health	Las Vegas, NV
Aaron Ritter, MD	Hoag Memorial Hospital	Newport Beach, CA
Yasar Torres-Yaghi, MD	Georgetown University Hospital	Washington, DC
Joseph Cahill, MD	Panhandle Research, LLC	Pensacola, FL
Angela Traylor, MD	Tandem Clinical Research	Marrero, LA
Anwar Ahmed, MD	Advent Health	Orlando, FL
Paul Dautzenberg, MD, PhD	Brain Research Center –Den Haag	Den Bosch, Netherlands
Daphne Troost, MD	Brain Research Center - AMS	Amsterdam, Netherlands
Lieza Exalto, MD, PhD	Brain Research Center - Zwolle	Zwolle, Netherlands
Prof. Dag Aarsland	Kings College	London, England, UK
Dr Saif Sharif	MARC	Hampshire, England, UK
Dr. Manpreet Kaur	Re:Cognition Health	London, England, UK
Dr Robert Barber	U of Newcastle	Newcastle, England, UK
Prof John O'Brien	Cambridgeshire and Peterborough NHS Trust	Cambridgeshire, England, UK
Dr Simon Vann Jones	U of Exeter Cornwall Partnership NHS Foundation Trust	Redruth, England, UK

https://clinicaltrials.gov/study/NCT05869669

Exhibit 99.4

CERVOMED

"Medicines for the Brain"

Corporate Overview

NASDAQ: CRVO

October 25th, 2023

cerveau (sair-voh), noun, in French for *brain* or *mind*

Forward-Looking Statements

This presentation 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 presentation speak only as of the October 25th (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 presentation, except to the extent required by law.

CervoMed at a Glance

Late Clinical Stage CNS Company	Differentiated approach to age-related neurologic disorders with a late-stage lead clinical asset; pipeline of additional indications and second asset
Leading drug candidate in major neurologic indication	Neflamapimod is poised to be the ***first to market treatment for dementia with Lewy bodies (DLB)***; positive phase 2a data published in *Nature Communications* and in *Neurology;* granted Fast Track designation by FDA
Attractive Commercial Opportunity in DLB	1.4M patients in the US and EU; 3rd most common neurodegenerative disease after Alzheimer's and Parkinson's disease >$3B US peak sales opportunity
Multiple Catalysts by the end of 2024	First patient dosing in 160-patient Phase 2b DLB clinical study August'23; complete enrollment in 1H24 and report primary efficacy results[1] in 2H24
Phase 2b Clinical Study Fully Funded	Awarded $21M grant from the NIH's National Institute on Aging (NIA) which will fully fund ongoing Phase 2b study[2].

1. Evaluated at the End of 16-week placebo-controlled portion of the study 2.The NIA grant funds will be disbursed over the course of study as costs are incurred.

CervoMed Management Team

John Alam, MD – President, CEO & Co-Founder, Director
- Former Chief Medical Officer and EVP Medicines Development, Vertex
- Former Global Head Alzheimer's R&D at Sanofi
- Led clinical development of Avonex for multiple sclerosis at Biogen

Robert J. Cobuzzi Jr., PhD – Chief Operating Officer
- President, Chief Executive Officer and Director of Diffusion since 2020
- More than 25 years of cross-functional leadership and operational experience in pharmaceutical and biotechnology industries, including Endo, Adolor, Centocor and AstraMerck

William Tanner, PhD – Chief Financial Officer
- 20 years+ prior experience as a biotech and biopharma research analyst for leading healthcare investment banks including Vector Securities, SG Cowen, Leerink Swann, Lazard Capital Markets and Guggenheim Securities.

William Elder – General Counsel, Corporate Secretary
- General Counsel and Corporate Secretary of Diffusion since 2020
- Nearly a decade of experience advising private and public companies in the pharmaceutical and biotechnology industry with Dechert LLP

Kelly Blackburn – SVP, Clinical Development
- Former VP, Clinical Affairs at aTyr Pharma; VP, Clinical Development Operations at Vertex
- Led global clinical operations for Kalydeco® for the treatment of cystic fibrosis, Incivek® for hepatitis C, and Velcade® for multiple myeloma

Non-Employee Directors and Advisors

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DIRECTORS

Sylvie Gregoire, PharmD (Chair)
- Former Executive Chair and Co-Founder of EIP Pharma
- Board member, Novo Nordisk, Revity (f/k/a Perkin Elmer), F2G
- Former President, Human Genetics Therapies, Shire
- Former Executive VP, Biogen; CEO, GlycoFi
- Former Board member at Vifor, Cubist, Board Chair at Corvidia

Jeff Poulton (Chair of Audit Committee)
- CFO, Alnylam Pharmaceuticals (Nasdaq:ALNY)
- Former CFO, Shire Pharmaceuticals; CFO, Indigo Agriculture

Jane H. Hollingsworth, JD
- Managing Partner, Militia Hill Ventures
- Former Chairman of the Board, Diffusion Pharmaceuticals
- Former Executive Chair, Immunome
- Former CEO, NuPathe (Nasdaq:PATH)

Marwan Sabbagh, MD
- Prof. of Neurology at the Alzheimer's and Memory Disorders division of the Barrow Neurological Institute at Dignity Health/St Joseph's Hospital in Phoenix, Arizona
- Camille and Larry Ruvo Endowed Chair for Brain Health and Director of Translational Research at Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas

Frank Zavrl
- Former Board Member, Puma Biotechnology
- Former Partner, Adage Capital
- Former Research Analyst at Merlin BioMed, Scudder Kemper Investments

Jill Davidson
- President of Fast Scripts LLC and Co-Manager of SkiProp LLC
- Former Vice President at Omnicare, Inc.
- Former Chief Operating Officer of Clasen Long Term Care Pharmacy

SCIENTIFIC ADVISORS

Ole Isacson, MD (Chair)
- Prof of Neurology (Neuroscience) Harvard Medical School

Lewis Cantley, PhD
- Professor of Cell Biology, Harvard Medical School, Dana-Farber Cancer Inst.
- Former Director of the Sandra and Edward Meyer Cancer Center and Professor of Cancer Biology in Medicine at Weill Cornell Medical College
- Co-Founder Petra Pharma, Agios Pharmaceuticals, Volastra Therapeutics

Jeff Cummings, MD, PhD
- Director, Chambers-Grundy Center for Transformative Neuroscience at UNLV

Heidi McBride, PhD
- Professor, Dept. of Neurology & Neurosurgery, McGill University

Dementia with Lewy Bodies (DLB)

CERVOMED

What is DLB?

- Disease associated with abnormal deposits of a protein called alpha-synuclein in the brain. These deposits, called Lewy bodies, affect chemicals in the brain whose changes, in turn, can lead to problems with thinking, movement, behavior, and mood1
- Patients incur greater rate of cognitive decline, higher healthcare costs, report lower quality of life, and have caregivers with higher levels of distress compared to patients with Alzheimer's disease (AD)

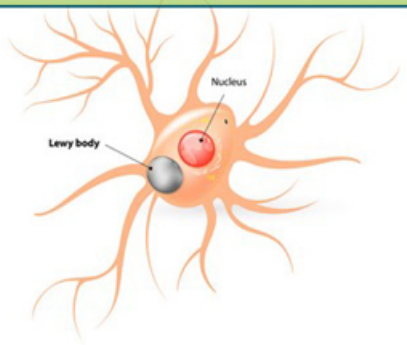
Treatment Landscape and Unmet Need

- No approved therapies; limited drugs in development
- Current standard of care is cholinesterase inhibitor therapy that only transiently improves cognition and does not impact motor component

Market Opportunity

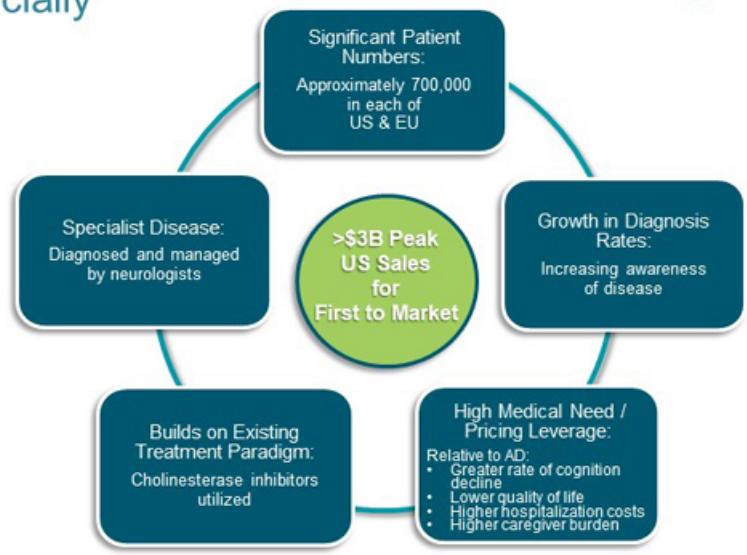
- 3rd most common neurodegenerative disease (after AD and PD)
- ~700,000 individuals in each of US and EU
- Neflamapimod has the potential to be the first disease-modifying approach because it treats the primary pathology - cholinergic degeneration in the basal forebrain

DLB affects ~1.4 million individuals in the US and EU



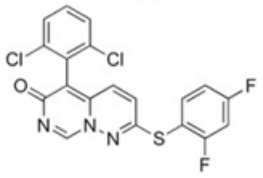
1. https://www.nia.nih.gov/health/what-lewy-body-dementia-causes-symptoms-and-treatments

Neflamapimod for DLB: Well-Positioned Commercially

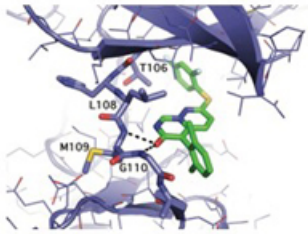


Neflamapimod Background

- Oral small molecule highly selective inhibitor of the protein kinase p38α, a major activator of the cellular stress response
- Licensed from Vertex Pharmaceuticals in 2014
  - Vertex had developed through to phase 2a clinical study in rheumatoid arthritis and discontinued program because brain concentrations 2X greater than in peripheral blood
  - Chronic repeat dose toxicology completed prior to licensing
- Safety profile well defined, with clinical safety data in > 300 study participants
- Phase 2 studies in AD conducted by EIP Pharma (renamed as CervoMed) demonstrated target engagement:
  - Reduction vs. placebo of CSF levels of p-tau and total tau
  - Reduction of CSF inflammatory marker (IL-8)



Crystal structure of neflamapimod bound to p38α



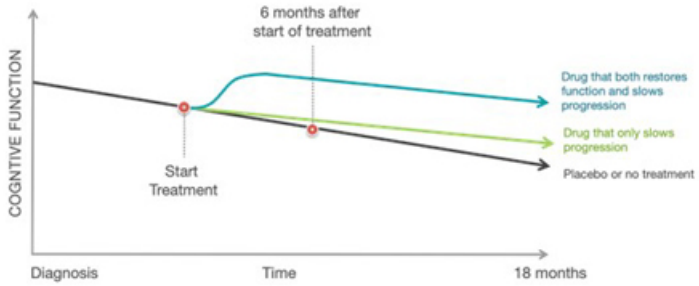
Targeting Synaptic Dysfunction To Treat Neurodegenerative Diseases

CERVOMED

Why Target Synaptic Dysfunction?

- Ahead of frank neuronal loss, there is degeneration and progressive loss of function of synapses (interconnection between nerve cells)
- In animals, treatment of synaptic dysfunction both restores function and arrests disease progression
- In DLB, synaptic dysfunction in the cholinergic system is the driver of symptoms and progression in the prodromal and mild dementia stages of disease

Reversing Synaptic Dysfunction Provides Ability to Demonstrate Efficacy in ≤ 6 Month Duration Clinical Study

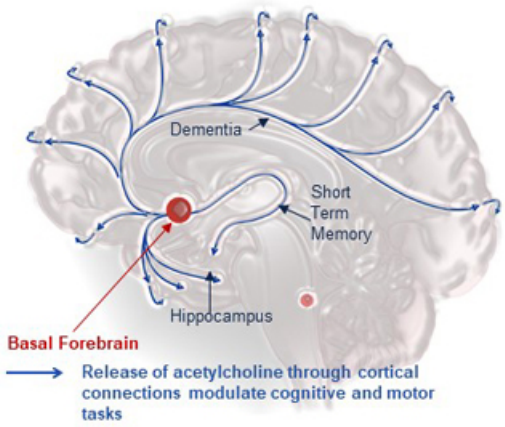


Opportunity for Therapeutics Targeting Basal Forebrain Cholinergic Degeneration

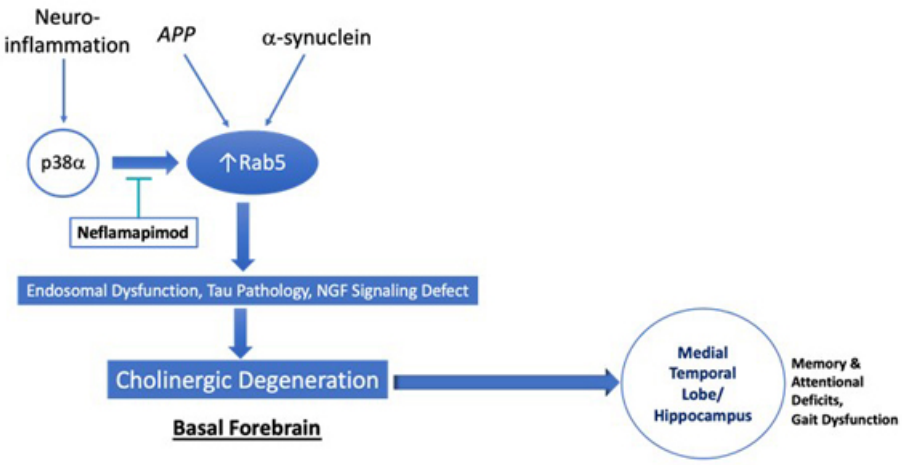
CERVOMED

- Age-related degeneration of the basal forebrain cholinergic system, the major source of the neurotransmitter acetylcholine, plays major role in many neurologic disorders:
  - Dementia with Lewy bodies (DLB), where it is the primary pathology
  - Early stages of Alzheimer's disease
  - Impaired functional recovery after stroke
- As it is due to synaptic dysfunction, and not frank neuronal loss, the neurodegenerative process in the basal forebrain is ***reversible*** through much of the disease course (Cooper et al, 2002; Nagara et al, 2009; etc.)

Basal Forebrain Cholinergic Complex



Neflamapimod Mechanism of Action



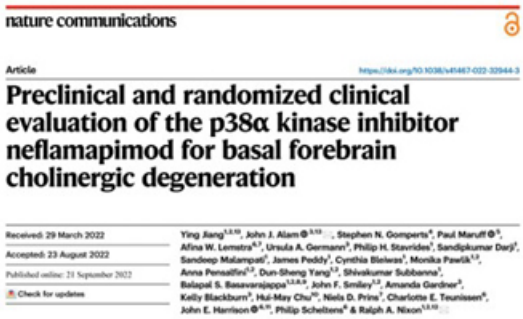
APP – Amyloid Precursor Protein; NGF – Nerve Growth Factor

Alam & Nixon, *Molecular Neurodegeneration, 2023*

Nature Communications Article

CERVOMED

"The authors show in an animal model and in a study in patients with dementia with Lewy bodies (DLB) that the drug neflamapimod has potential to treat diseases, such as DLB, associated with loss of neurons that produce the neurotransmitter acetylcholine."



nature communications

Article

https://doi.org/10.1038/s41467-022-32944-3

Preclinical and randomized clinical evaluation of the p38α kinase inhibitor neflamapimod for basal forebrain cholinergic degeneration

Received: 29 March 2022

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Published online: 21 September 2022

Check for updates

Ying Jiang[1,2,10], John J. Alam[3,11] ✉, Stephen N. Gomperts[4], Paul Maruff[5], Afina W. Lemstra[6,7], Ursula A. Germann[8], Philip H. Stavrides[1], Sandipkumar Darji[1], Sandeep Malampati[1], James Peddy[1], Cynthia Bleiwas[1], Monika Pawlik[1,2], Anna Penatifin[1,2], Dun-Sheng Yang[1,2], Shivakumar Subbanna[1], Balapal S. Basavarajappa[1,2,8,9], John F. Smiley[1,2], Amanda Gardner[3], Kelly Blackburn[3], Hui-May Chu[10], Niels D. Prins[7], Charlotte E. Teunissen[6], John E. Harrison[3,4,11], Philip Scheltens[6] & Ralph A. Nixon[1,2,12] ✉

Neflamapimod ***Reverses*** Cholinergic Dysfunction and Degeneration

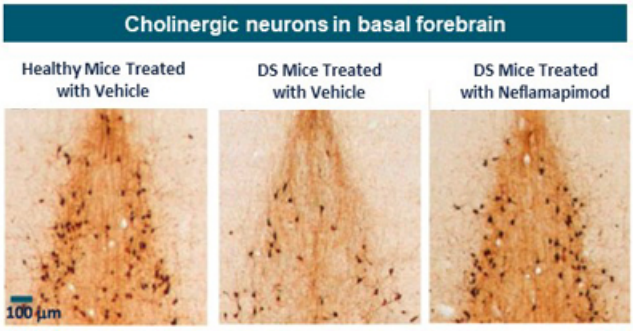
CERVOMED

Down Syndrome (DS) mice

- Ts2 transgenic mice that have both DS-like defects during early development and adult-onset basal forebrain cholinergic degeneration
- Treated with vehicle or 3 mg/kg neflamapimod twice daily x 28 days, starting at month 6

Reversed basal forebrain cholinergic neuron loss and restored cholinergic function

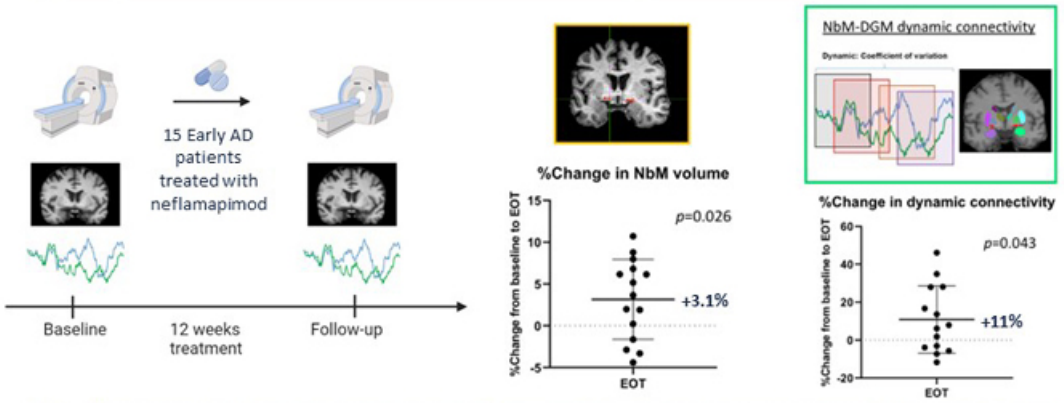
- Significantly increased (+30% vs. controls, $p<0.001$) number of cholinergic neurons in basal forebrain
- Normalized performance in Open field and NOR behavioral test



Cholinergic neurons identified by staining for choline acetyl transferase expression

Neflamapimod Appears to Reverse Basal Forebrain Atrophy, assessed by MRI

Neflamapimod treatment is associated with increased basal forebrain volume and functional connectivity



NbM – Nucleus basalis of Meynert, the largest cluster of cholinergic neurons in the basal forebrain; DGM – Deep Grey Matter

Lin C-P, Noteboom S, Bet M, Alam J, Prins N, Barkhof F, Jonkman L, Schoonheim M, Oral Presentation at AD/PD™ 2023, Gothenburg, Sweden, 1 April 2023

Phase 2a ("AscenD-LB") Clinical Trial Results in Patients with DLB

- 91-patient, exploratory, 16-week treatment, double-blind placebo-controlled study in patients with mild-to-moderate DLB
- In the study, neflamapimod:
  - Significantly improved outcomes compared to placebo on Clinical Dementia Rating Sum of Boxes (CDR-SB, dementia severity scale, p=0.023) and Timed Up and Go (TUG, measure of mobility, p=0.044)
  - Significantly (p=0.049) improving vs. placebo results on cognitive testing at the higher (40mg TID) of two dose levels in the study dose level, particularly with respect to attention (p=0.023)
  - Well tolerated, with no treatment discontinuations at 40mg TID dose level

Clinical Dementia Rating Sum of Boxes (CDR-SB, Total Score = 0-18)

Cognitive Domains:
- Memory (0-3)
- Orientation (0-3)
- Judgement and Reasoning (0-3)

Functional Domains:
- Community Affairs (0-3)
- Home & Hobbies (0-3)
- Personal Care (0-3)

Nature Communications, 13, Article number: 5308 (2022). https://www.nature.com/articles/s41467-022-32944-3

AscenD-LB results stratified by presence of AD Co-Pathology (by plasma ptau181 levels)

CERVOMED

- Efficacy results analyzed after stratification presence (44% of patients in study) or absence (56%) of AD co-pathology at study entry, as assessed by prospectively defined cut-off for plasma ptau181
  - Analysis by presence/absence of AD co-pathology pre-specified in protocol
  - Ptau181 cut-off prospectively defined from an independent cohort in patients with AD

RESEARCH ARTICLE OPEN ACCESS

Association of Plasma Phosphorylated Tau With the Response to Neflamapimod Treatment in Patients With Dementia With Lewy Bodies

John J. Alam, MD, Paul Maruff, PhD, Susan R. Doctrow, PhD, Hui-May Chu, PhD, Jennifer Conway, BS, Stephen N. Gomperts, MD, PhD, and Charlotte Teunissen, PhD

Neurology® 2023;101:e1708-e1717. doi:10.1212/WNL.0000000000207755

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Published online Sept 1st, 2023
In print, Oct 24th, 2023

Patients in Phase 2a without AD Co-pathology show substantial response to neflamapimod

CERVOMED

AscenD-LB

	Overall Study Population				Patients Without AD Co-pathology (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

[1] Difference between neflamapimod and placebo.

NTB: Neuropsychological Test Battery (6-test cognitive test battery); ISLT – International Shopping List Test. Improvement reflected by negative sign for CDR-SB and TUG and positive sign for other measures. By convention Cohen's d 0.2-0.4=small effect, 04-0.8=moderate, ≥0.8=large

Potential Biomarker Effects Identified in Phase 2a

- EEG: Functional Connectivity in the beta band (13-30 Hz) significantly increased with neflamapimod TID (n=6) vs all placebo (n=17), p=0.03; and vs. placebo TID (n=6), p=0.01.
- Plasma Biomarker: In patients without Alzheimer's related co-pathology at study entry, neflamapimod 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)

Learnings from Phase 2a Study That Enhance Probability of Success in Phase 2b

- Optimal dose is 40mg TID
- Clinical endpoints that can detect effects on both cognitive and motor function (specifically, CDR-SB and TUG) perform better than endpoints that are purely focused on evaluating cognition
  - In Alzheimer's disease, CDR-SB accepted by regulatory authorities as an approval endpoint
- Patients without AD co-pathology have a substantially greater response to treatment
  - Excluding patients with AD co-pathology as assessed by plasma ptau181 in phase 2b study substantially increases statistical power in the study

With incorporation of above, Phase 2b has >95% (approaching 100%) statistical power to meet its primary endpoint: change in CDR-SB vs. placebo

PARTICIPANTS

- DLB by consensus criteria, including abnormal DaTscan™
- Global CDR score of 0.5 or 1.0
- No AD co-pathology, assessed by plasma ptau181

RewinD-LB

INTERVENTION

- Randomized on a blinded basis 1:1 to neflamapimod 40mg capsules (n=80) or matching placebo capsules (n=80), TID for 16 weeks, followed by 32-week open-label neflamapimod treatment extension

OUTCOME MEASURES

- Primary: Clinical Dementia Rating Sum of Boxes (CDR-SB)
  - >95% (approaching 100%) statistical power to detect treatment effect on CDR-SB
- Secondary: Timed Up and Go (TUG) test, Neuropsychological Test Battery (NTB), Clinical Global Impression of Change (CGIC)
- EEG: beta functional connectivity (primary), eyes-closed to eyes-open alpha reactivity
- MRI: atrophy of basal forebrain, and its functional connectivity

Major Value Creation Potential with Positive Phase 2b Clinical Trial

CERVOMED

Phase 2b success (statistical significance on primary endpoint) will provide a clear path to market in a high value indication

- DLB is an indication with **high unmet medical need** and **high commercial return potential**
- Phase 3 design, based on prior discussions with FDA and pending confirmation in an end-of-phase 2 meeting with the FDA after Phase 2b:
  - Single clinical trial
  - 24-weeks treatment duration, with CDR-SB as primary endpoint
  - Approximately 300 patients (final sizing based on phase 2b results)
  - Anticipated $50-75M cost

➢ **Efficacy risk in phase 3 is in extending treatment duration to 24 weeks from 16 weeks in phase 2b**

Key Upcoming Anticipated Milestones/Catalysts

CERVOMED

1H 2023

- ✓ NIA approves $21M grant for Phase 2b
- ✓ Signed merger agreement with Diffusion Pharma
- ✓ Present data at AD/PD 2023
- ✓ Initiate Phase 2b DLB study

2H 2023

- ✓ FPD in Phase 2b DLB study
- ✓ Close merger transaction; begin trading as a public company
- ✓ Publish additional Phase 2a data[1] from DLB study in a major neurology journal
- ✓ Oral presentation at CTAD conference

2024

- ❑ Complete enrollment in Phase 2b DLB study (1H)
- ❑ Additional presentations at scientific conferences and publications
- ❑ Report data from placebo-controlled portion of Phase 2b DLB study (2H)

1. Plasma ptau181 stratified results.

Financial Overview[1]

- Approximately 5.7M shares outstanding, all common stock
  - 0.5M pre-funded warrants; 0.1M out of the money warrants
  - Other than officers and directors, and certain affiliated trusts, no shareholders subject to contractual lock-ups
- CervoMed has cash runway to fund company operations through to anticipated primary efficacy readout in the study in H2'24

(1) As of September 30, 2023. Refer to the Company's Current Report on Form 8-K/A filed with the SEC on September 29, 2023 for additional financial and other information

Summary

- Differentiated Approach to Age-related Neurologic Disorders with a Late-Stage Asset
- Major value creation potential in phase 2b read-out in dementia with Lewy bodies
- Experienced Management Team and Board of Directors
- Potential to broaden opportunity through additional indications and 2nd asset
- Significant news flow through to end of 2024

CERVOMED

"Medicines for the Brain"

Corporate Overview

NASDAQ: CRVO

October 25th, 2023

cerveau (sair-voh), noun, in French for *brain* or *mind*