CERVOMED

Medicines for the Brain

September 2024

Corporate Overview

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

NASDAQ: CRVO

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; the anticipated timing and achievement of clinical and development milestones, including the completion and achievement of primary endpoints of the RewinD-LB Phase 2b clinical trial and the Company's announcement of topline data therefrom; any other expected or implied benefits or results, including that any initial clinical results observed with respect to neflamapimod in the AscenD-LB Trial or RewinD-LB Trial will be replicated in later trials; the Company's clinical development plans and related timelines; the potential commercial opportunity of neflamapimod, if approved; and the Company's anticipated cash runway. Terms such as "believes," "estimates," "anticipates," "expects," "plans," "aims," "seeks," "intends," "may," "might," "could," "might," "will," "should," "approximately," "potential," "target," "project," "contemplate," "predict," "forecast," "continue," 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 Company's ability to design, initiate, enroll, execute, and complete its planned studies evaluating neflamapimod; 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, but not limited to: changes in the competitive and highly regulated industry in which the Company operates; the issuance of additional shares of the Company's common stock, including upon the issuance of outstanding warrants or otherwise; 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, including the continued availability of funding for the U.S. federal government to support disbursements under the Company's grant from the National Institute on Aging; and the other factors discussed under the heading "Risk Factors" in the Company's most recent Annual Report on Form 10-K for the year ended December 31, 2023 filed with the U.S. Securities and Exchange Commission ("SEC") on March 29, 2024, and other filings that the Company may file from time to time with the SEC. Any forward-looking statements in this presentation speak as of September 3, 2024 (or such earlier date as may be identified) and the Company does not undertake any obligation to update such forward-looking statements to reflect events or circumstances after this date, except to the extent required by law.

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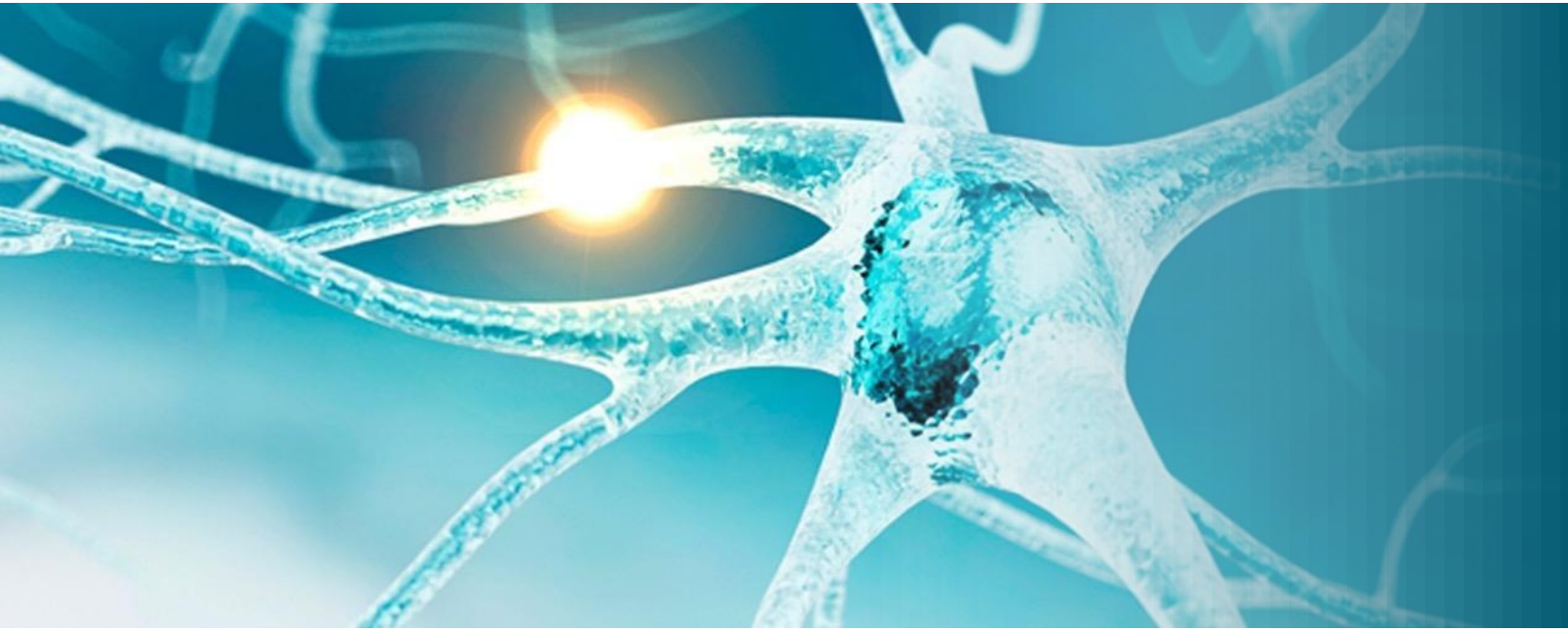
Company Overview

Targeting Synaptic Dysfunction to Treat Age-Related Neurologic Disorders



CervoMed began trading on NASDAQ (CRVO) in August 2023 following a completed merger between EIP Pharma, Inc. and Diffusion Pharmaceuticals Inc.

Headquartered: Boston, MA

Lead program: Oral neflamapimod for the treatment of Dementia with Lewy bodies

Licensed from Vertex Pharmaceuticals; developed for CNS indications by EIP Pharma/CervoMed

Neflamapimod IP covered by multiple issued patents around method of use for specific disease indications and formulations, expiring at various dates through to 2039

Experienced Leadership 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

William Elder

Chief Financial Officer & General Counsel

Principal Financial Officer of CervoMed since March 2024
General Counsel and Corporate Secretary of Diffusion (2020-23)
J.D. from University of Pennsylvania School of Law, M.S. Finance from Villanova University, B.A. Economics from Tufts University

Robert J. Cobuzzi Jr., PhD

Chief Operating Officer, Director

President, Chief Executive Officer and Director of Diffusion (2020-23)
More than 25 years of cross-functional leadership and operational experience in pharmaceutical and biotechnology companies, including Endo, Adolor, Centocor and AstraMerck

Kelly Blackburn, MHA

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

DIRECTORS

Joshua Boger, PhD (Chair)
Executive Chair, Alkeus Therapeutics.
Founder, former CEO, Vertex Pharmaceuticals

Sylvie Gregoire, PharmD
Co-Founder; Board member, Novo Nordisk, F2G, Former Executive VP, Biogen; Former President, HGT Division, Shire Pharmaceuticals; Former Board member, Revitty, ViFor, Corvidia, Cubist

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

Jane H. Hollingsworth, JD
Managing Partner, Militia Hill Ventures
Former Chairman of the Board, Diffusion Pharmaceuticals

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

Frank Zavrl
Former Board Member, Puma Biotechnology
Retired Partner, Adage Capital

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 Institute; Laureate, Breakthrough Prize in Life Sciences

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

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

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Financial Overview[1]

CervoMed has an expected cash runway through the end of 2025

Cash Resources and Grant Funding

- $50.9M in cash, cash equivalents and marketable securities
- $21.0M NIA Grant awarded January 2023, disbursed over 3 years
    - $6.8M in remaining funding yet to be received

Operating Expenses

- $6.5M in research and development expenses during 1H24

Capitalization

- 8.3 million shares outstanding as of August 8, 2024
- 3.1 million shares underlying outstanding warrants, including 0.4 million pre-funded warrants
    - CervoMed may receive up to $99.4 million of gross proceeds upon the exercise of 2.5 million shares underlying outstanding Series A warrants (Exercise Price = $39.24)
    - With positive top-line data from ongoing Phase 2b trial, exercise permitted no later than 180 days after data announcement

1. Unless otherwise indicated, all financial information is approximate and as of June 30, 2024. For additional, important information regarding the Company's financial position and results of operations, please refer to the Company's Quarterly Report on Form 10-Q for the three months ended June 30, 2024, filed with the SEC on August 9, 2024.

CervoMed at a Glance

Late Clinical Stage CNS Company	**Targeting synaptic dysfunction to treat age-related neurologic disorders;** modulating drivers of the early phase of the degenerative process in the brain, including neuronal stress and inflammatory pathways
Attractive Commercial Opportunity in Dementia with Lewy bodies (DLB)	Major neurologic indication with 700,000 patients in the US; **>$3B US peak sales opportunity**
First-to-market Potential in DLB	Neflamapimod granted Fast Track designation by FDA and is poised to be the **first to market treatment for DLB;** positive phase 2a data published in *Nature Communications, Neurology,* and *JPAD*
Phase 2b Clinical Study Optimally Designed and Fully Enrolled	159 patient study in early-stage DLB with Clinical Dementia Rating Scale Sum of Boxes (CDRS SB) as primary endpoint; 16-week placebo controlled with 32-week open label extension. Funded by $21M grant from National Institutes of Aging (NIA)[1]
Multiple Value-Driving Milestones Over Next 12 Months	**Completed enrollment into phase 2b study in June 2024 and plan to report efficacy results[2] and other topline data in December 2024.** With positive Phase 2b data, anticipate starting Phase 3 in mid 2025

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

Neflamapimod Background

Oral brain penetrant small molecule highly selective inhibitor of the protein kinase p38α, a major activator of the cellular stress pathways in response to neuroinflammation

Licensed from Vertex Pharmaceuticals in 2014

Neflamapimod offers first to market treatment option for dementia with Lewy bodies (DLB) with the potential to **reverse the underlying disease process** in the basal forebrain and address **cognitive, functional and motor** aspects of the disease

Supported by robust dataset:

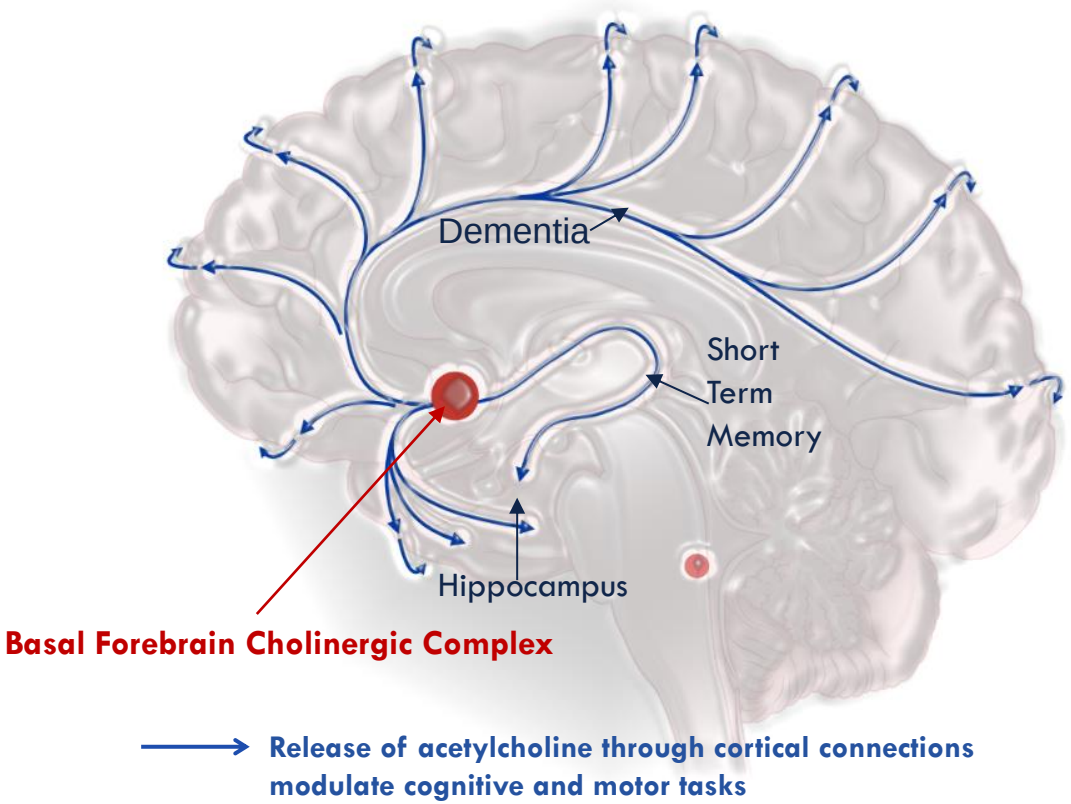
- In preclinical and clinical studies, neflamapimod reverses the underlying disease process in the basal forebrain
- Chronic, repeat dose toxicology studies completed, with 10-fold safety margin at 40mg TID in humans to NOAEL in those studies
- In phase 2a trial in patients with DLB, neflamapimod versus placebo improved cognitive, functional and motor aspects of the disease, and demonstrated effects on EEG and a plasma biomarker. Effects most prominent in patients with early-stage DLB
- Safety profile well defined, with clinical safety data in greater than 300 study participants

Prior phase 2 studies in Alzheimer's disease (AD) demonstrated target engagement:

- Reduction vs. placebo of CSF levels of ptau and total tau; increased volume and functional connectivity of basal forebrain by MRI

Neflamapimod Mechanism of Action

Synaptic dysfunction in basal forebrain is the primary driver of disease in DLB



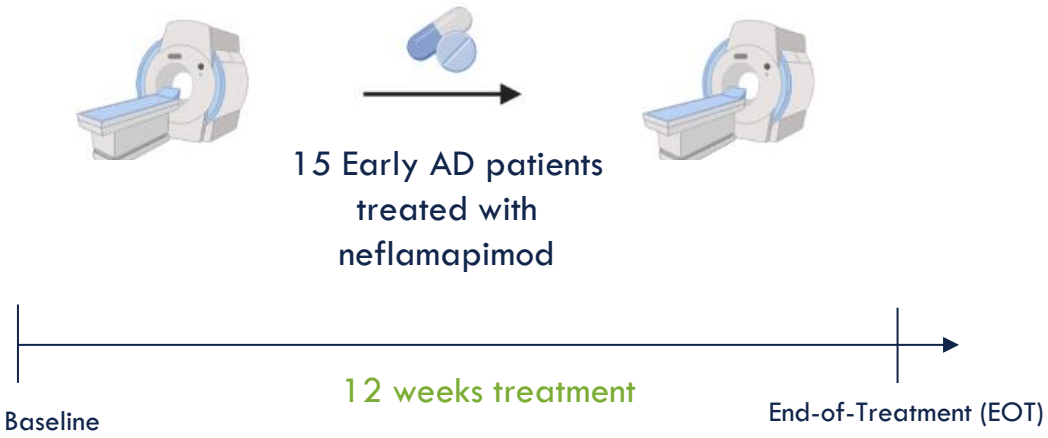
Disease processes in basal forebrain are reversible

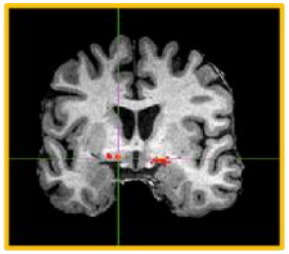
- Through inhibiting p38a targets specifically targets molecular mechanisms underlying synaptic dysfunction in the basal forebrain cholinergic system[1]
- In published studies[2] conducted in the laboratory of Prof. Ralph Nixon at NYU Langone Medical Center, in mice that develop basal forebrain cholinergic degeneration neflamapimod:
  - Reduced phosphorylation levels of downstream targets of p38a (i.e., demonstrated target engagement)
  - Reversed early (Rab5+) endosomal pathology
  - Restored the number of cholinergic (choline acetyl transferase expressing) neurons in the basal forebrain to wild-type levels
  - Normalized performance in behavioral tests linked to cholinergic function

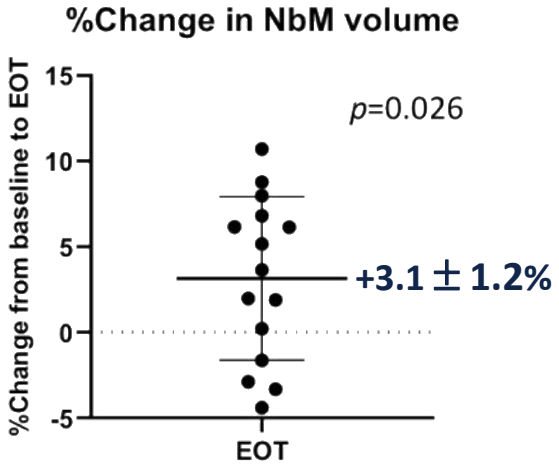
1. Alam & Nixon, *Molecular Neurodegeneration*, 2023. 2. Nature Communications, 13: 5308 (2022). https://www.nature.com/articles/s41467-022-32944-3

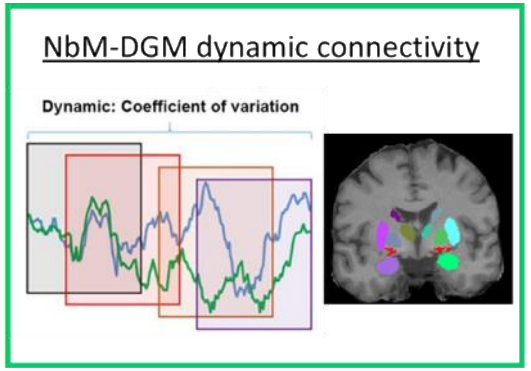
Neflamapimod Appears to Reverse Synaptic Dysfunction in the Basal Forebrain, As Assessed by Structural and Functional MRI

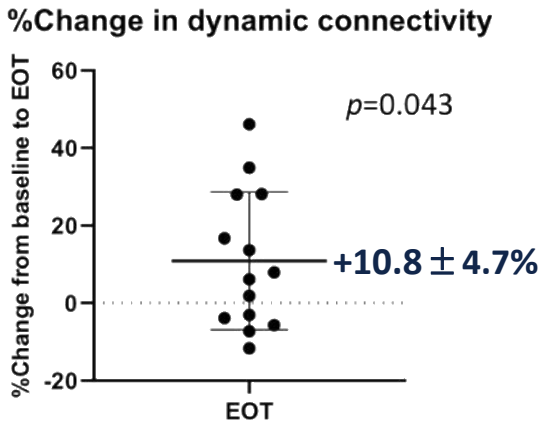
Neflamapimod treatment is associated with a significant increase of basal forebrain volume and functional connectivity











Findings based on AscendD-LB Phase 2a Results

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

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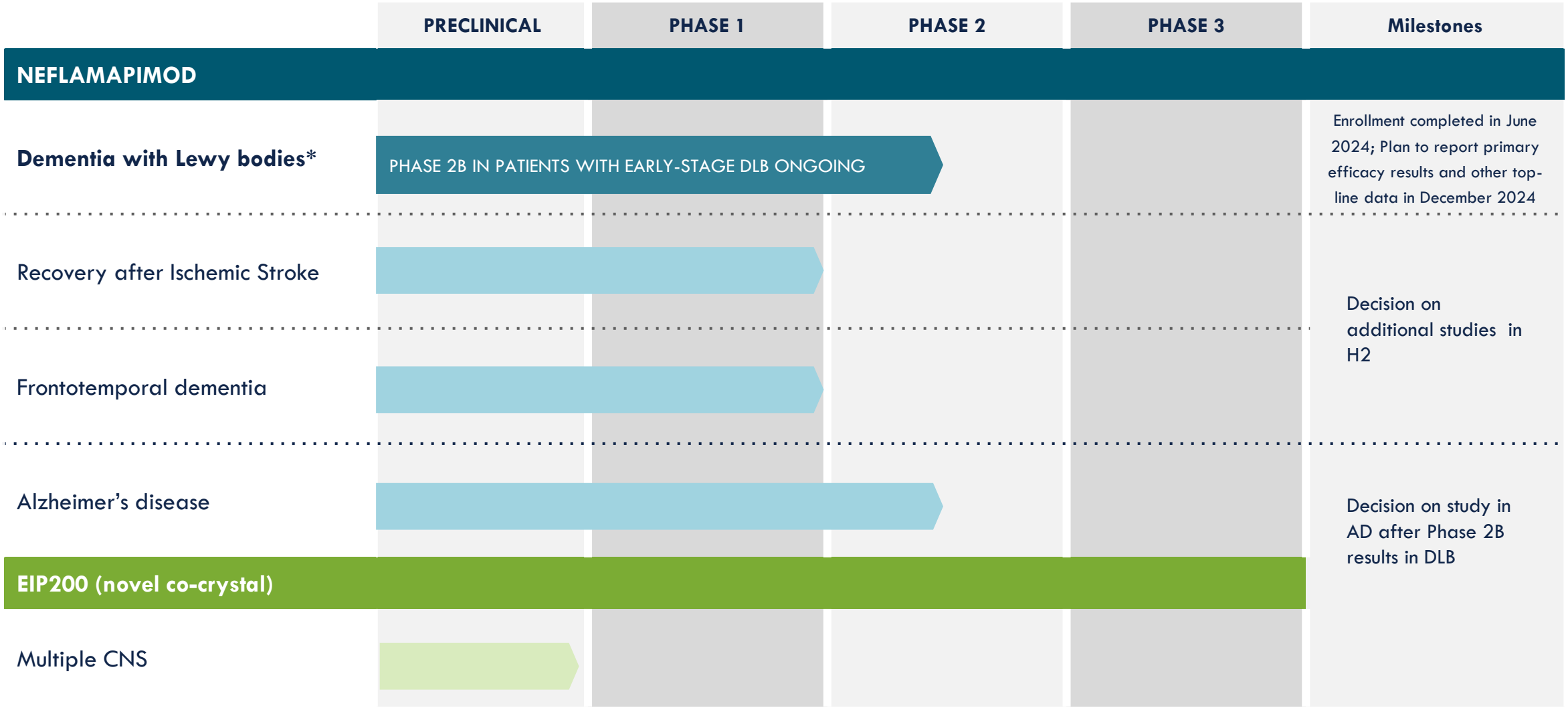
CervoMed Pipeline



Worldwide commercial rights across programs
*Received FDA Fast Track designation

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Dementia with Lewy Bodies (DLB)

What is DLB?

Disease associated with abnormal deposits ("Lewy bodies") within neurons of a protein called alpha-synuclein in the brain, with primary site of pathology being in basal forebrain

Clinically, characterized by dementia (deficits in attention, executive function) and ≥ 2 of the following: fluctuating attention, visual hallucinations, REM sleep disorder, and/or parkinsonism (motor deficits)[1]

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)

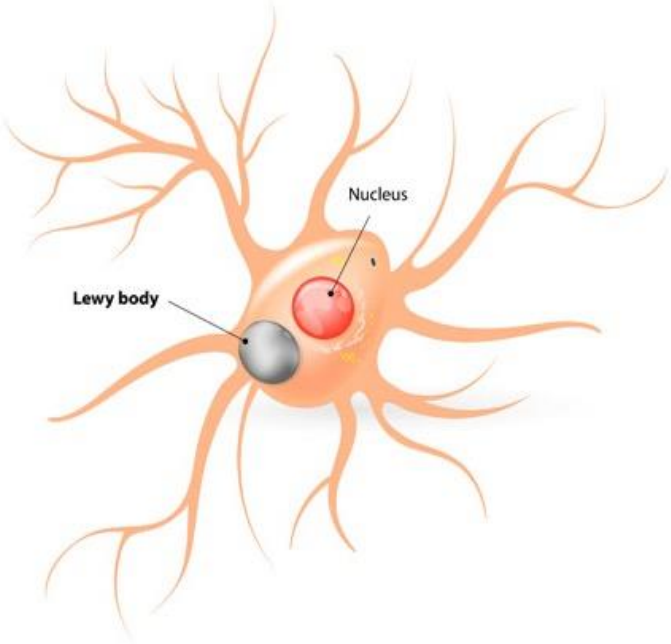
Treatment Landscape and Unmet Need

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 degenerative disease of the brain (after AD and PD)
- ~700,000 individuals in each of US and EU, half of which are in the early-stage of their disease
- High pricing leverage because of medical need and DLB being a specialty disease (i.e., neurologist managed)
- Projected >$3B in sales in US alone



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

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Distinctions between "Early-Stage DLB" and "Advanced DLB"

Early-Stage DLB (~50% of All DLB Patients)

Without biomarker evidence of AD (e.g., positive amyloid or tau PET scan, elevated phosphorylated tau in CSF or blood)

Disease limited to synaptic dysfunction in basal forebrain, with no to limited neuronal loss in hippocampus

Have a reversible component of disease

Ability to obtain approval based on 6-month treatment duration in phase 3

Advanced DLB (~50% of All DLB Patients)

Have biomarker evidence of AD (e.g., positive amyloid or tau PET scan, elevated phosphorylated tau in CSF or blood)

Have significant neuronal loss in hippocampus

Have primarily irreversible deficits

Approval would likely require demonstrating disease progression effect with 12 to 18-month treatment duration in phase 3

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Therapeutic Opportunity in Early-Stage Dementia with Lewy Bodies (DLB)

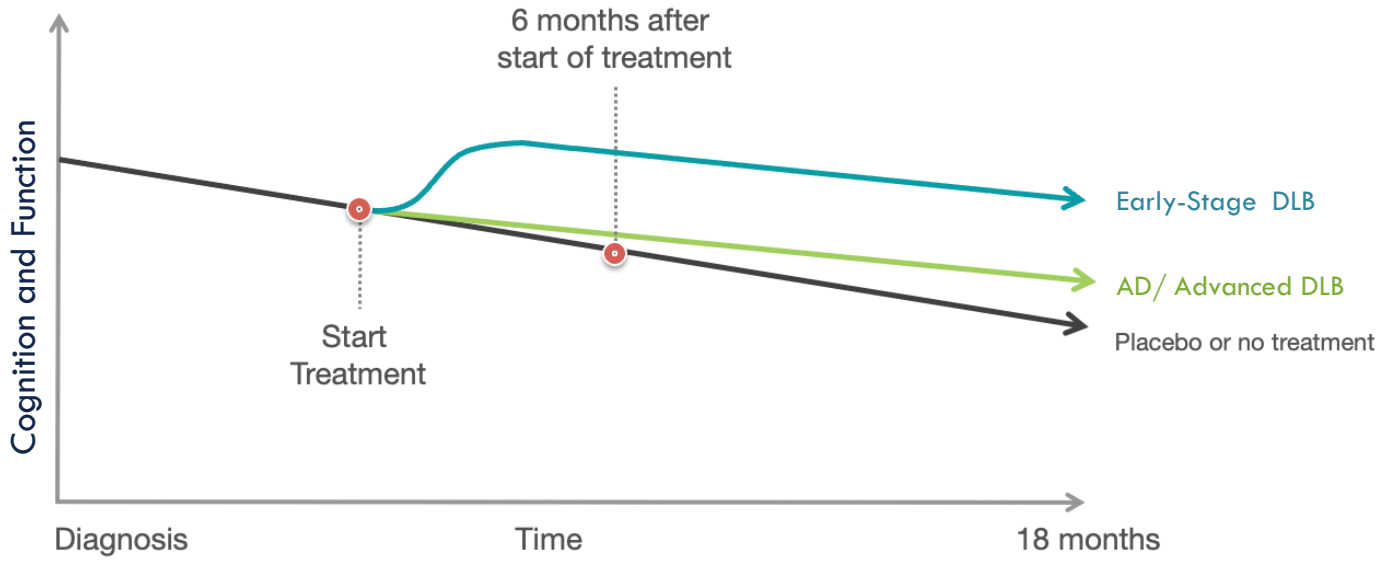
Early-stage DLB is primarily a disease of reversible synaptic dysfunction in the basal forebrain cholinergic system

Advanced DLB also has neuronal loss in the hippocampus

Successful treatment of the underlying disease process in early stage DLB would lead to both reversal of progression (**restore function**) in the near term, as well as slowing of further decline in the long-term

Provides opportunity to demonstrate efficacy in phase 2 and go to market with 6-month treatment duration in phase 3

Reversing Clinical Progression Provides Ability to Demonstrate Efficacy in ≤ 6 Month Duration Clinical Studies



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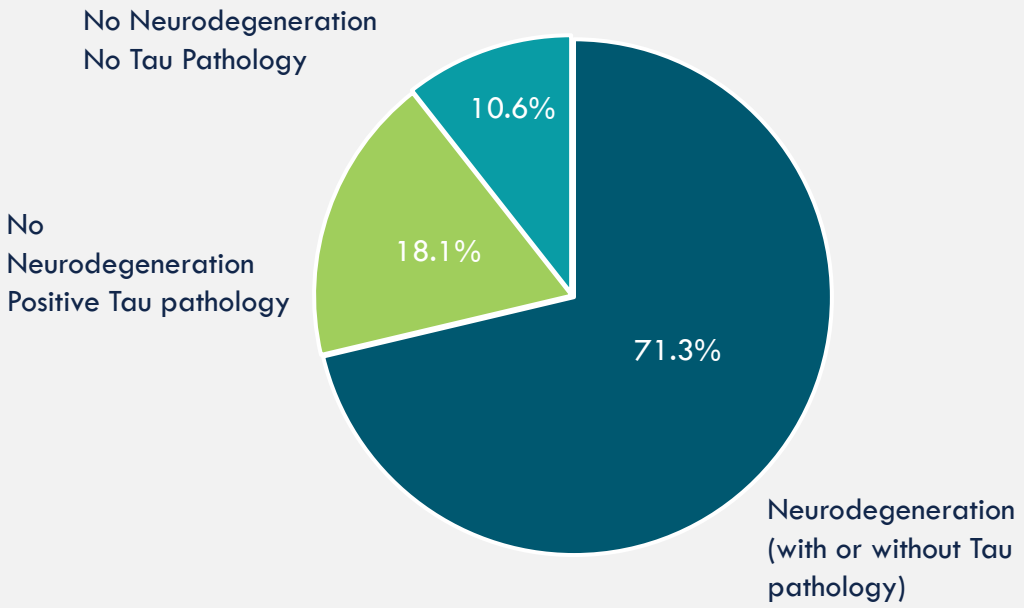
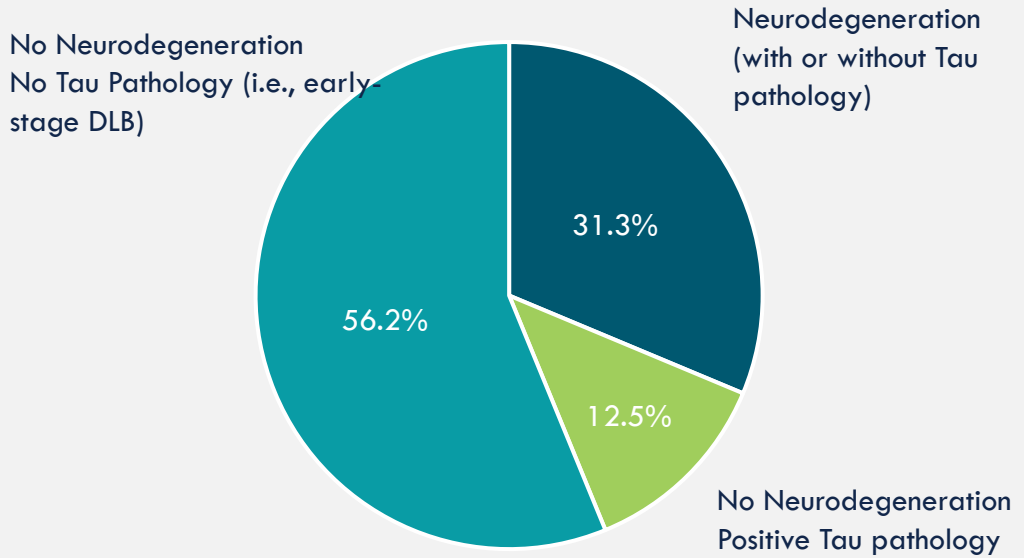
Approximately 50% of Diagnosed DLB Patients are in the Early-Stage of Their Disease (versus ~10% of AD Patients)

Presence of Neurodegenerative Marker Elevation in CSF (Cerebrospinal Fluid)

Alzheimer's Disease (n=133)



Dementia with Lewy Bodies (n=109)



[1] Positive Tau: increased CSF levels of ptau181; "Neurodegeneration": Increased CSF levels total tau
Jain et al, *Alzheimer's & Dementia*, 2023

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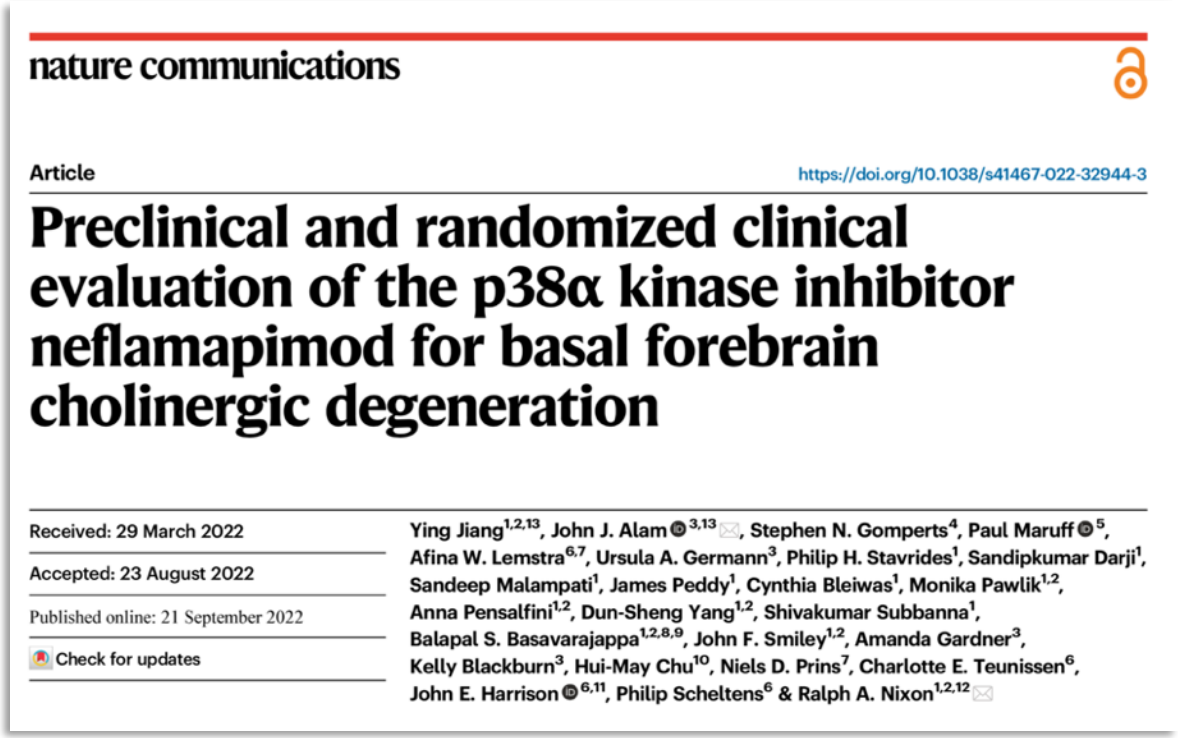
Positive Phase 2a Clinical Results in Dementia with Lewy Bodies Published in High Impact Factor Scientific and Clinical Journals



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

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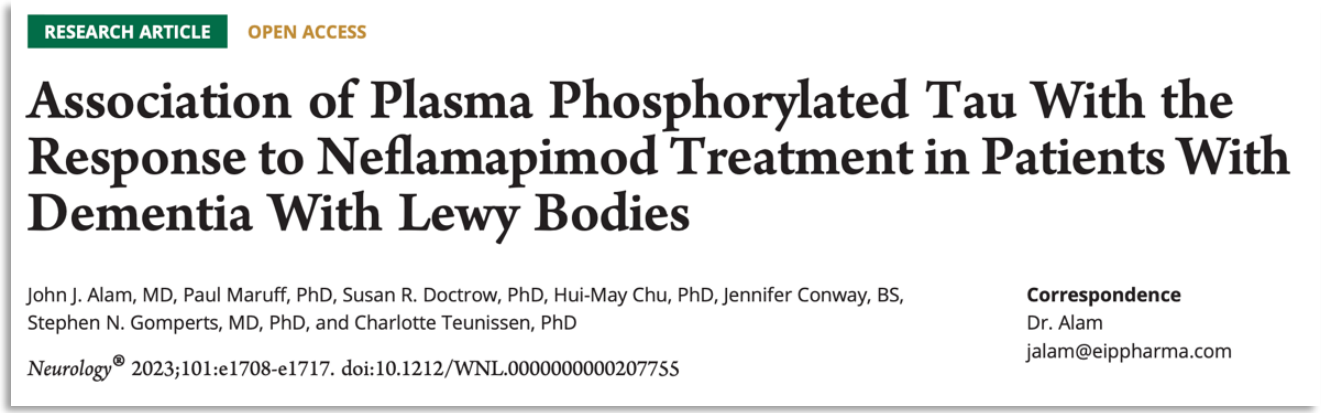
Published online: 21 September 2022

Check for updates

Ying Jiang[1,2,13], John J. Alam[3,13] ✉, Stephen N. Gomperts[4], Paul Maruff[5], Afina W. Lemstra[6,7], Ursula A. Germann[3], Philip H. Stavrides[1], Sandipkumar Darji[1], Sandeep Malampati[1], James Peddy[1], Cynthia Bleiwas[1], Monika Pawlik[1,2], Anna Pensalfini[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[6,11], Philip Scheltens[6] & Ralph A. Nixon[1,2,12] ✉



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

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

Alam and Nixon
Molecular Neurodegeneration (2023) 18:74
https://doi.org/10.1186/s13024-023-00663-y

Molecular Neurodegeneration

RESEARCH HIGHLIGHT Open Access

Drug development targeting degeneration of the basal forebrain cholinergic system: its time has come

John J. Alam[1*] and Ralph A. Nixon[2,3]

Abbreviations: CDR-SB: Clinical Dementia Rating Scale, measure of dementia severity. TUG: Timed Up and Go test, measure of functional mobility.
Nature Communications, 13, Article number: 5308 (2022)

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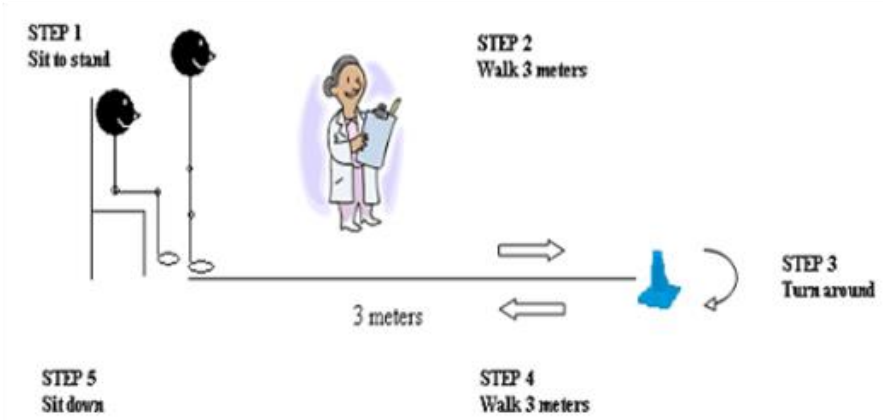
Phase 2a Clinical ("AscenD-LB") Study Outcome Measures

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)

Timed Up and Go Test (TUG, scored in seconds)



Neuropsychological Test Battery (NTB)*:

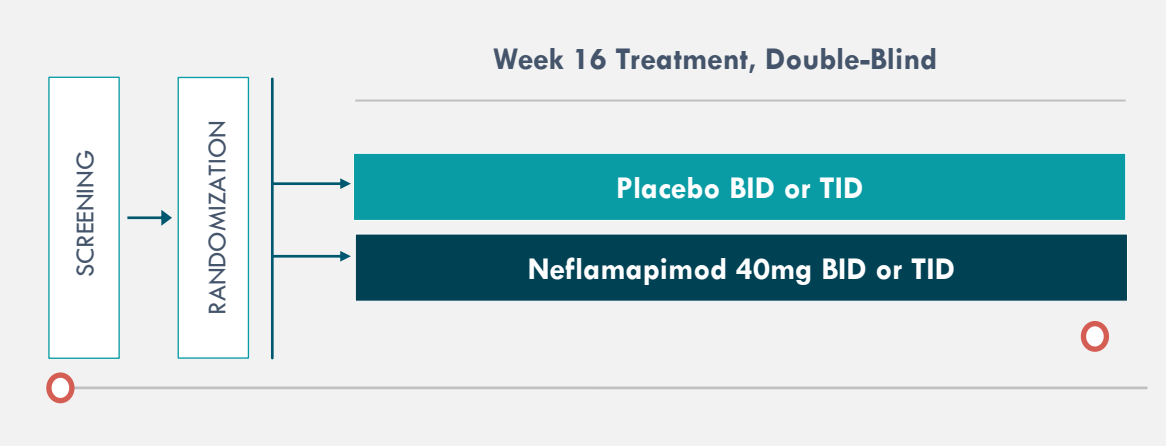
- Detection
- Identification
- One Card Learning
- One Back
- Letter Fluency Test
- Category Fluency Test

*Study-specific cognitive test battery designed to assess attention and executive function

NTB composite: results of all six tests combined into single z-score

Attention composite: Detection and Identification tests combined into single z-score

AscenD-LB Phase 2a Clinical Trial



PARTICIPANTS

Mild-to-Moderate DLB by consensus criteria[1]

Abnormal dopamine uptake by DaTscan™

On background cholinesterase inhibitor therapy

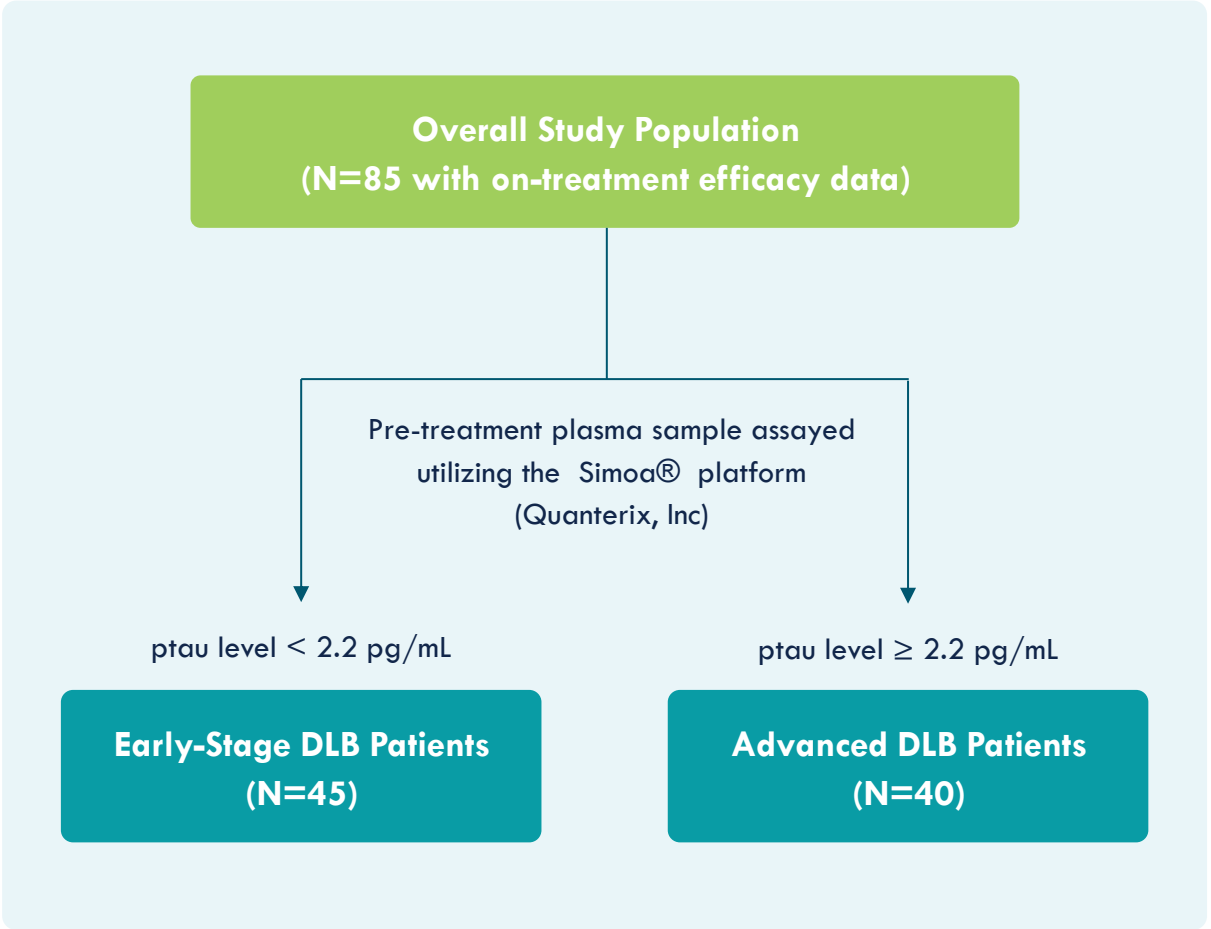
MAIN RESULTS[2]

- In mITT analysis (all patients randomized ≥1 efficacy data point) neflamapimod significantly improved dementia severity (assessed by CDR-SB, p=0.023 vs. placebo) and gait (assessed by Timed Up and Go, TUG, *p*=0.044 vs. placebo); no significant effects on cognitive testing
- In secondary analysis, results at the higher (40mg TID) of two dose levels of neflamapimod, significantly improved cognitive testing results (*p*=0.049 vs. placebo), particularly with respect to attention (*p*=0.023 vs. placebo)
- Well-tolerated, with no treatment discontinuations at 40mg TID dose level

1. McKeith, *Neurology*, 2017) 2. Nature Communications, 13, Article number: 5308 (2022). https://www.nature.com/articles/s41467-022-32944-3

Phase 2a AscenD-LB Results Stratified by Plasma ptau181 Levels

- Conducted after study was completed (i.e., formally post-hoc).
- While stratification and analysis was pre-specified in protocol, independent data that validated plasma ptau181 in DLB was not published until after the study was completed.
- Plasma ptau181 cut-off (i.e., early-stage DLB v. advanced DLB) prospectively defined based on publication[2] that 2.2 pg/mL in the assay utilized correctly identified patients with CSF-biomarker (amyloid & tau) confirmed AD dementia
- Results published in *Neurology*, a major, peer-reviewed medical journal[3]



1. Hall et al, *Movement Disorders,* 2021. 2.Bayoumi et al, *Alz Res & Ther*, 2022 3. Alam et al, *Neurology*, 2023

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Response in Phase 2a is primarily due to effects of neflamapimod in patients with early-stage DLB

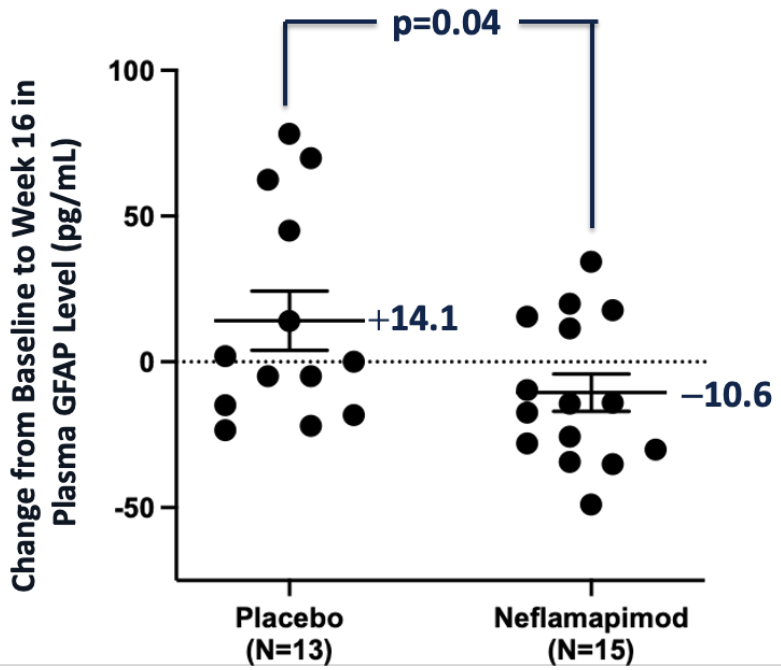
	Overall Study Population				Patients With Early-Stage DLB (Plasma ptau181 < cutoff)			
	N= NFMD TID, Placebo	Difference[1] (95% CI)	p-value	Cohen's d Effect size	N= NFMD TID, Placebo	Difference[1] (95% CI)	p-value	Cohen's d Effect size
NTB	19,37	+0.17 (0.00,0.35)	0.049	0.47	11,19	+0.21 (-0.07,0.49)	0.13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

- Patients without baseline plasma ptau181 elevation (i.e., patients with early-stage DLB) show greater treatment effect than seen in the study overall, and significant and substantial improvement over placebo on CDR-SB, TUG, Attention and Recognition Memory
- By convention Cohen's d of 0.2-0.4=small effect, 04-0.8=moderate, ≥0.8=large

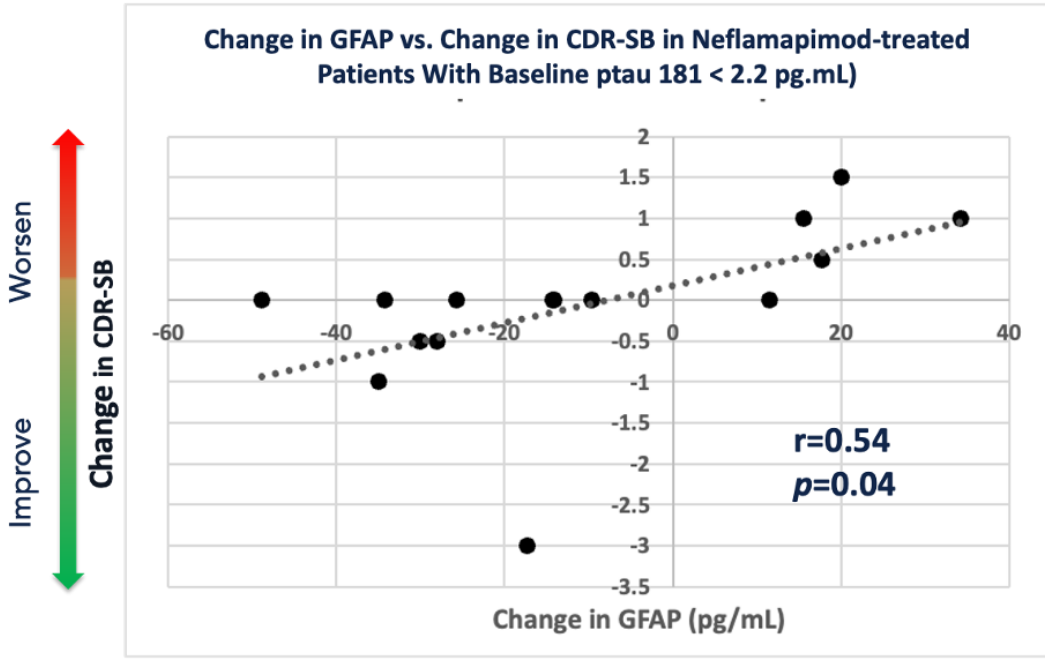
Early-stage DLB: plasma ptau181 < cutoff at study entry; NTB – Neuropsychological Test Battery, ISLT – International Shopping List Test. Improvement reflected by negative sign for CDR-SB and TUG and positive sign for other measures. Table adapted from Prins et al, *JPAD*, 2024

Plasma Biomarker Effect Further Supports Neflamapimod is Clinically Efficacious in Early-Stage DLB

Neflamapimod Reduces Plasma GFAP in Early-Stage DLB Patients (plasma ptau181 < cutoff)



Effect of Neflamapimod on plasma GFAP is Correlated to the Clinical Outcome[1]



Glial Fibrillary Acidic Protein (GFAP) has emerged as a leading plasma biomarker to evaluate the underlying disease process in early-stage DLB

Includes BID and TID treated patients in all analyses 1. Correlation not seen in placebo-recipeints with baseline ptau181 < 2.2 pg/mL

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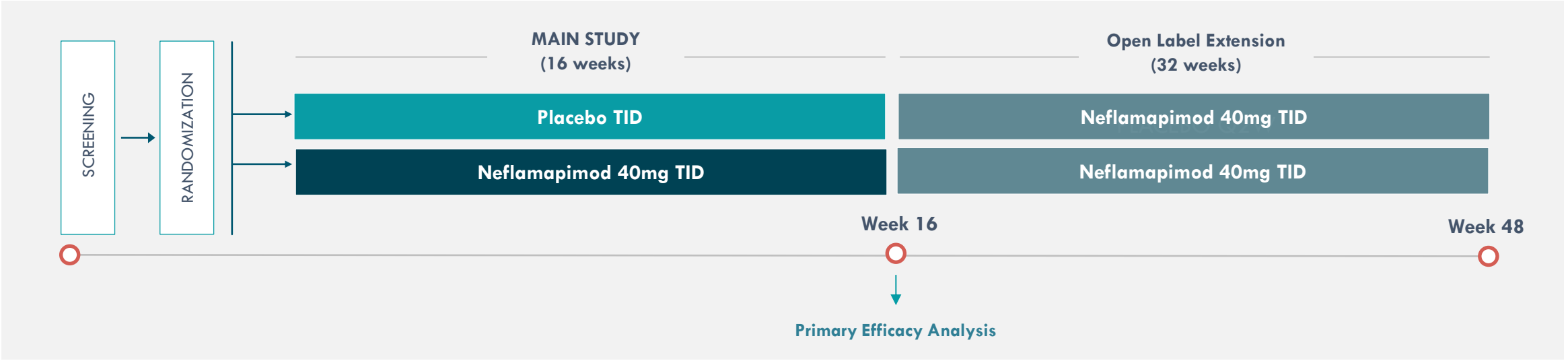
RewinD-LB Phase 2b Clinical Trial Ongoing



PARTICIPANTS

DLB by consensus criteria

Pre-treatment plasma ptau181 <2.4 pg/ml (i.e., only enrolled patients with early-stage DLB)

INTERVENTION

159 participants randomized on a blinded basis 1:1 to neflamapimod 40mg capsules or matching placebo capsules, 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

Plasma biomarker: GFAP

RewinD-LB Study Has Potential to De-risk Planned Phase 3 Study

AscenD-LB

Full primary results published September 2022

16-week placebo-controlled Phase 2a study

91 DLB patients with mild to moderate cognitive impairment

Placebo vs. Neflamapimod 40 mg (randomized 1:1); BID (weight < 80 kg) or TID (weight ≥ 80 kg)

Results vs. placebo:

- ✓ Significant improvement on CDR-SB and TUG in full efficacy population (mITT)
- ✓ Significant improvement on NTB (cognitive test battery) at 40mg TID, particularly with respect to attention
- ✓ Results most prominent in patients with early-stage DLB

RewinD-LB

Topline results expected in December 2024

16-week placebo-controlled Phase 2b study with 32-week open label extension

159 patients with early-stage DLB

Placebo vs. neflamapimod 40mg TID (randomized 1:1)

Optimized, based on learnings from AscenD-LB:

- Exclude patients with advanced DLB, assessed by plasma ptau181
- Identified optimal dose (40mg TID) only dosing regimen
- CDR-SB primary endpoint, TUG, CGIC, NTB secondary endpoints, better distinguish drug treatment effect from placebo by evaluating motor function in addition to cognition
- High statistical power to demonstrate significance on primary endpoint

Planned Phase 3 Study Design[1]

Assuming positive result in Phase 2b, anticipated initiation in mid 2025 following end-of-Phase 2 meeting

24-week placebo-controlled Phase 3 study with long-term extension

Approximately 300 patients with early-stage DLB

Will be designed to replicate RewinD-LB findings over 24 weeks

- Replicates RewinD-LB with respect to primary and secondary clinical endpoints and patient population
- Also replicates RewinD-LB with respect to dosing regimen (40 mg ID); potential to also include 80mg BID for additional dosing flexibility
- Longer duration should increase statistical power
- Basal forebrain atrophy by MRI as an additional, major secondary endpoint

Estimated trial cost of $50M-$75M (n = 300 patients)

1. Based previous discussions with FDA. Initiation, final design, size and cost of planned Phase 3 trial subject to change based on results of RewinD-LB Trial, potential feedback from FDA and other factors.

Early-Stage DLB is a High-Value Indication

Potential to reverse the degenerative processes, address cognitive, functional and motor aspects of DLB

01

Significant Patient Numbers:

Approximately 700,000 in each of US & EU, approximately half of which are in the early-stage of their disease

02

Growth in Diagnosis Rates:

Increasing awareness of disease

03

Opportunity to Improve Existing Treatment Paradigm:

High unmet treatment needs remain with currently utilized cholinesterase inhibitors

04

Diagnosed and managed by neurologists

Specialist Disease

05

High Medical Need /Pricing Leverage: *Relative to Early AD*

Higher rate of cognition decline, lower quality of life, higher hospitalization costs, higher caregiver burden. Potential to deliver more value than anti-Aβ therapies provide in AD

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Key Recent Accomplishments and Upcoming Milestones

2023

- ✓ NIA approved $21M grant for Phase 2b
- ✓ First Patient Dosed in Phase 2b DLB study
- ✓ Closed merger transaction; began trading as a public company (NASDAQ: CRVO)
- ✓ Published additional Phase 2a data[1] from DLB study in *Neurology®*
- ✓ Oral presentation featured at CTAD conference

2024

- ✓ Completed private placement for aggregate gross proceeds of up to $149.4M from leading healthcare investors (April 2024)
- ✓ Completed enrollment in Phase 2b DLB study (June 2024)
- ✓ Published comprehensive phase 2a results, including EEG and MRI data, in JPAD (February 2024)
- ✓ Presented GFAP (plasma biomarker) data at AD/PD and AAIC meetings
- ❑ **Report topline efficacy data from Phase 2b DLB study (December 2024)**

2025

- ❑ **Present and publish Phase 2b results**
- ❑ **Meet with FDA to finalize Phase 3 study design**
- ❑ **Initiate Phase 3 DLB study[2]**

1. Plasma ptau181 stratified results. 2. Initiation, final design, size and cost of planned Phase 3 trial subject to change based on results of RewinD-LB Trial, potential feedback from FDA and other factors.

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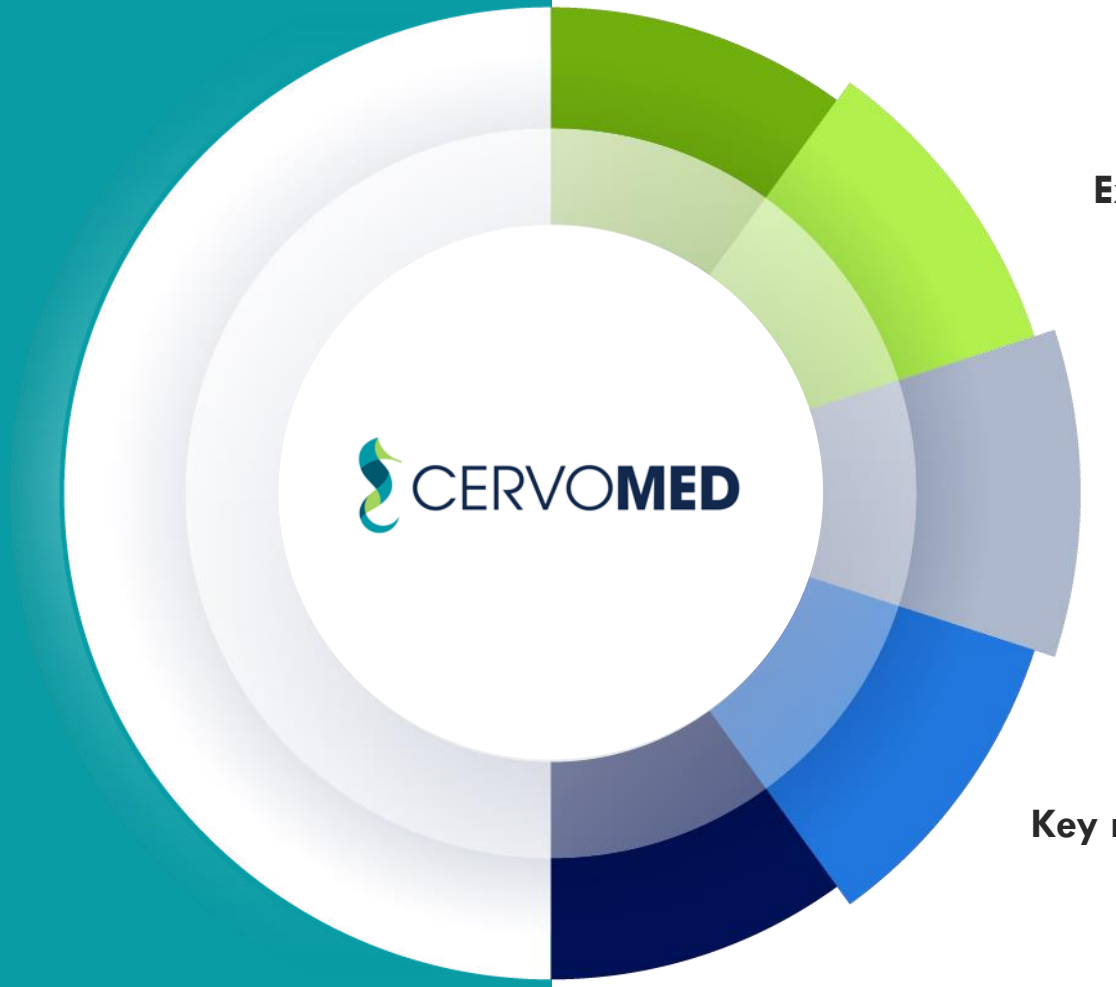
Summary



Late-stage asset with differentiated approach, targeting synaptic dysfunction to treat age-related neurologic disorders

Experienced management team and board of directors

Major value creation potential in Phase 2b read-out in early-stage DLB, expected in December 2024; positive result may provide cost-effective path to significant market opportunity

Key milestones expected over next 12 months

Potential to broaden opportunity through additional indications

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Medicines for the Brain

August 2024

Corporate Overview

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

NASDAQ: CRVO

Appendix

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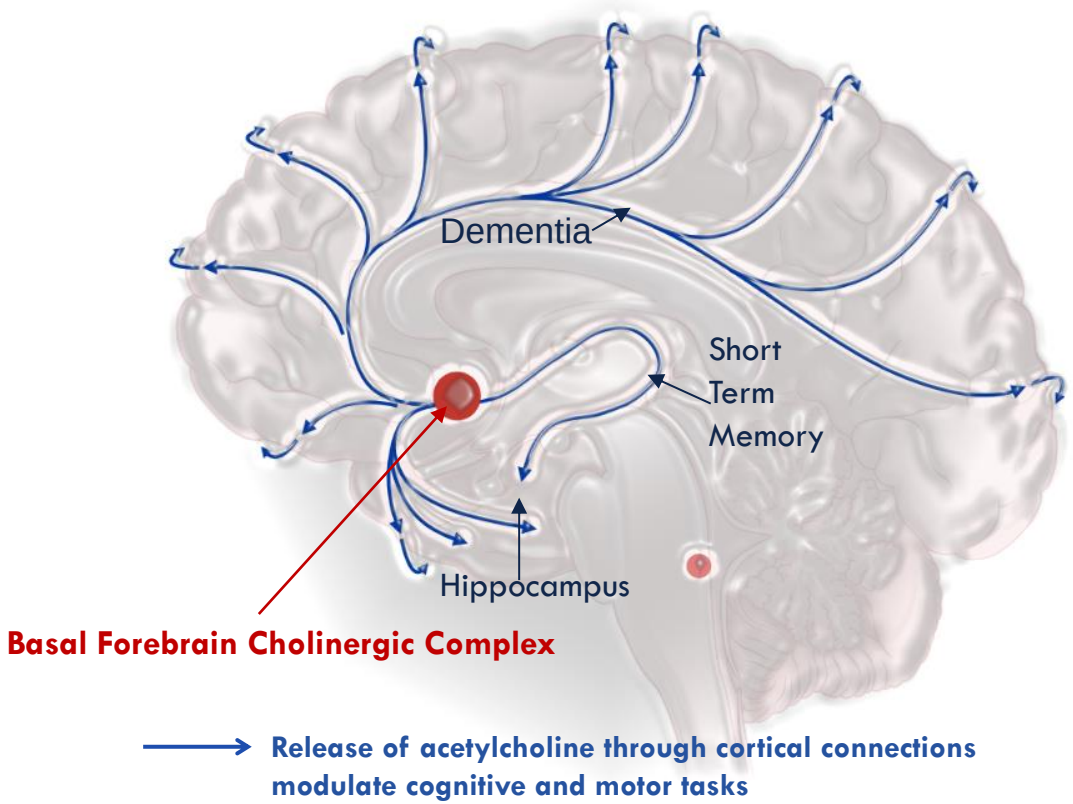
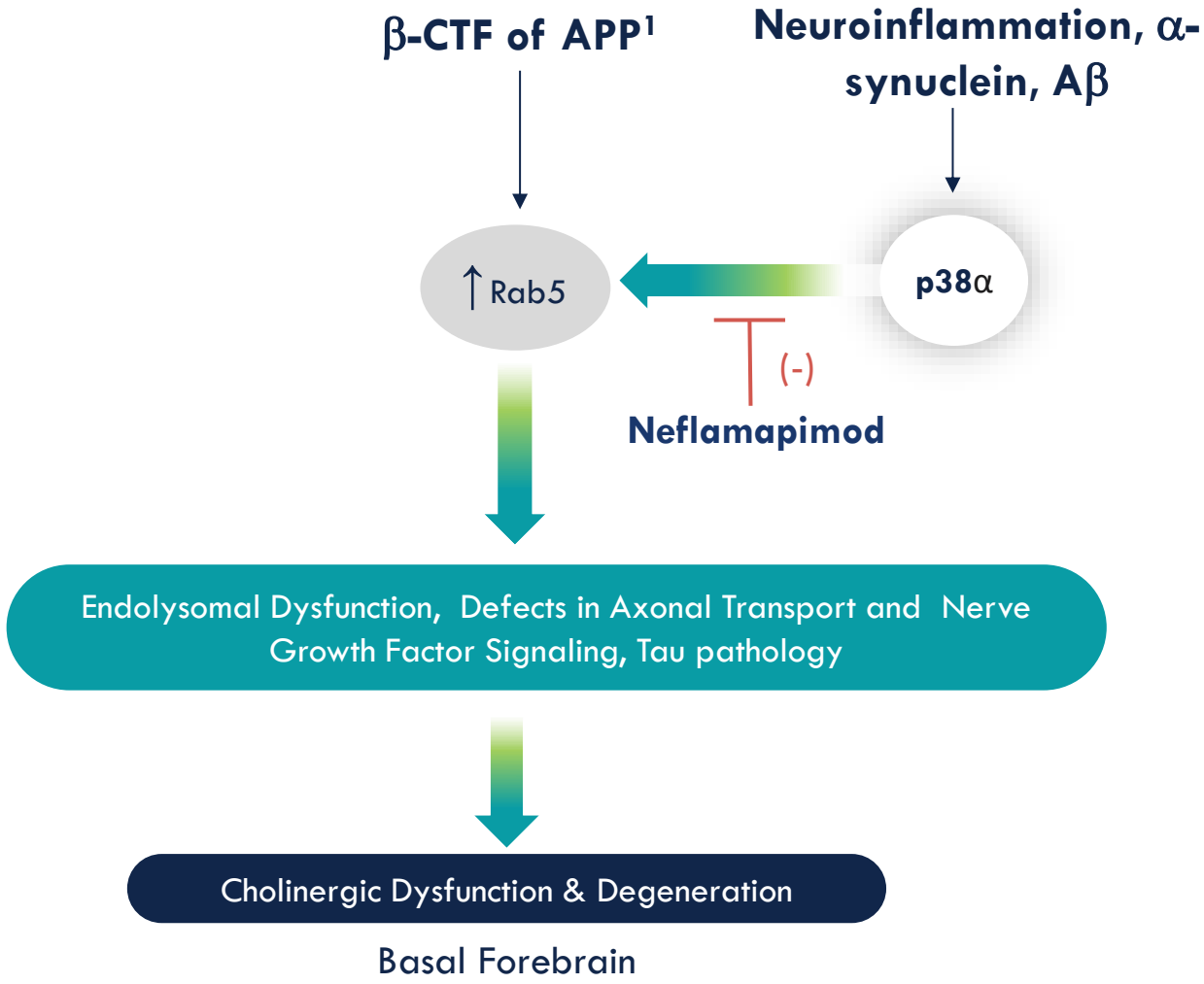
Medicines for the Brain

Neflamapimod Mechanism of Action

Synaptic disfunction in basal forebrain is the primary driver of disease in DLB



Disease processes in basal forebrain are reversible



NGF: Nerve Growth Factor

Adapted from Alam & Nixon, *Molecular Neurodegeneration*, 2023. 1. APP: Amyloid Precursor Protein

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Neflamapimod Reverses Cholinergic Dysfunction and Degeneration in Preclinical Study

TS2 mouse model of Down Syndrome (DS)

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

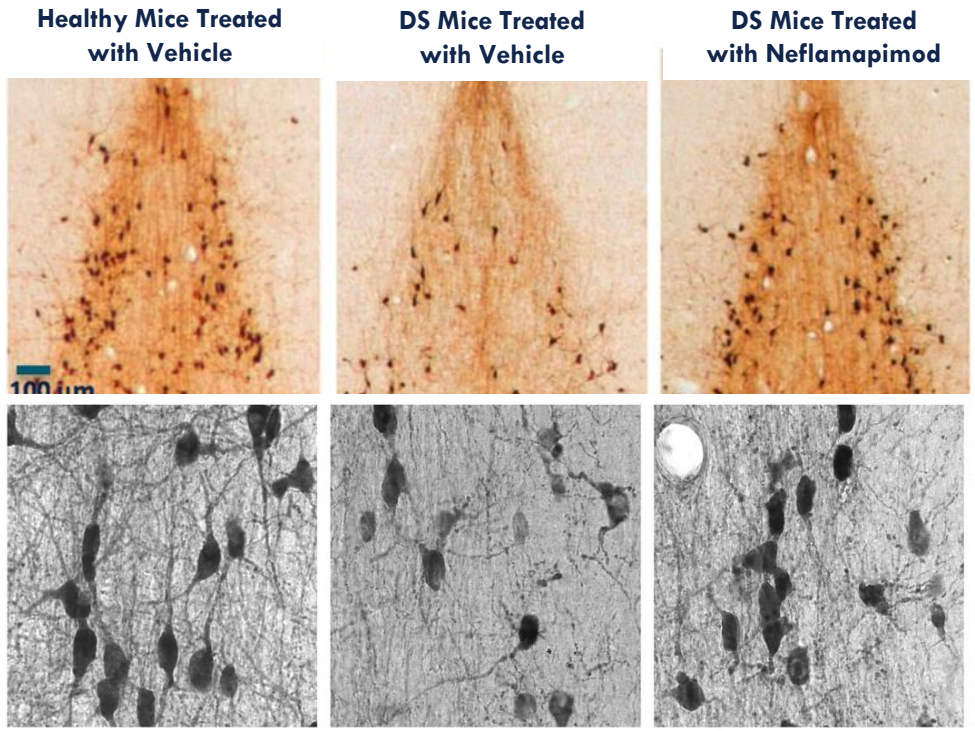
Reversed basal forebrain cholinergic neuron loss and restored cholinergic function

- Significantly increased (+30% vs. controls, $p<0.001$) and normalized the number of cholinergic neurons in basal forebrain
- Normalized performance in both open field and novel object recognition behavioral tests of cholinergic function

Mechanistic effects of neflamapimod

- Decreased Rab5 activation and reversed Rab5+ endosomal pathology
- Normalized levels of activated (phosphorylated) p38α and its downstream targets MK2 and MNK1

Cholinergic neurons in basal forebrain



Cholinergic neurons identified by staining for choline acetyl transferase expression

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

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AscenD-LB Demonstrated Neflamapimod Improved Cognition and Function

		40mg BID + 40mg TID (mITT Analysis)		40mg TID	
		Mean difference vs. placebo (95% CI)	*p*-value	*Mean difference 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
Cognitive Testing	**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

Improvement reflected by negative sign for CDR-SB and TUG and positive sign for cognitive tests

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

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Performance of Clinical Endpoints in Phase 2a

- Clinical endpoints that can detect effects on both cognition and motor function (specifically, CDR-SB and TUG) performed better in DLB with respect to detecting improvement over placebo than endpoints purely focused on evaluating cognition
- Performance of Neuropsychological Test Battery (NTB, six-test cognitive test battery), original primary outcome measure, also limited by "ceiling effects":
  - As all patients were receiving cholinesterase inhibitors, while the NTB was modeled after a cognitive test battery that showed responsiveness to treatment in a study of rivastigmine.
  - Absence of deficits of executive function at baseline, tests for which were a major component of the NTB

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

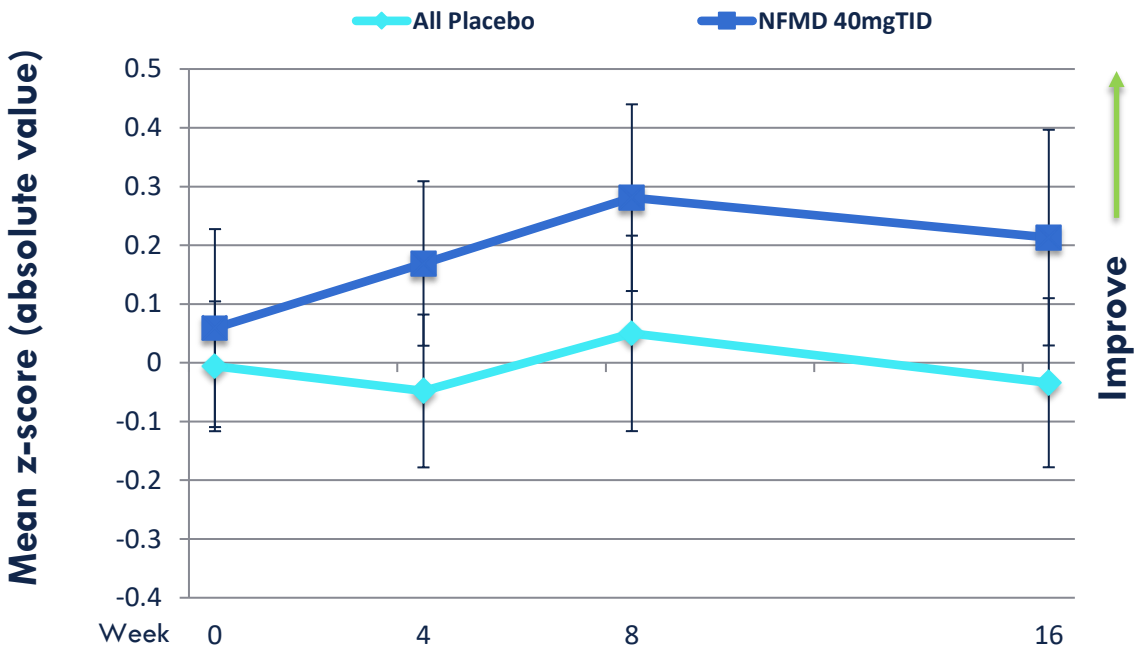
Cognitive Domains:
- Memory (0-3)
- Orientation (0-3)
- Judgement and Reasoning (0-3)

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

1. McKeith, *Neurology*, 2017)

Phase 2a Results Demonstrated Neflamapimod 40mg TID Improved Cognition in Patients with DLB (Overall Patient Population)

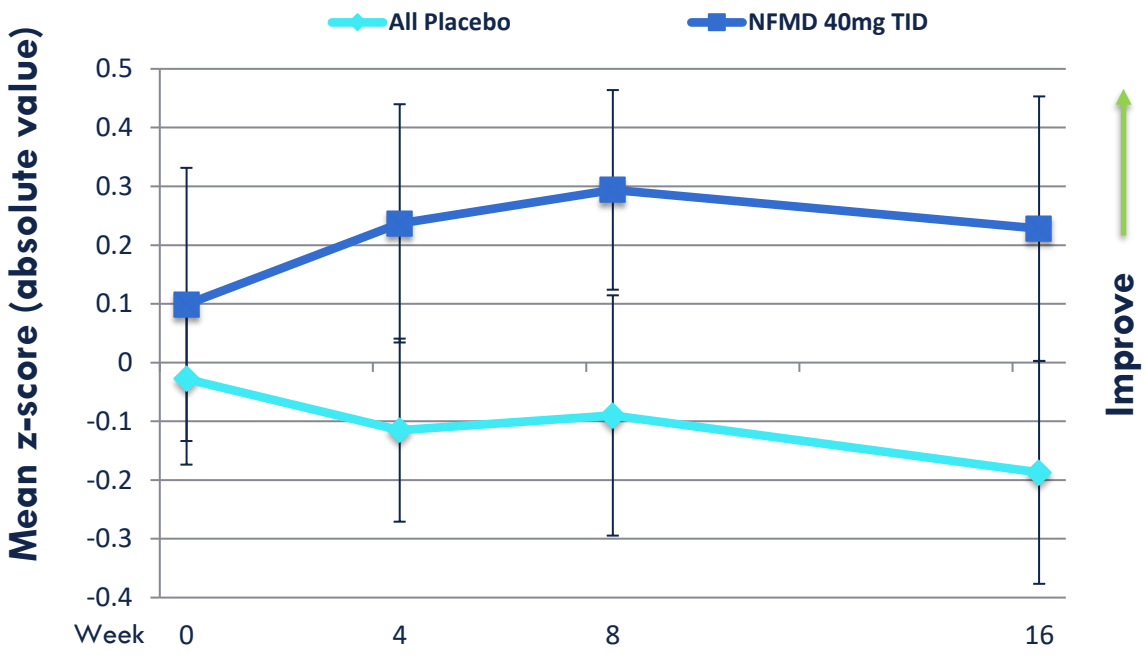
Neuropsychological Test Battery (NTB) Composite



Number of Participants with Data at Each Timepoint			
Placebo	36	27	29
NFMD TID	16	7	17

p=0.049 for NFMD 40mg TID vs. placebo (MMRM analysis using all timepoints)

Attention Composite



Number of Participants with Data at Each Timepoint			
Placebo	36	27	29
NFMD TID	16	7	17

p=0.023 for NFMD 40mg TID vs. placebo (MMRM analysis using all timepoints)

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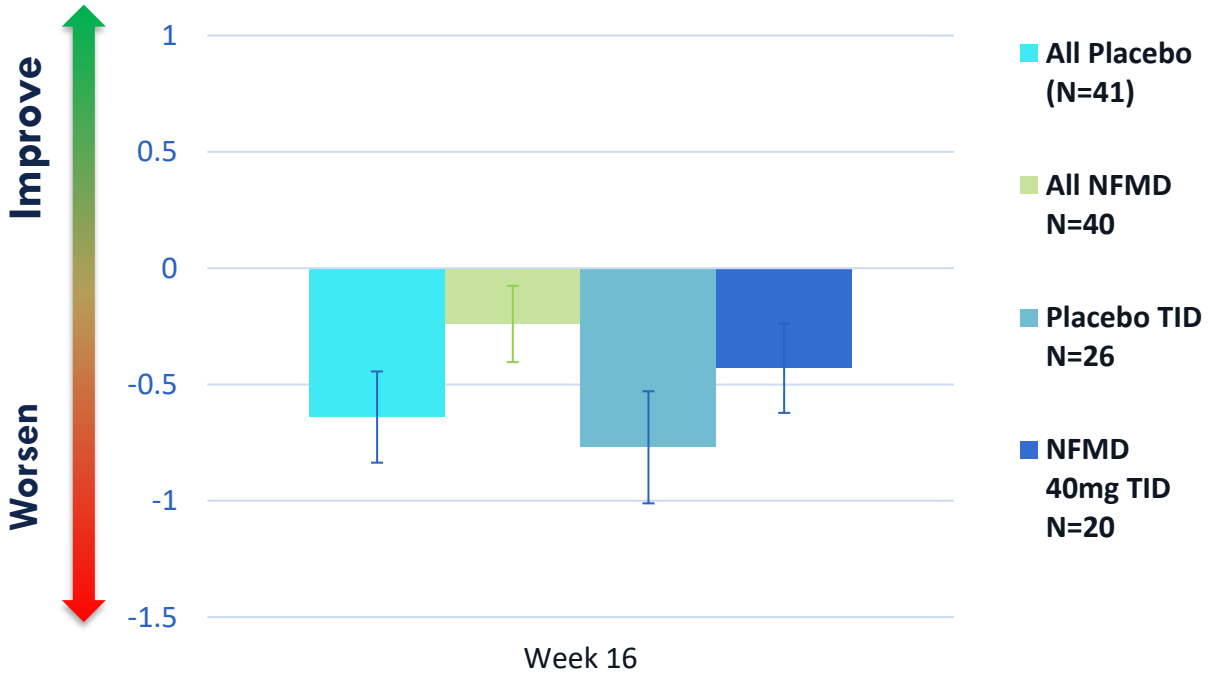
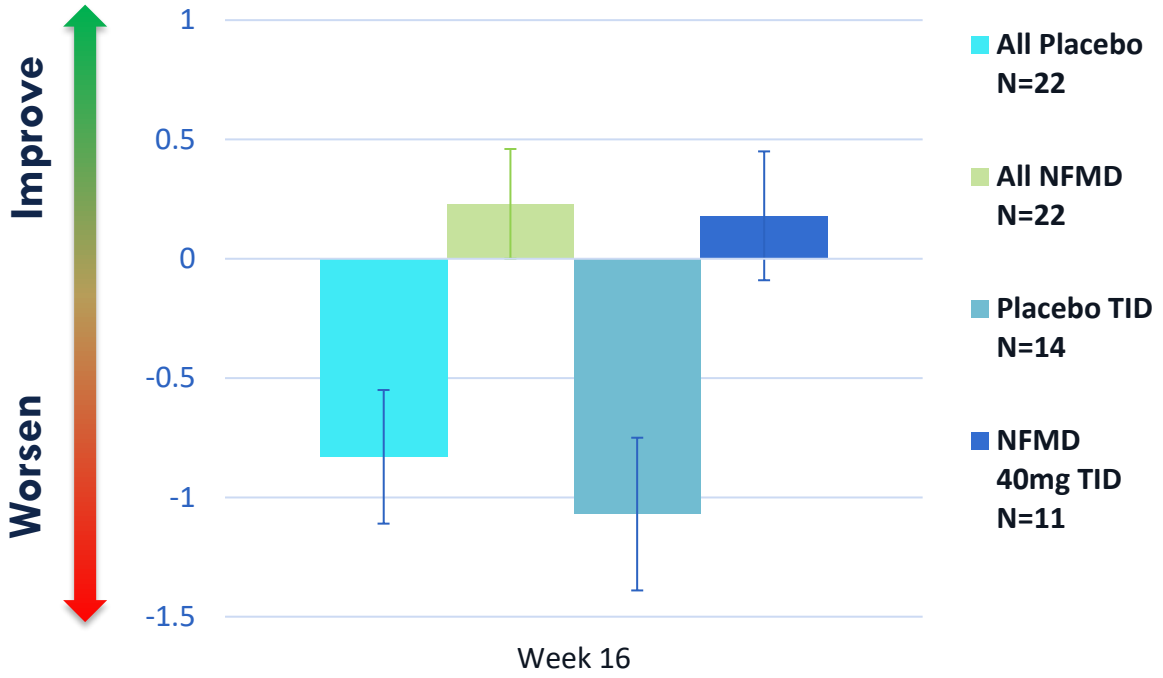
Neflamapimod Treatment in Patients with DLB Demonstrated Substantial Effect on Change from Baseline in CDR-SB in Phase 2a

Overall Patient Population



Patients with Early DLB (Baseline plasma ptau181 < 2.2 pg/)



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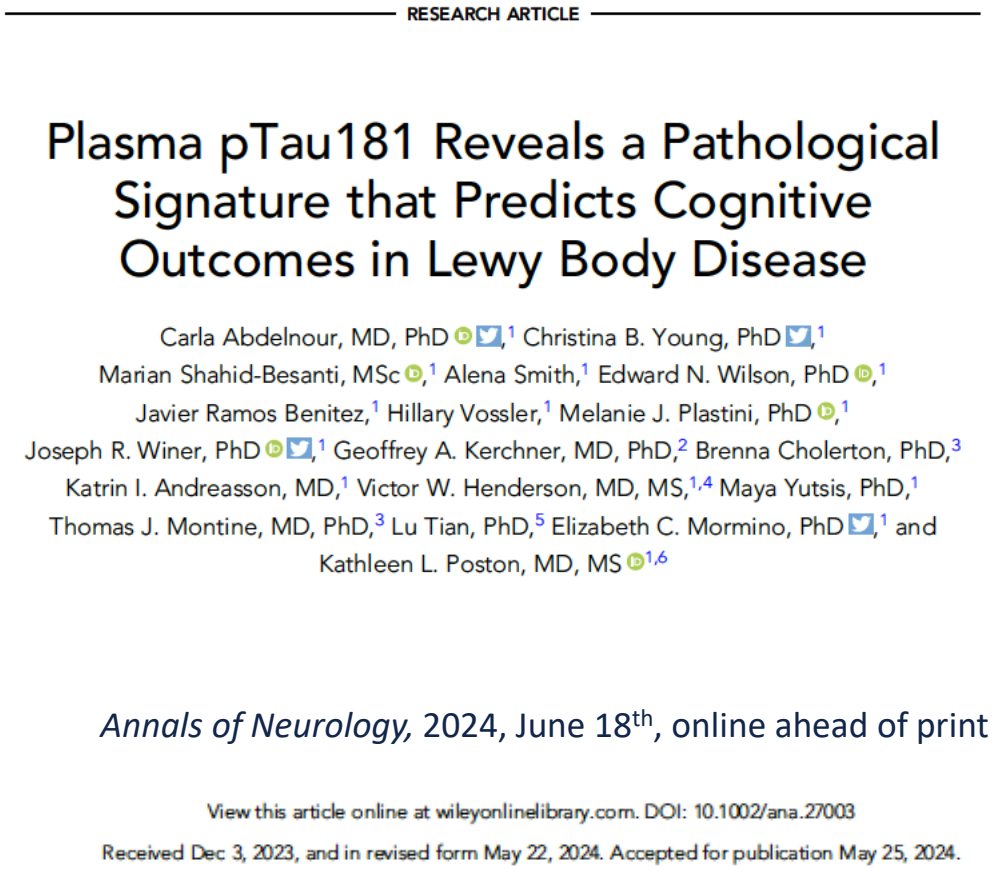
Plasma ptau181 and underlying pathology in dementia with Lewy bodies

- 2.2 pg/mL cut-off utilized in Neurology paper (Alam et al, 2023) was based on published report that indicates that value was optimal cut-off for CSF biomarker positive (A+T+) confirmed AD dementia
- In DLB, plasma ptau181 correlated to:
  - PET amyloid status, but more strongly associated with tau PET status (positive "AD signature tau signal") status, with optimal cut-off for tau PET status being 2.3 pg/mL (Diaz-Galvan et al, 2024)
  - CSF ptau181/Aβ42 ratio, with optimal cut-off of 2.5 pg/mL (Abdelnour et al, 2024) providing 78% positive predictive value and 95% negative predictive value
    - Plasma ptau181 also correlated to baseline CDR-SB and accelerated decline in CDR-SB (with stronger association for ptau181 compared to NfL)
  - Medial temporal lobe atrophy by MRI, with optimal cutoff of 2.4 pg/mL (unpublished data from Charlotte Teunissen, Amsterdam Medical Center)



RESEARCH ARTICLE

Plasma pTau181 Reveals a Pathological Signature that Predicts Cognitive Outcomes in Lewy Body Disease

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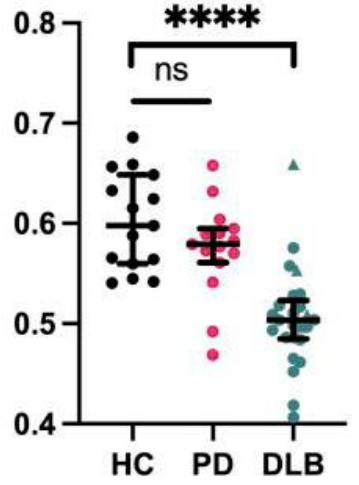
“Right Patient” for Optimal Response to Neflamapimod Treatment

- Patient whose disease is driven primarily by basal forebrain cholinergic dysfunction and degeneration
  - Matches mechanism of action
  - Disease is reversible
- Profile met by:
  - Patient who meets clinical criteria for DLB consistently have significant basal forebrain atrophy and/or cholinergic terminal loss
    - DLB consensus clinical criteria also predicts patient with alpha synuclein pathology by skin biopsy (96% skin biopsy positive vs. 3% in healthy controls; Gibbons et al, *JAMA*,2024)

AND

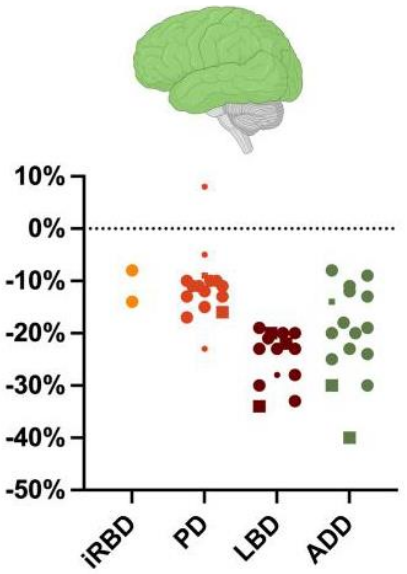
  - Patient who does not have elevated plasma ptau181, which excludes patients who also have significant hippocampal atrophy

Posterior Basal Forebrain Volume by MRI



BRAIN 2023: 146; 3690–3704

Cholinergic Terminal Loss in Neocortex by PET



BRAIN 2024: 147; 2308–2324

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Plasma Glial Fibrillary Acidic Protein (GFAP) as a Biomarker of the Neurodegenerative Process in DLB

- Across a range of dementia plasma GFAP shown to be a sensitive marker of neurodegeneration and is correlated to cognition
- Elevated in MCI-DLB, while other plasma biomarkers (NfL, ptau) are not (Diaz-Galvan et al, 2024)
  - As patients at this stage have cholinergic degeneration without hippocampal atrophy (Kantarci et al, 2022), GFAP elevation in this context reflects basal forebrain disease
- In DLB (Bolsewig et al, 2024), plasma GFAP is associated with rate of cognitive decline, but not with CSF Aβ42 status, suggesting that GFAP elevation has potential to evaluate DLB-specific disease processes in these patients