CERVOMED

Medicines for the Brain

February 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; anticipated milestones related to the Company's clinical development programs, including timelines for trial enrollment and reporting of data; the potential therapeutic value of neflamapimod; the Company's anticipated cash runway; and the potential commercial opportunity of neflamapimod, if approved. 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 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 changes in the competitive and highly regulated industry in which the Company operates; variations in operating performance across competitors; changes in laws and regulations affecting the Company's business; the Company's ability to remediate its previously disclosed material weaknesses in its internal controls over financial reporting in a timely manner; the Company's ability to successfully integrate the historical businesses of EIP and Diffusion and realize the anticipated benefits of the recent merger; 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 Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission ("SEC") on November 13, 2023, and other filings that the Company may file from time to time with the SEC. Any forward-looking statements in this presentation speak as of February 6th, 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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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* and in *Neurology*
Phase 2b Clinical Study Optimally Designed and Fully Funded	Well-powered trial, stratified to identify patients most likely to benefit from neflamapimod **supports development success and path to market, while reducing overall cost;** awarded $21M grant from the NIH's National Institute on Aging (NIA) which will fully fund ongoing Phase 2b study[1]
Multiple Value-Driving Milestones Through 2024	First patient dosed in 160-patient Phase 2b DLB clinical study August'23; plans **to complete enrollment in 1H24 and report primary efficacy results[2] in 2H24**

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

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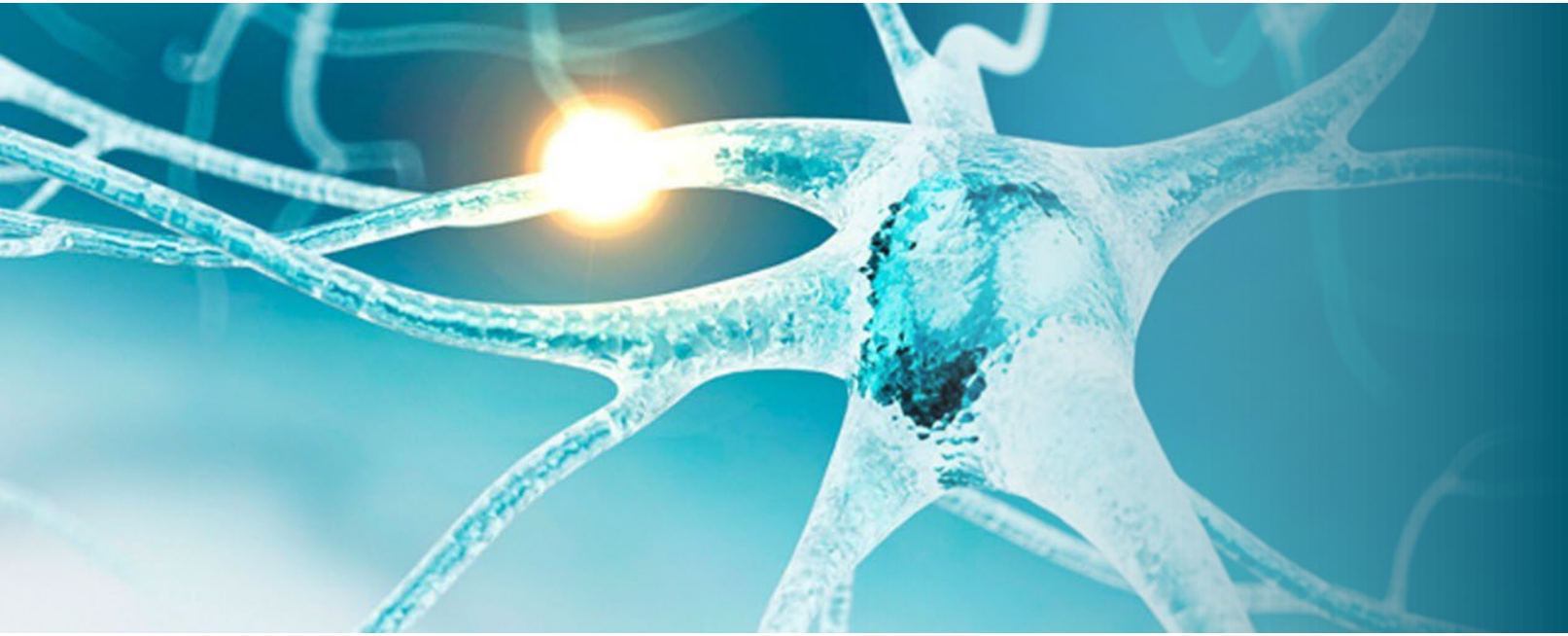
Company Overview

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: Neflamapimod

Licensed from Vertex Pharmaceuticals in 2014

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

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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 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, Guggenheim Securities and Cantor Fitzgerald

Robert J. Cobuzzi Jr., PhD

Chief Operating Officer, Director

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 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, retired CEO and Board Chair, Vertex Pharmaceuticals

Sylvie Gregoire, PharmD
Co-Founder; Board member, Novo Nordisk, Revity (f/k/a Perkin Elmer), F2G, Former Executive VP, Biogen; Former President, HGT Division, Shire Pharmaceuticals

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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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

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

Supported by growing positive data:

- In preclinical and clinical studies, neflamapimod reversed degenerative processes in basal forebrain
- In phase 2a trial in patients with DLB, neflamapimod versus placebo improved cognitive, functional and motor aspects of the disease. Effects most prominent in patients with pure 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

Opportunity in Dementia with Lewy Bodies (DLB)

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Why Dementia with Lewy Bodies (DLB)

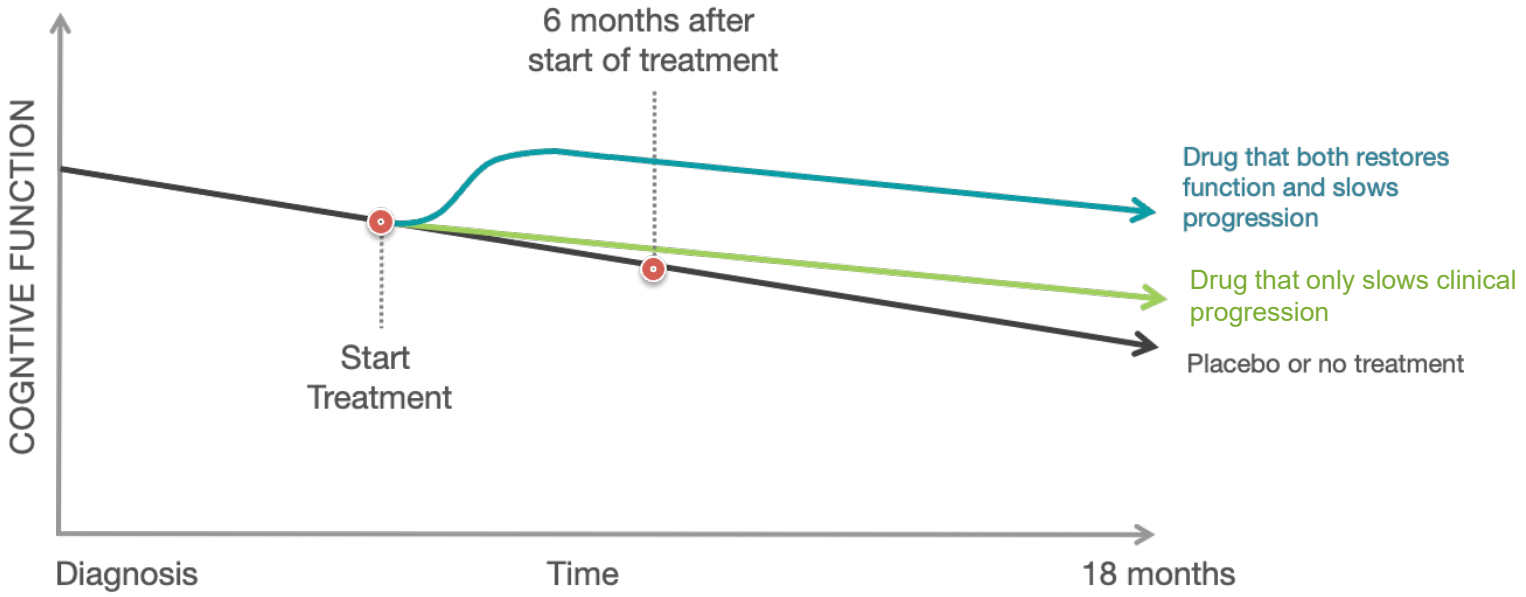
High unmet medical need, no approved therapies, significant commercial opportunity

Early-stage (very mild and mild dementia) is primarily a disease of synaptic dysfunction in the basal forebrain cholinergic system, rather than frank neuronal loss

Successful treatment of the underlying disease process in early stage DLB would lead to both reversal and slowing of clinical progression

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

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



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Dementia with Lewy Bodies (DLB)

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 mood[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

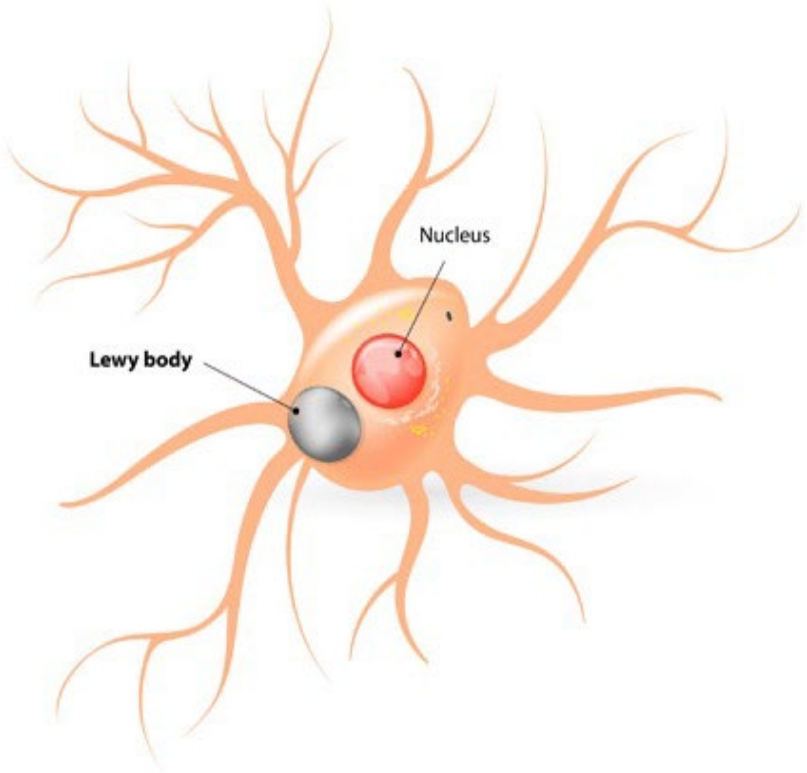
Current standard of care is cholinesterase inhibitor therapy that only transiently improves cognition and does not impact motor component

Market Opportunity

3rd most common degenerative disease of the brain (after AD and PD)

~700,000 individuals in each of US and EU

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

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Neflamapimod for DLB: Well-Positioned Commercially

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

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 AD*

Greater rate of cognition decline, lower quality of life, higher hospitalization costs, higher caregiver burden

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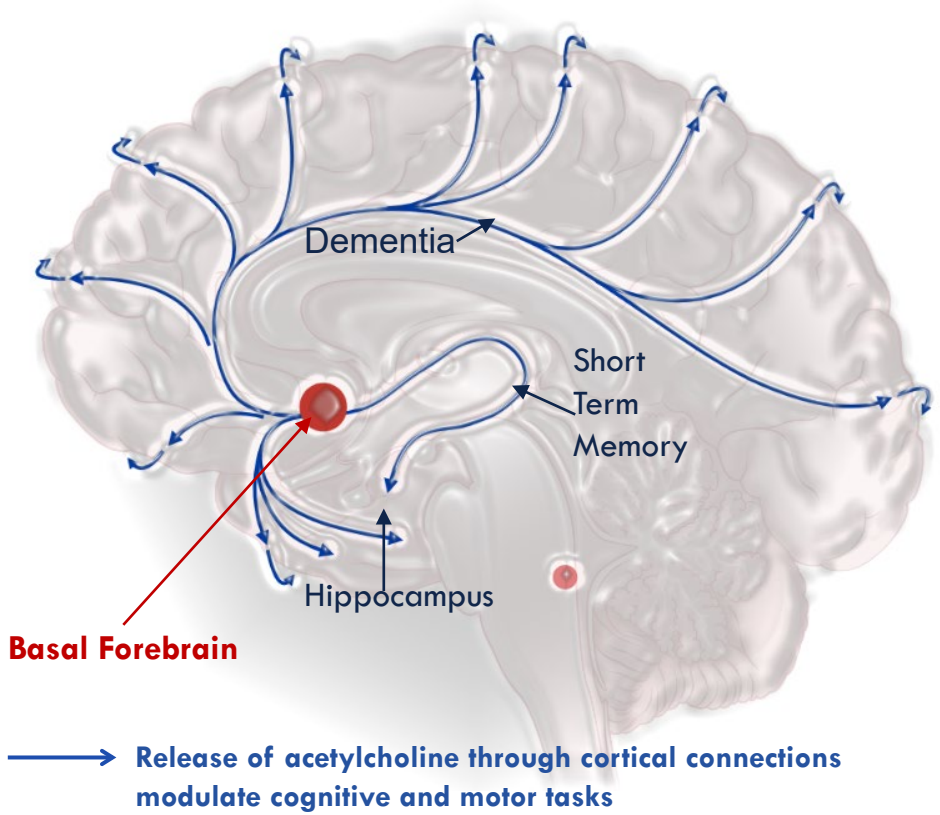
Opportunity for Therapeutics Targeting Basal Forebrain Cholinergic Dysfunction and Degeneration

- Age-related dysfunction of the basal forebrain cholinergic system, the major source of the neurotransmitter acetylcholine, plays major role in many neurologic disorders and is the primary pathology for DLB

- As it is due to synaptic dysfunction, and not frank neuronal loss, the disease processes in the basal forebrain is ***reversible*** through much of the disease course[1]

Basal Forebrain Cholinergic Complex



1. Cooper et al, 2002; Nagara et al, 2009; etc.

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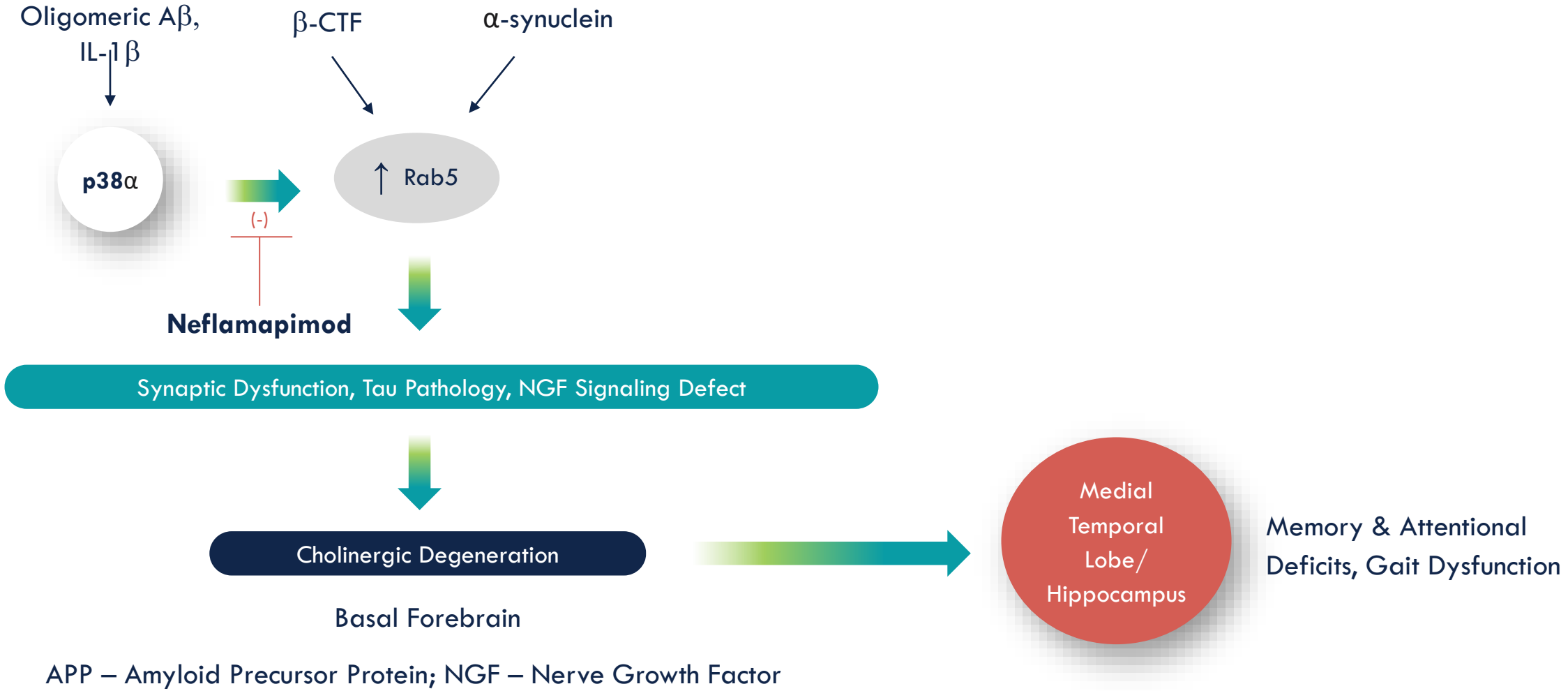
Neflamapimod Mechanism of Action



APP – Amyloid Precursor Protein; NGF – Nerve Growth Factor

Adapted from Alam & Nixon, *Molecular Neurodegeneration, 2023*

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Distinctions between “Pure DLB” and “DLB-AD”

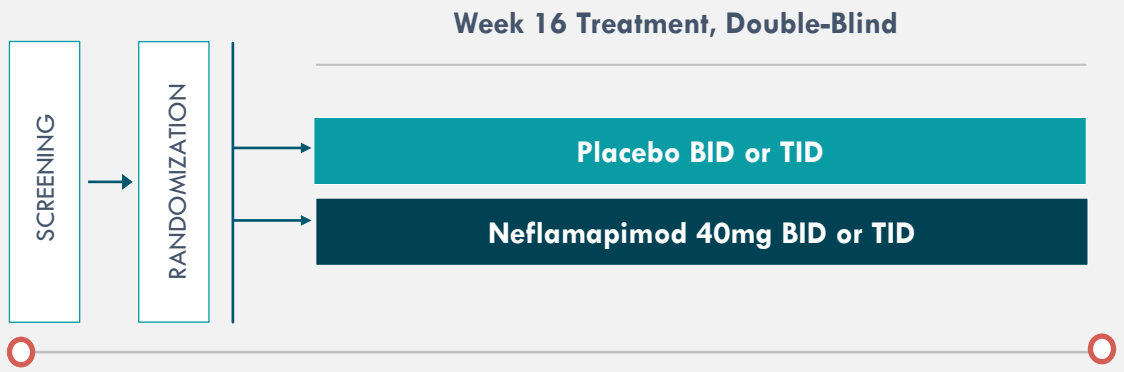
Pure DLB (~50% of All DLB Patients)

- Patients with Early Stage DLB, without biomarker evidence of Alzheimer’s disease (AD)
- 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

DLB-AD (~50% of All DLB Patients)

- Have biomarker evidence of AD (e.g., elevated plasma ptau181)
- Advanced disease, with 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

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

INTERVENTION

Randomized on a blinded basis 1:1 to neflamapimod 40mg capsules (n=46) or matching placebo capsules (n=45), Twice daily (BID) if weight < 80kg or three times daily (TID) if weight ≥ 80kg

OUTCOME MEASURES

DLB-specific Neuropsychological Test Battery (NTB, a cognitive test battery)

Dementia Severity, assessed by CDR-SB

Motor Function, assessed by Timed Up and Go (TUG) test

PERFORMANCE OF CLINICAL ENDPOINTS

- Clinical endpoints that can detect effects on both cognition and 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. Additionally, patients had modest level of deficits of executive function at baseline, tests for which were a major component of the NTB

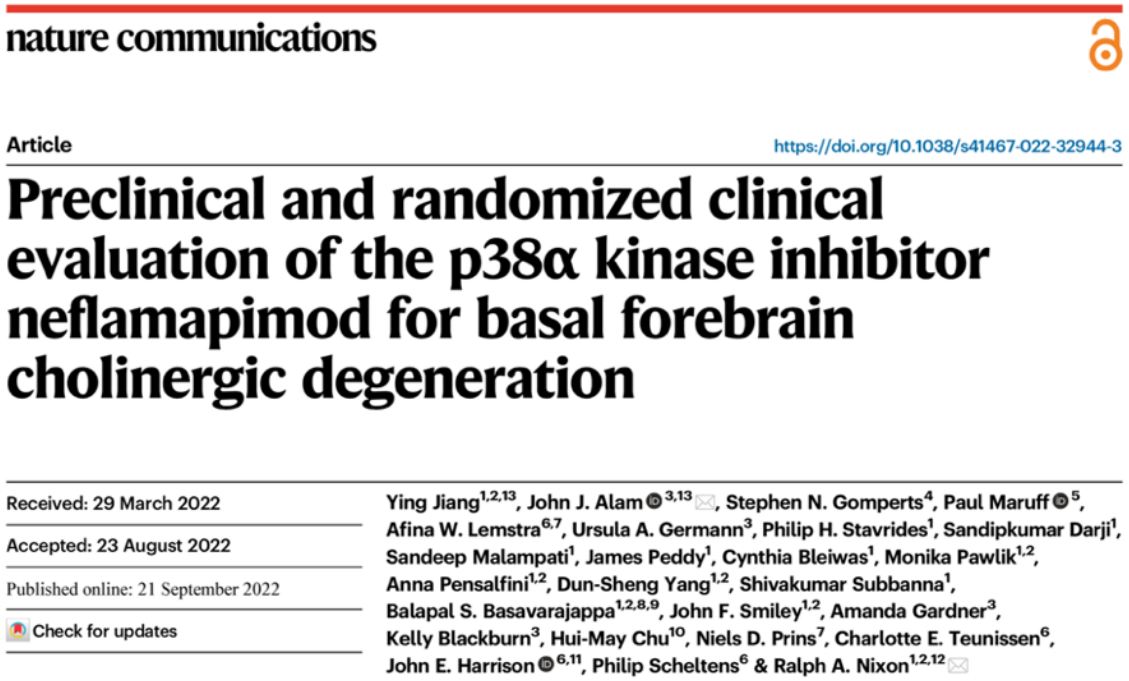
1. McKeith, *Neurology*, 2017)

Positive Preclinical and Phase 2a Clinical Results in Dementia with Lewy Bodies

Pre-clinical: In Down Syndrome transgenic mice, neflamapimod reverses cholinergic neuronal loss and restores function

Clinical: 91-patient, exploratory, 16-week treatment, double-blind placebo-controlled study in patients with mild-to-moderate DLB

- 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)
- In secondary analysis, results at the higher (40mg TID) of two dose levels of neflamapimod, significantly improved original primary outcome measure (*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



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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Accepted: 23 August 2022

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] ✉

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 results stratified by abnormal or normal plasma ptau181 levels

40mg TID vs. placebo efficacy results analyzed after stratification for abnormal (46% of patients in study) or normal (54% of patients) levels of plasma tau phosphorylated at position 181 ("ptau181")

Patients with normal plasma ptau181 level represent patients with pure DLB (i.e., DLB without biomarker evidence of Alzheimer's disease), who have minimal neuronal loss in the hippocampus

Patients with abnormal plasma ptau181 level represent patients with DLB-AD (i.e., DLB with biomarker evidence of AD), who have more advanced disease, including significant neuronal loss in the hippocampus

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

Correspondence
Dr. Alam
jalam@eippharma.com

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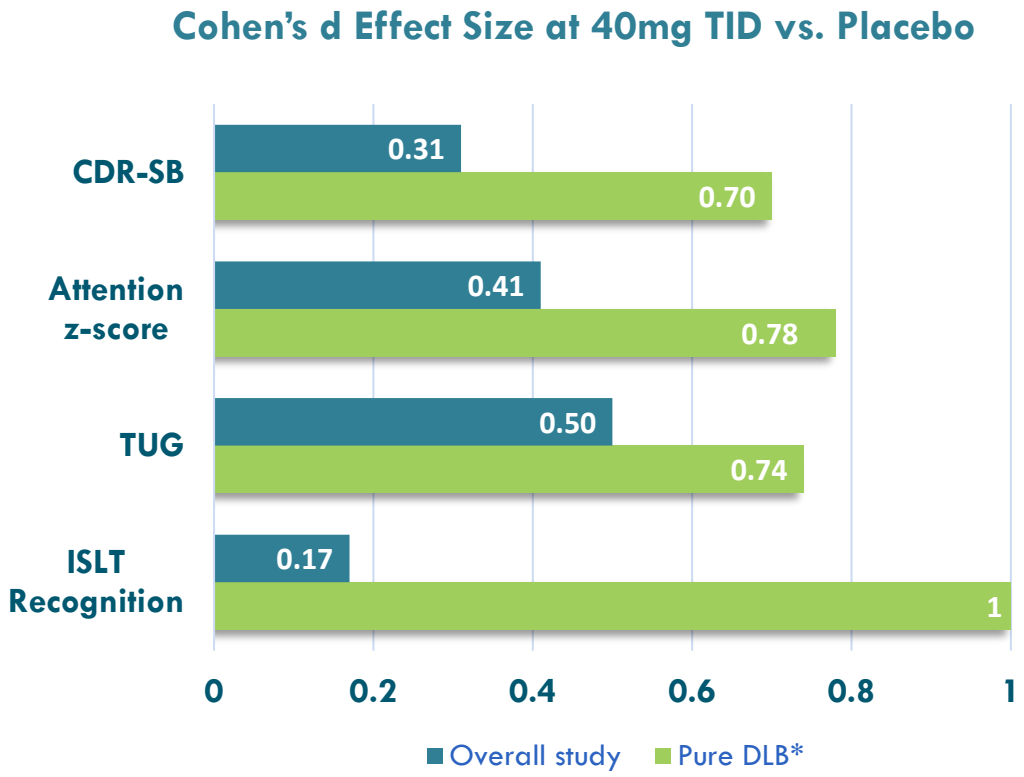
Patients in Phase 2a with pure DLB show substantial response to neflamapimod

	Overall Study Population			Patients With Pure DLB (plasma ptau181 < cutoff)		
	N= NFMD TID, Placebo	*p*-value	Cohen's *d* Effect size	*N*= NFMD TID, Placebo	*p*-value	Cohen's *d* Effect size
CDR-SB	20,38	0.007	0.31	11,22	0.031	0.7
Attention	19,36	0.023	0.41	11,18	0.023	0.78
TUG	20,38	0.024	0.50	11,20	<0.001	0.74
ISLT-Recognition	19,39	0.15	0.17	10,21	0.024	1



- Patients without baseline plasma ptau181 elevation (i.e., patients with pure 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

*Pure DLB: plasma ptau181 < cutoff at study entry
ISLT – International Shopping List Test. Improvement reflected by negative sign for CDR-SB and TUG and positive sign for other measures.

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Potential Biomarker Effects Identified in Phase 2a

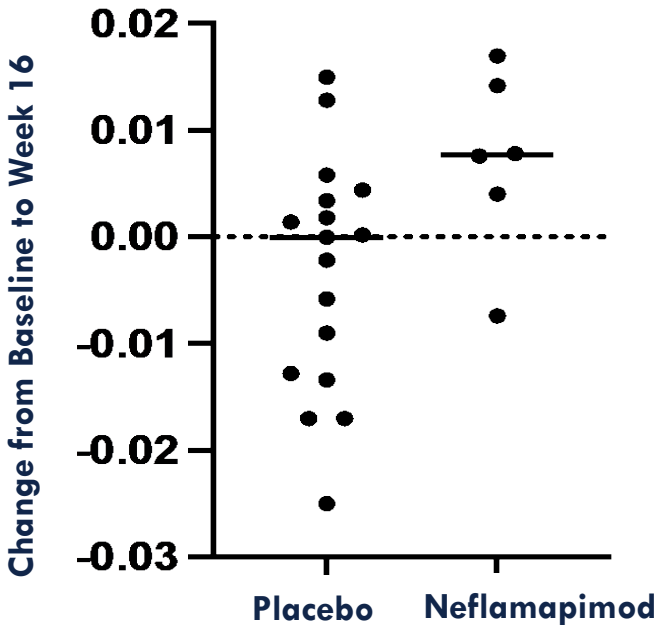
EEG: Functional Connectivity in the beta band (13-30 Hz) significantly increased with neflamapimod TID vs placebo

- Abnormal beta band functional connectivity differentiates DLB from AD (Mehraram et al, 2019)

Plasma Biomarker: In pure DLB patients, neflamapimod led to significant improvement compared to placebo in the change in plasma levels of glial fibrillary acidic protein (GFAP)

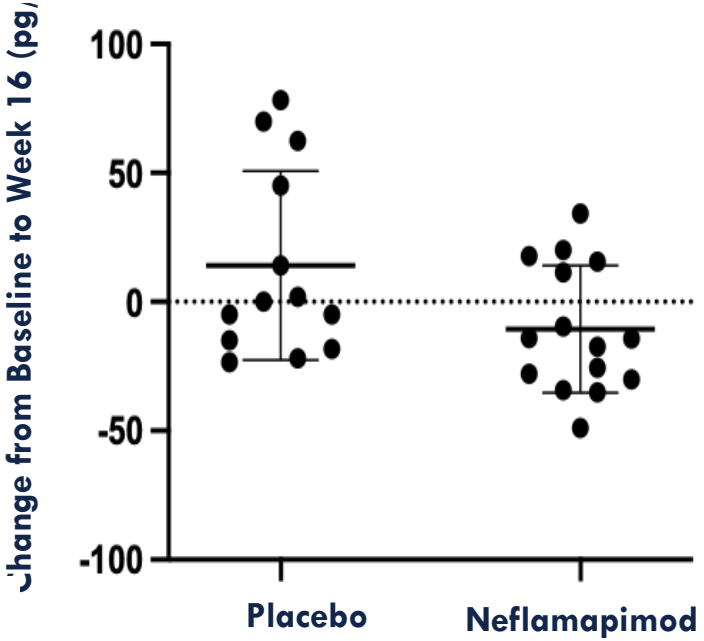
- GFAP recently identified as a potential biomarker for DLB (Hamilton et al, 2023)

Beta Band Functional Connectivity by EEG



NFMD TID (n=6) vs all placebo (n=17) (p=0.03) and vs placebo TID (n=6) (p=0.01)

Change in plasma GFAP in Pure DLB Patients (plasma ptau181 < cutoff)



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

Functional Connectivity by EEG assessed as corrected Amplitude Envelope Correlation (AECc)

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Learnings from Phase 2a Study De-Risks Phase 2b Trial

- 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 with pure DLB (i.e., those without biomarker evidence of AD) have a substantially greater response to treatment
  - Excluding patients with biomarker evidence of AD, 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

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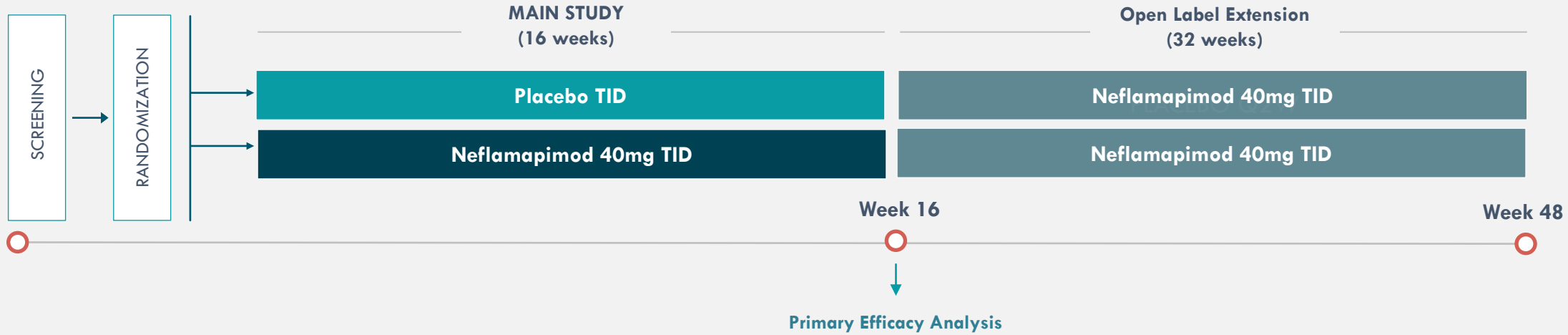
RewinD-LB Phase 2b Clinical Trial Ongoing



PARTICIPANTS

DLB by consensus criteria, including abnormal DaTscan™

Global CDR score of 0.5 or 1.0

No biomarker evidence of AD, as assessed by plasma ptau181

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

Potential for Major Value Creation with Well-defined Path Forward

DLB is an indication with **high unmet need** and **high commercial return potential;** currently no approved treatment options for patients with DLB

Phase 2b is optimized for success, builds on Phase 2a learnings and is expected to **provide a clear path to market in a high value indication;** neflamapimod granted Fast Track designation by FDA

Based on prior discussions with FDA, and pending alignment in an end-of-phase 2 meeting, **potential Phase 3 design:**

Single Phase 3 clinical trial (Est. Cost: $50 – $75M)	CDR-SB as primary endpoint	Treatment duration of 24 weeks	Approximately 300 patients (final sizing based on Phase 2b results)

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Summary

Key Milestones

1H 2023

- ✓ NIA approved $21M grant for Phase 2b
- ✓ Signed merger agreement with Diffusion Pharmaceuticals
- ✓ Presented data at AD/PD 2023
- ✓ Initiated Phase 2b DLB study

2H 2023

- ✓ 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

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

1. Plasma ptau181 stratified results.

Financial Overview

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 through the end of 2024[1],

by which time Phase 2b Main Study clinical data are expected to be available

1. As of September 30, 2023. Refer to the Company's current Quarterly Report on Form 10-Q filed with the SEC on November 13, 2023 for additional financial and other information

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 DLB; success in Phase 2b would provide a clear, cost-effective path to market

Key milestones expected in 2024

Potential to broaden opportunity through additional indications

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Medicines for the Brain

February 2024

Corporate Overview

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

NASDAQ: CRVO

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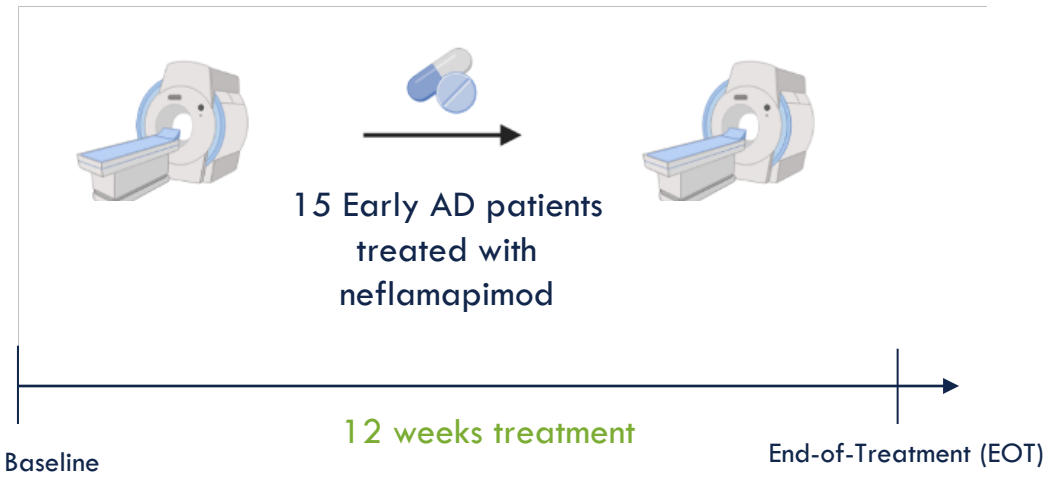
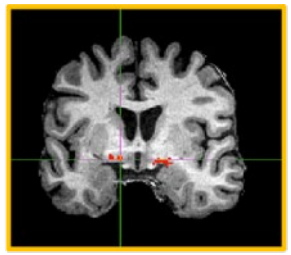
Medicines for the Brain

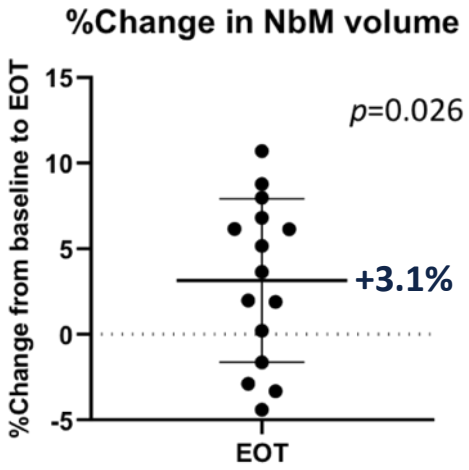
Appendix

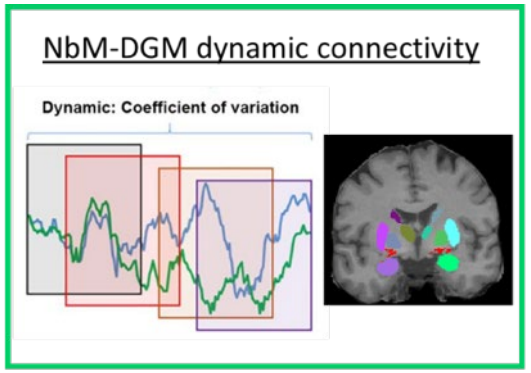
Neflamapimod Appears to Reverse Basal Forebrain Atrophy, Assessed by MRI

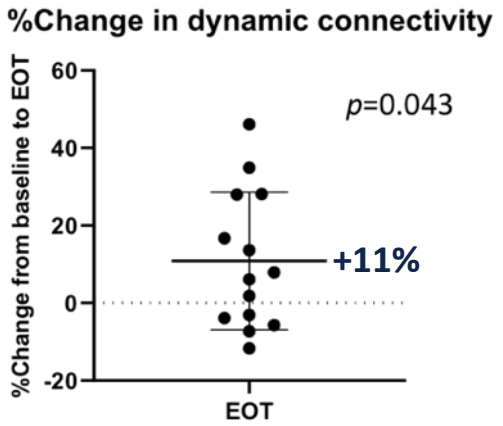
Neflamapimod treatment is associated with a significant increase of basal forebrain volume and functional connectivity











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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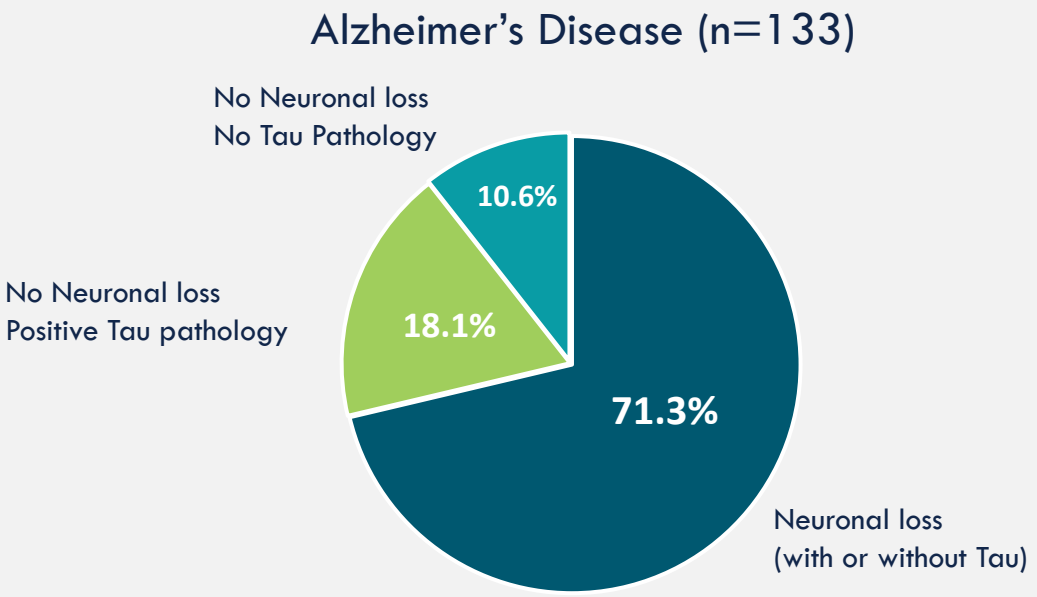
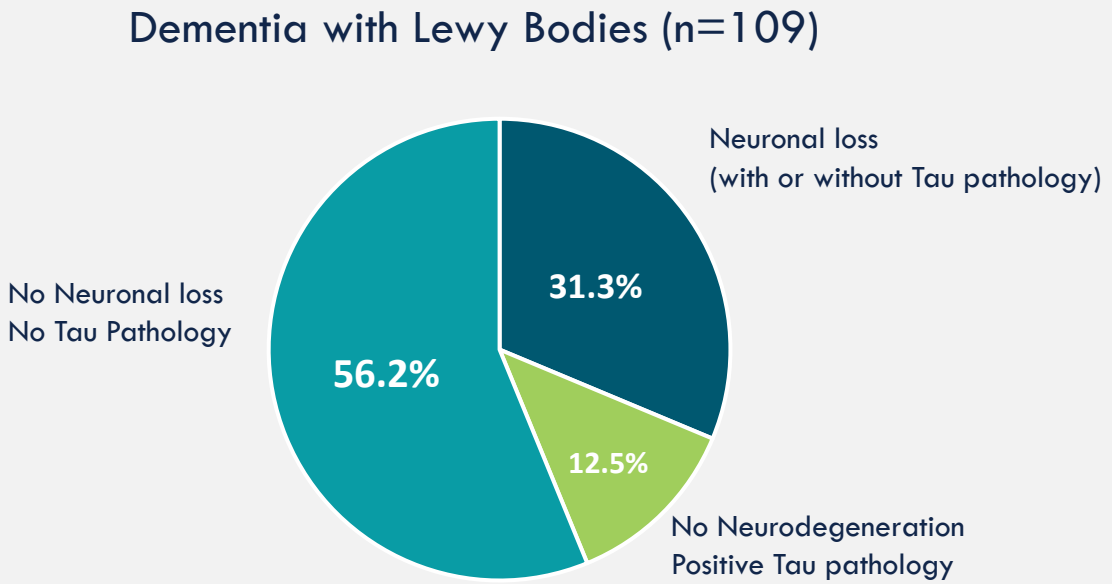
DLB is Associated with Significantly Less Neuronal Loss than AD





[1] Positive Tau: increased ptau; Neuronal loss: Increase total tau; in CSF
Jain et al, *Alzheimer's & Dementia*, 2023

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AscenD-LB 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

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AscenD-LB Demonstrated Neflamapimod Improved Cognition and Function

		40mg BID + 40mg TID		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
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://wwwnature.com/articles/s41467-022-32944-3

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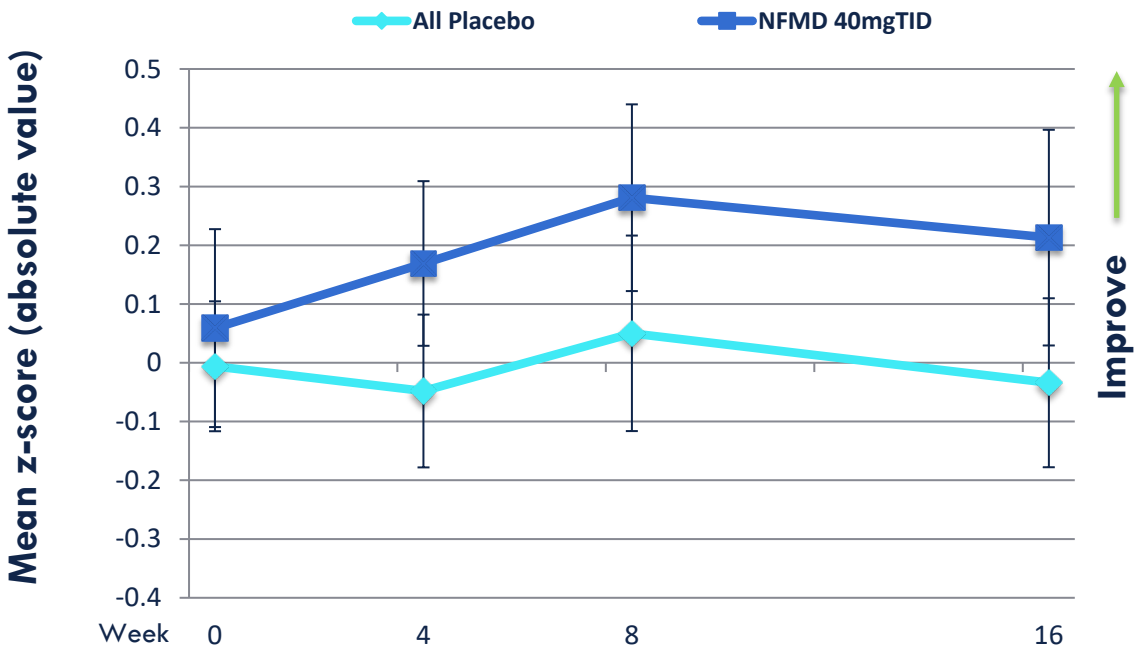
Phase 2a Results Demonstrated Neflamapimod 40mg TID Improved Cognition in Patients with DLB (Overall Patient Population)

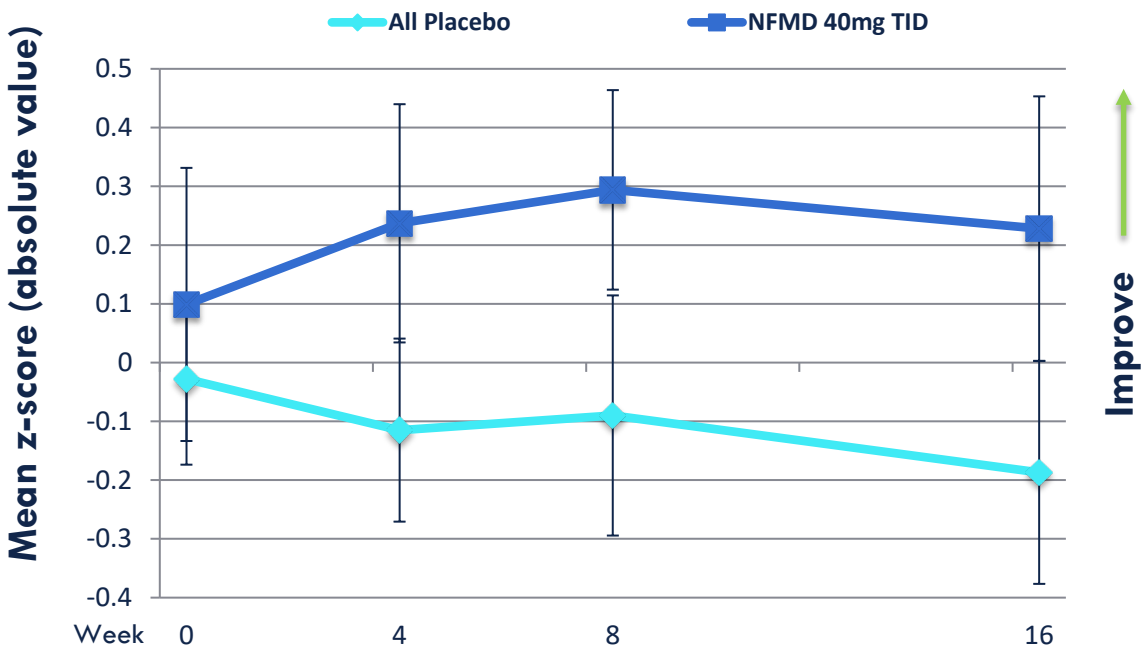
Neuropsychological Test Battery (NTB) Composite



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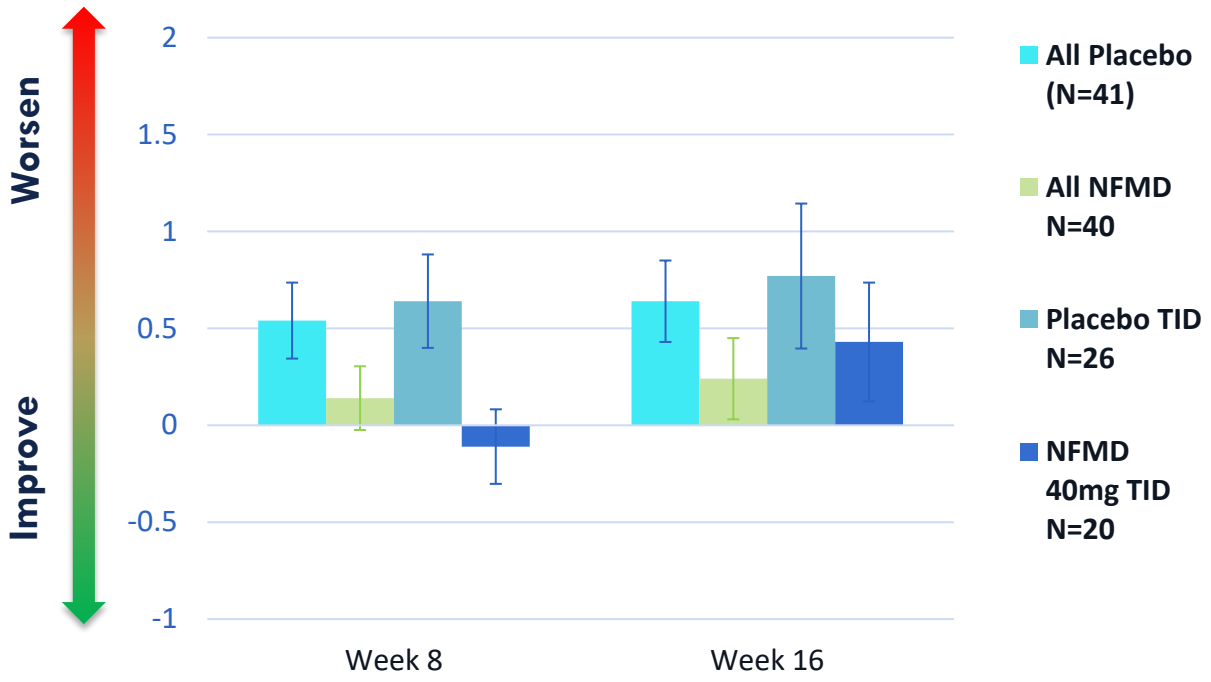
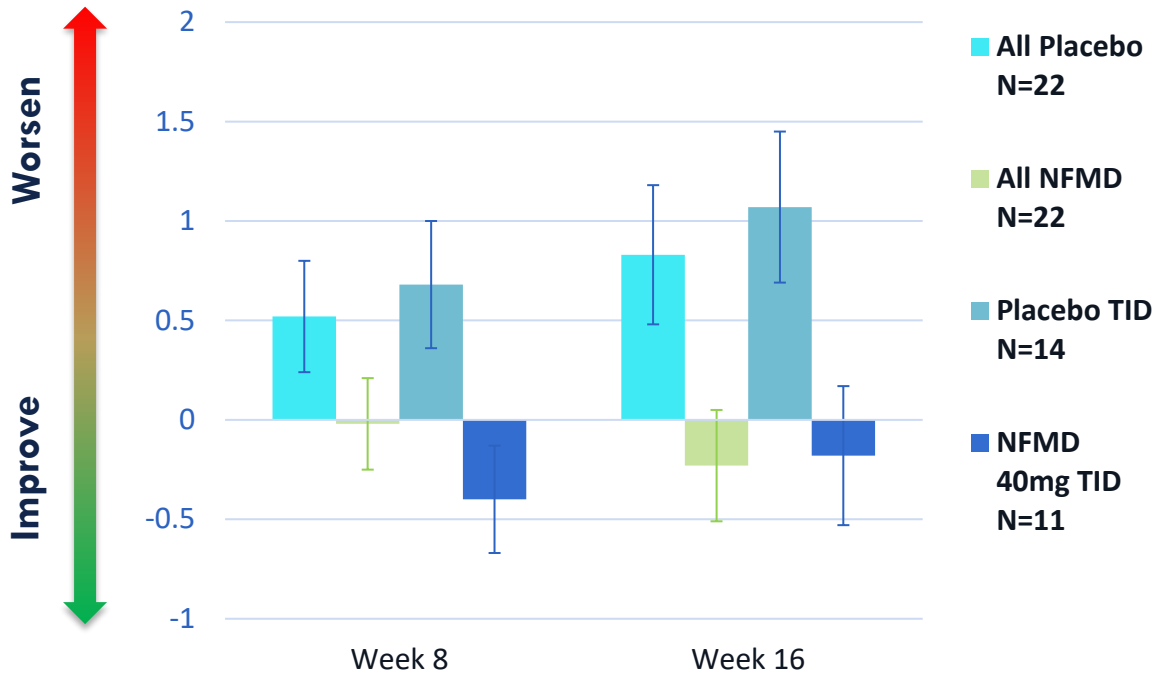
Neflamapimod Treatment in Patients with DLB Demonstrated Substantial Effect on Change from Baseline in CDR-SB in Phase 2a

Overall Patient Population



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



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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

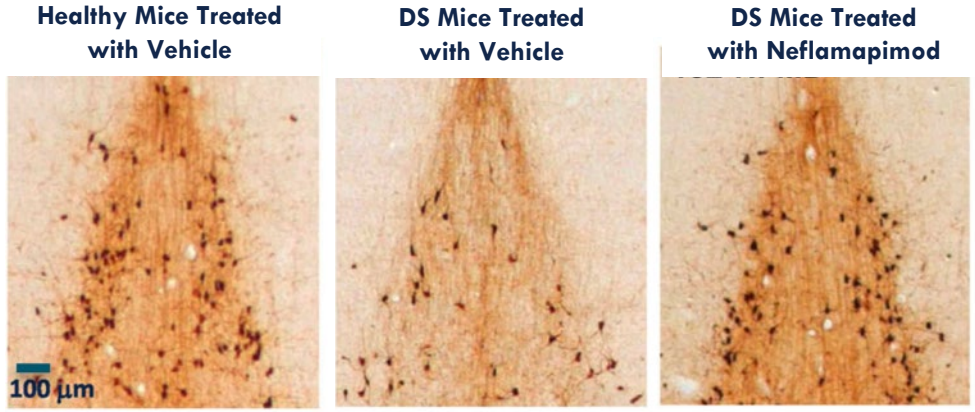
Reversed basal forebrain cholinergic neuron loss and restored cholinergic function

- 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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Results of 24-week Placebo-controlled Study of Neflamapimod 40mg BID in Early AD

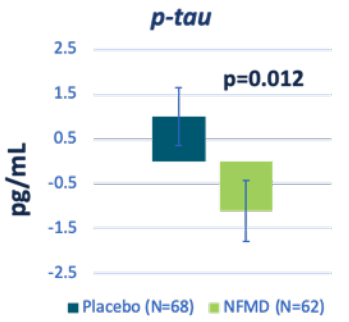
161 patients with CSF-biomarker (Ab42, ptau181) confirmed AD randomized to neflamapimod 40mg BID or placebo for 24 weeks

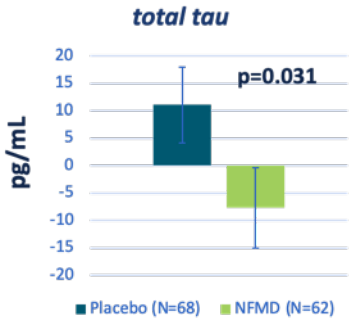
Significant effect vs. placebo on CSF markers of disease progression (ptau, total tau)

No significant effect on clinical endpoints for neflamapimod 40mg BID vs. placebo for overall population. However, PK-PD analysis shows potential effect on progression on the primary outcome measure (HVLT Total and Delayed Recall) in patients with C_{trough} > 4 ng/mL

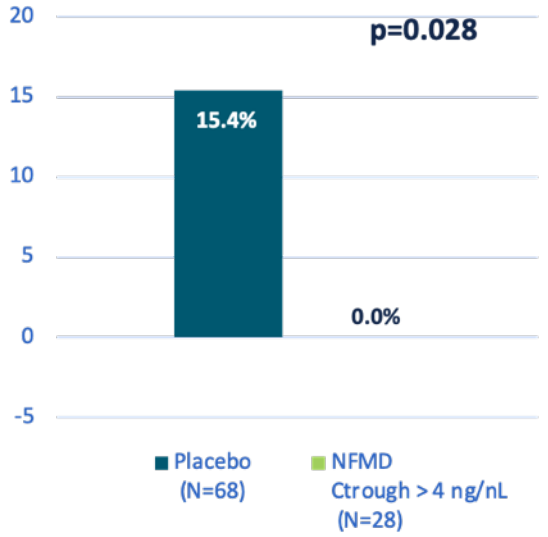
- Suggests 40mg TID or 80mg BID would slow disease progression

CSF Markers of Disease Progression





Proportion of Patients with Progression (one SD decline) on Primary Outcome Measure (HVLT)



HVLT: Hopkins Verbal Learning Test; results analyzed as change in z-score for combined total and delayed recall

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Roadmap to Success: Planned Phase 3 Study

AscenD-LB | RewinD-LB | Phase 3 Study Design

91-patient, 16-week placebo-controlled study

Placebo vs. Neflamapimod 40 mg (randomized 1:1); BID (weight < 60 kg) or TID (weight ≥ 60 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
- ✓ Significant positive effects on EEG and plasma GFAP
- ✓ Results most prominent in patients with pure DLB

160-patient 16-week placebo-controlled study with 32-week open label extension

Optimized, based phase 2a learnings:

- Placebo vs. neflamapimod 40mg TID (randomized 1:1)
- CDR-SB primary endpoint; TUG, CGIC, NTB secondary endpoints
- Exclude patients with AD co-pathology, assessed by plasma ptau181 (i.e., include patients with pure DLB)
- High statistical power for significant positive effect on change in CDR-SB vs. placebo

Plans to enroll approximately 300 patients in a 24-week placebo-controlled study with long-term extension

- Placebo vs. neflamapimod 40mg TID (randomized 1:1); potential to include 80mg BID
- Replicates phase 2b with respect to primary and secondary clinical endpoints and patient population
- Basal forebrain atrophy by MRI as a major secondary endpoint

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