CERVOMED

Medicines for the Brain

April 2024

Corporate Overview

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

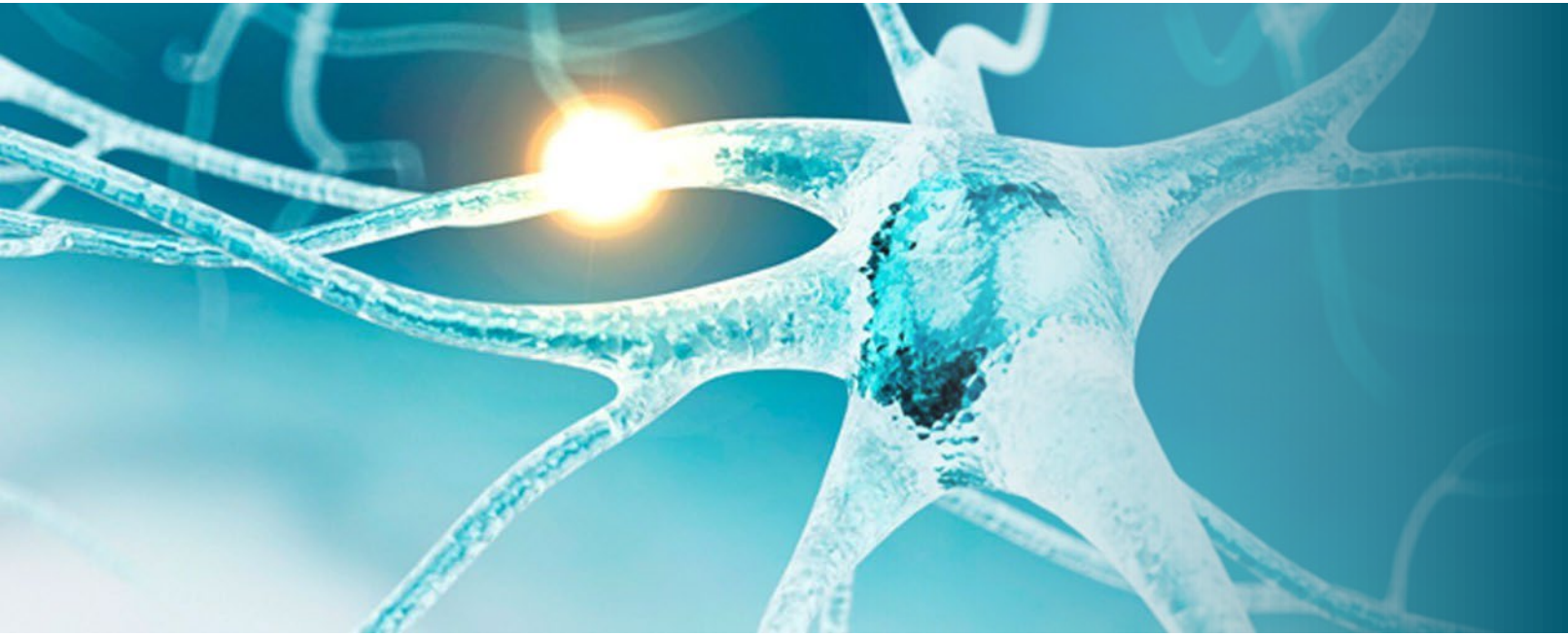
NASDAQ: CRVO

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 and the completion and achievement of primary endpoints in the Company's ongoing Phase 2b clinical Trial; the potential therapeutic value of neflamapimod; the Company's anticipated cash runway and use of proceeds from its recent private placement; 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 or 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 April 22nd, 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.

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

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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, former CEO, 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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Financial Overview[1]

Post-offering,
8,253,741 shares
outstanding, all
common stock

- Completed private placement with leading healthcare investors on April 1, 2024
- Upfront gross proceeds of $50.0 million
- Up to an additional $99.4 million of gross proceeds tied to exercise of Series A warrants; with positive top-line data from ongoing Phase 2b trial, exercise permitted no later than 180 days after data announcement

CervoMed has cash runway through the end of 2025,
not including any additional proceeds that may be received upon the exercise of Series A warrants

1. As of April 2, 2024, and inclusive of the upfront proceeds and issuance of shares of common stock in connection with the Company's private placement completed April 1, 2024. For additional financial and other information, refer to (i) the Company's Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on March 29, 2024, and (ii) the Company's Current Report on Form 8-K filed with the SEC on March 28, 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 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; plan **to complete enrollment in 2Q24 and report primary efficacy results and other top-line data[2] in 4Q24**

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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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. Effects most prominent in patients with pure DLB
- Safety profile well defined, with clinical safety data in greater than 300 study participants

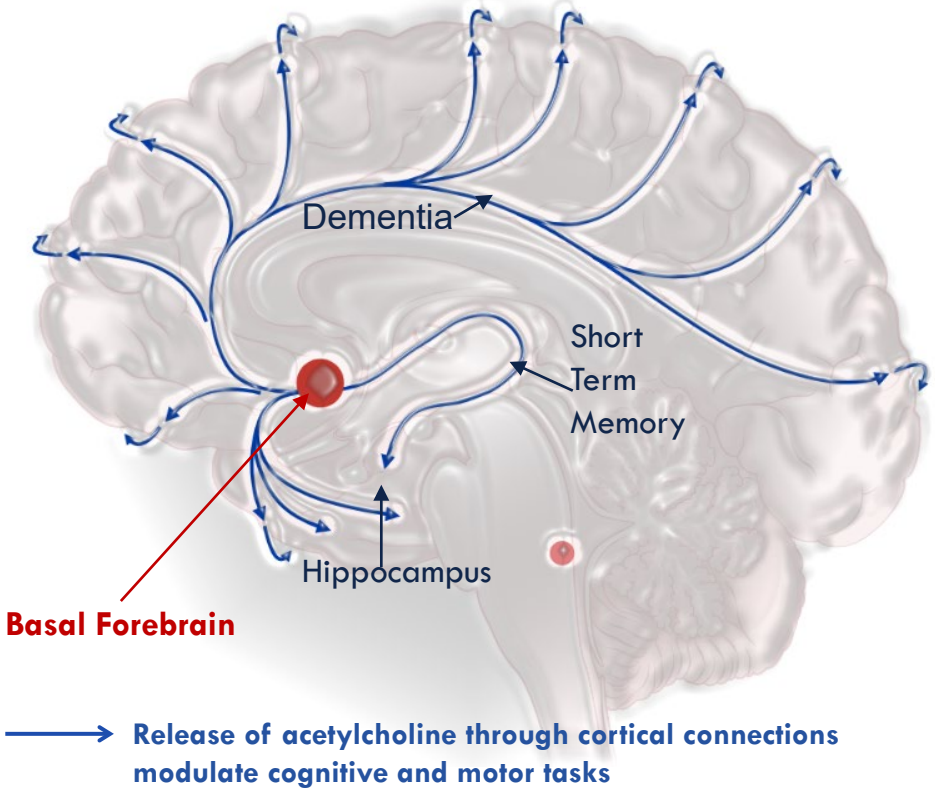
Prior phase 2 studies in Alzheimer's disease (AD) demonstrated target engagement:

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

Neflamapimod Mechanism of Action

Basal Forebrain Cholinergic Complex

Primary site of pathology in DLB



Neuroinflammation,
Aggregated Proteins (e.g., α-synuclein)

p38α ⊣ (-) **Neflamapimod**

↑ Rab5

Tau Pathology, Defects in Axonal Transport and NGF Signaling

Cholinergic Dysfunction & Degeneration

Basal Forebrain

NGF: Nerve Growth Factor

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

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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

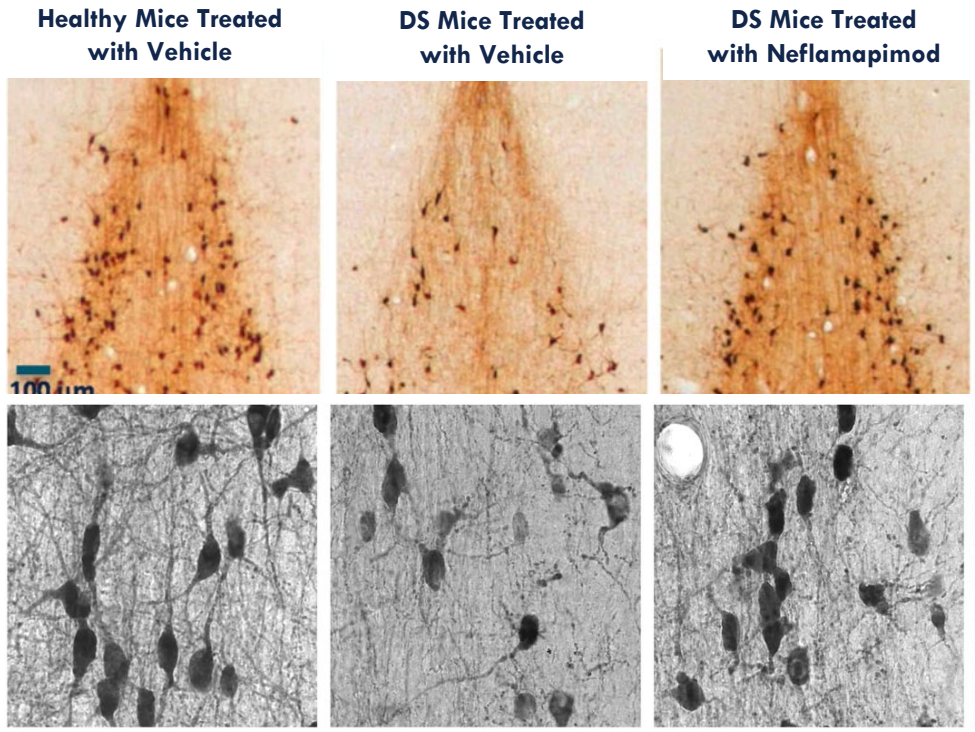
Reversed basal forebrain cholinergic neuron loss and restored cholinergic function

- 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://www.nature.com/articles/s41467-022-32944-3

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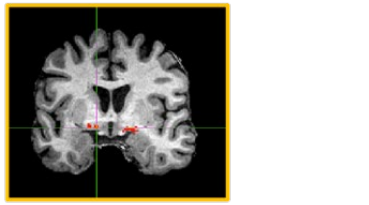
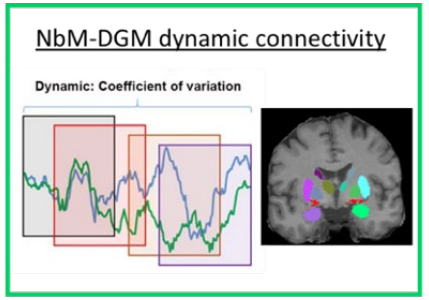
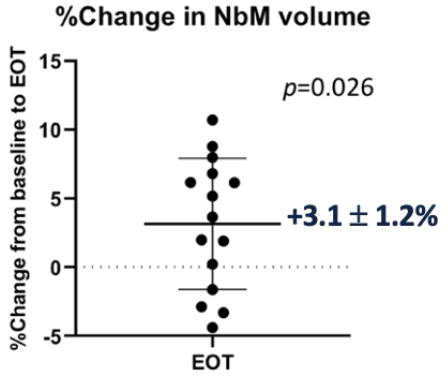
Neflamapimod Appears to Reverse Basal Forebrain Atrophy, Assessed by MRI

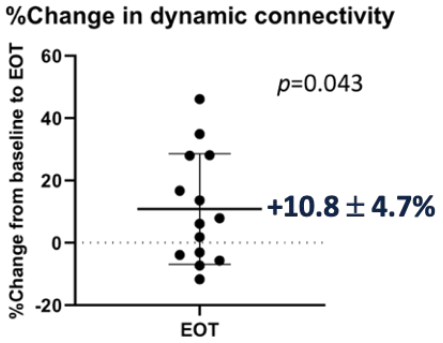
Neflamapimod treatment is associated with a significant increase of basal forebrain volume and functional connectivity in patients with Early (Amyloid PET+) AD

MRI scans obtained before and after 12-weeks neflamapimod treatment in 15 Early AD Patients





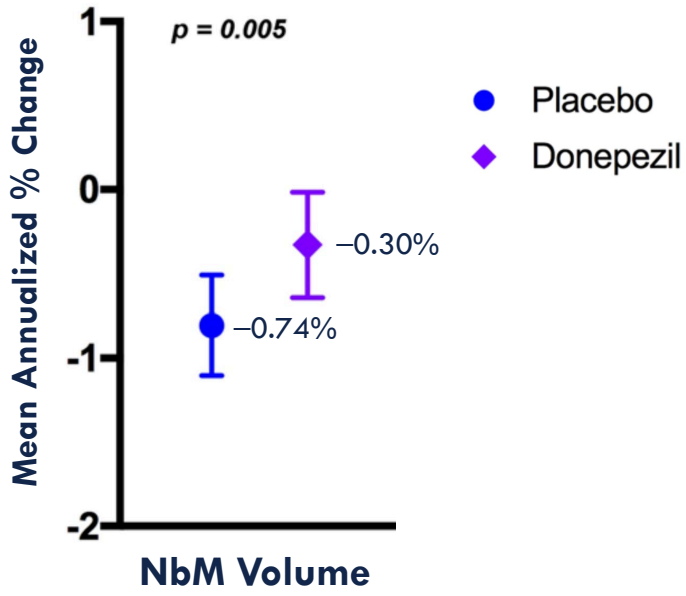




Prins et al, *JPAD*, 2024

Donepezil (cholinesterase inhibitor) treatment only slows decline in basal forebrain volume in a similar patient population (prodromal AD)

MRI scans before and after donepezil 10mg/day (N=75) or Placebo (N=88) for 12 months



Cavedo et al, *Scientific Reports*, 2017

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

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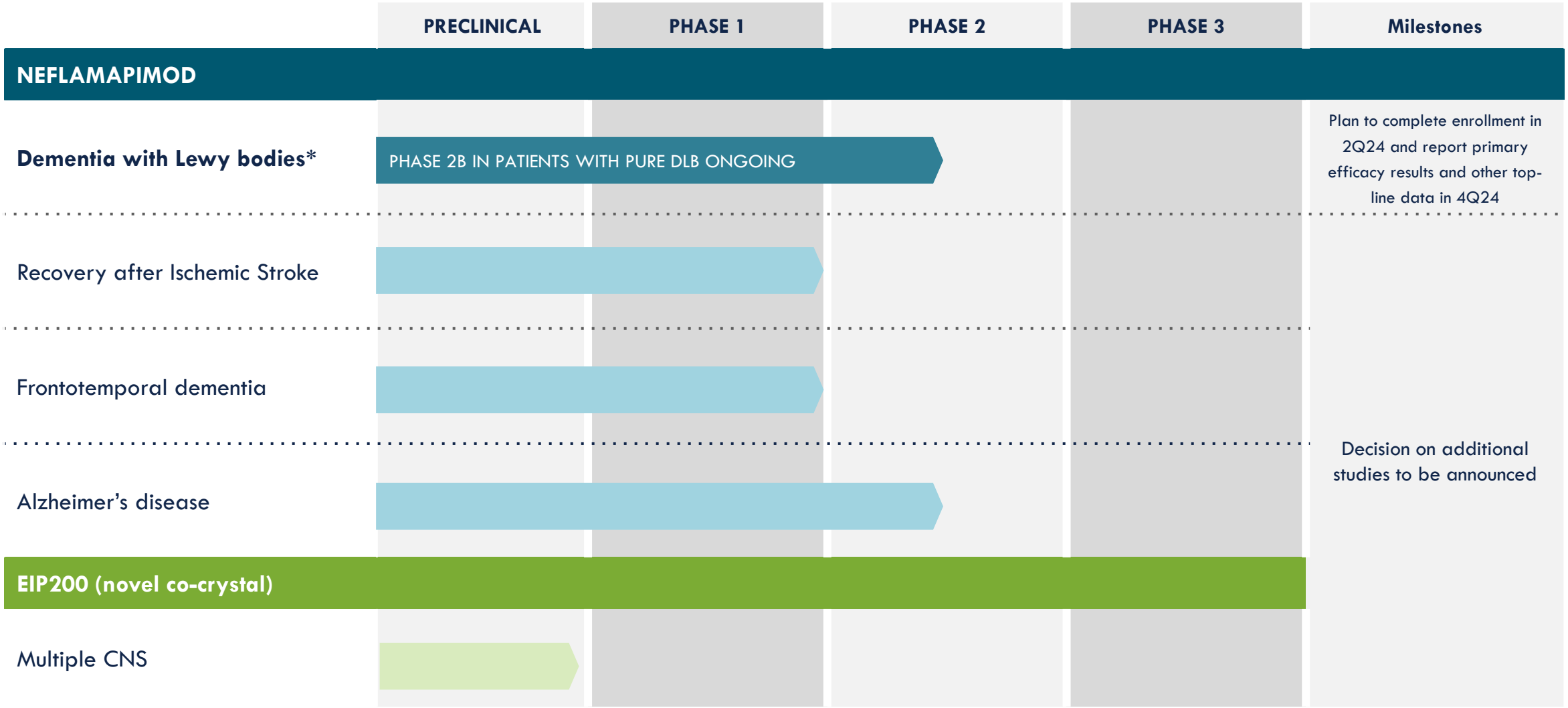
CervoMed Pipeline



Worldwide commercial rights across programs
*Received FDA Fast Track designation

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

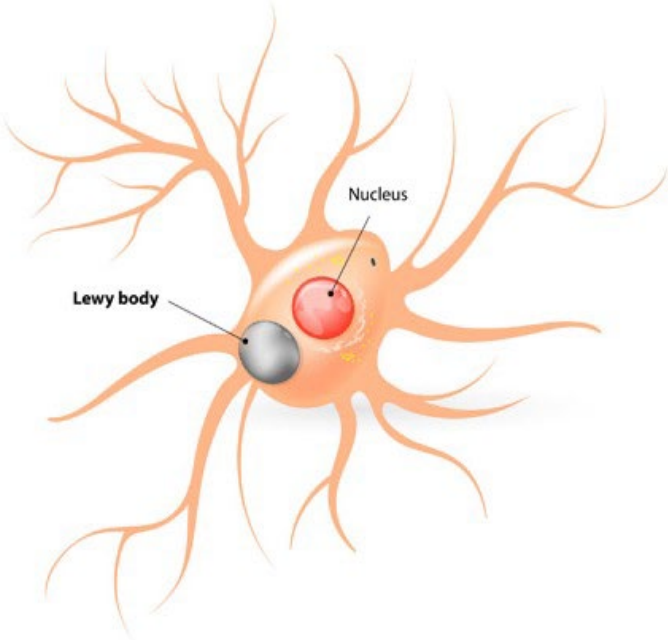
Market Opportunity

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

~700,000 individuals in each of US and EU

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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Basal Forebrain Cholinergic Dysfunction and Degeneration is Primary Driver of Disease Expression and Progression in Early DLB

In vivo nucleus basalis of Meynert degeneration in mild cognitive impairment with Lewy bodies

Julia Schumacher[a,*], John-Paul Taylor[a], Calum A. Hamilton[a], Michael Firbank[a], Ruth A. Cromarty[a], Paul C. Donaghy[a], Gemma Roberts[a], Louise Allan[a,c], Jim Lloyd[b], Rory Durcan[a], Nicola Barnett[a], John T. O'Brien[d], Alan J. Thomas[a]

[a] *Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL, United Kingdom*
[b] *Nuclear Medicine Department, Newcastle upon Tyne Hospitals NFS Foundation Trust, Newcastle upon Tyne, United Kingdom*
[c] *Institute of Health Research, University of Exeter, Exeter, United Kingdom*
[d] *Department of Psychiatry, University of Cambridge School of Medicine, Cambridge CB2 0SP, United Kingdom*

NeuroImage: Clinical 30 (2021) 102604

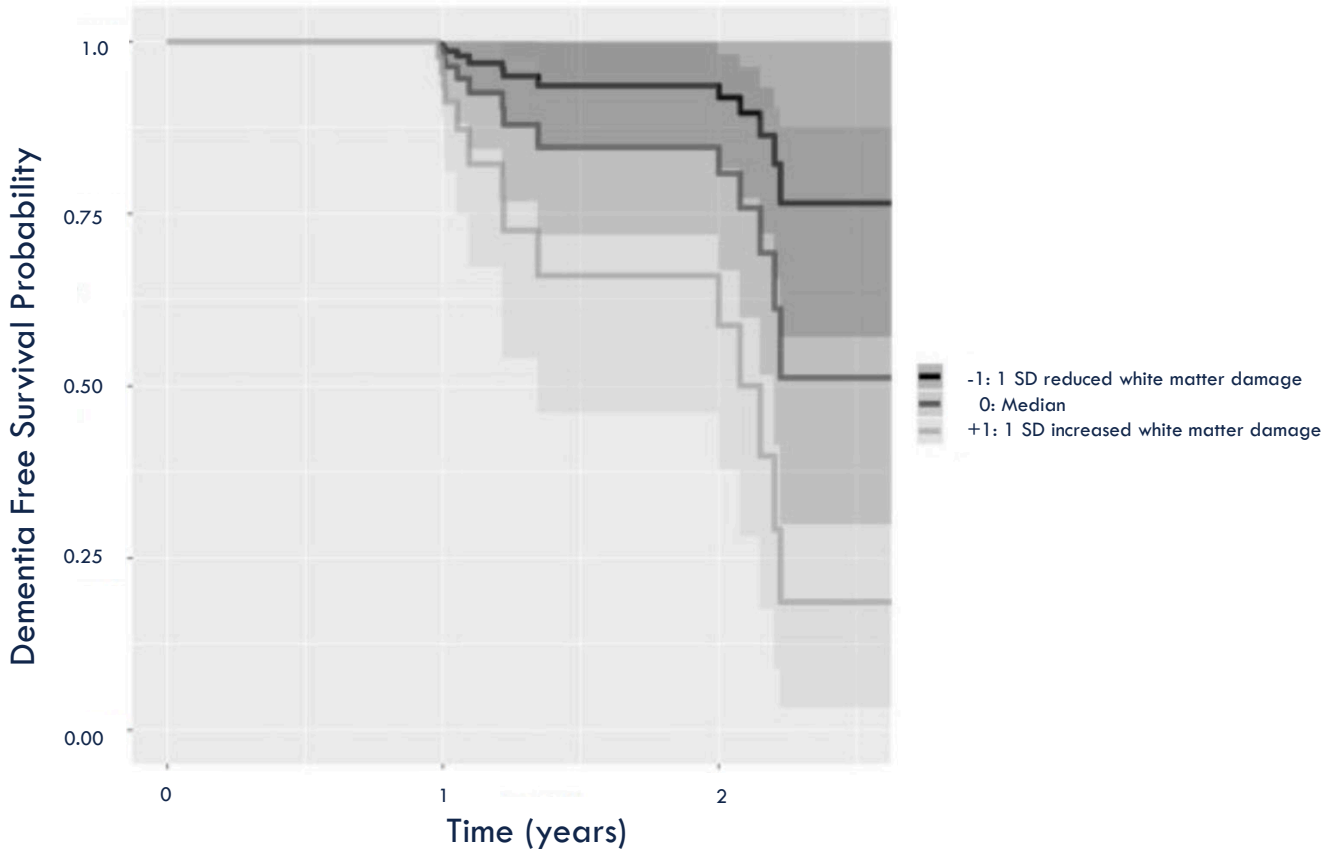
https://doi.org/10.1093/braincomms/fcac013 BRAIN COMMUNICATIONS 2022: Page 1 of 12 | 1

BRAIN COMMUNICATIONS

Longitudinal atrophy in prodromal dementia with Lewy bodies points to cholinergic degeneration

Kejal Kantarci,[1] Zuzana Nedelska,[1,2] Qin Chen,[1,3] Matthew L. Senjem,[1] Christopher G. Schwarz,[1] Jeffrey L. Gunter,[1] Scott A. Przybelski,[4] Timothy G. Lesnick,[4] Walter K. Kremers,[4] Julie A. Fields,[5] Jonathan Graff-Radford,[6] Rodolfo Savica,[6] David Jones,[6] Hugo Botha,[6] David S. Knopman,[6] Val Lowe,[1] Neill R. Graff-Radford,[7] Melissa M. Murray,[8] Dennis W. Dickson,[8] R. Ross Reichard,[9] Clifford R. Jack Jr,[1] Ronald C. Petersen,[6] Tanis J. Ferman[10] and Bradley F. Boeve[6]

Damage to Cholinergic Pathways Predicts Progression to Dementia



Schumacher et al, *Brain* 2022: 145; 1773–1784

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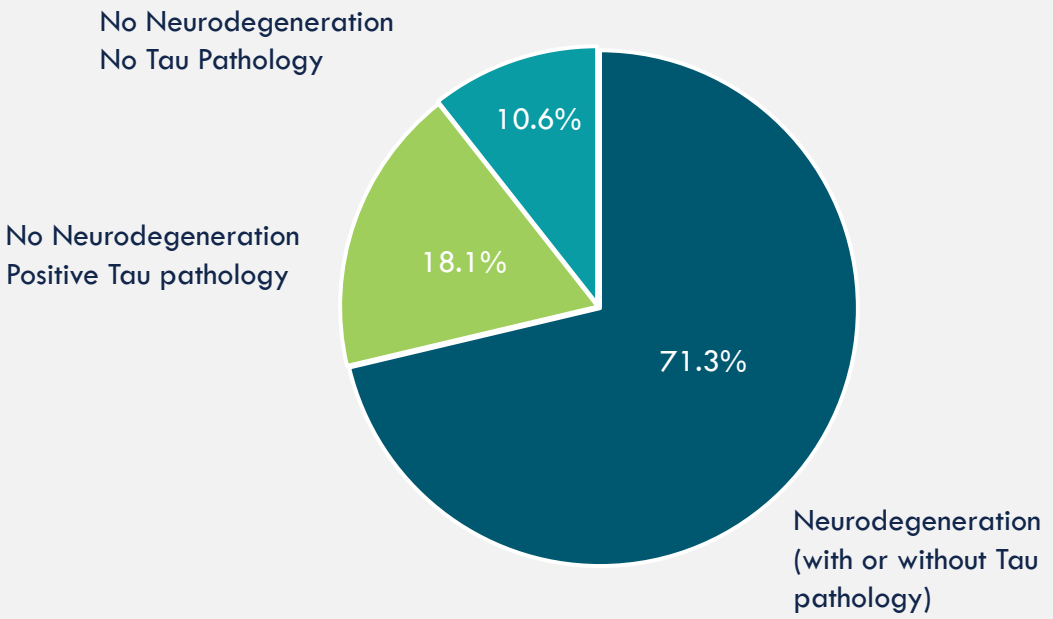
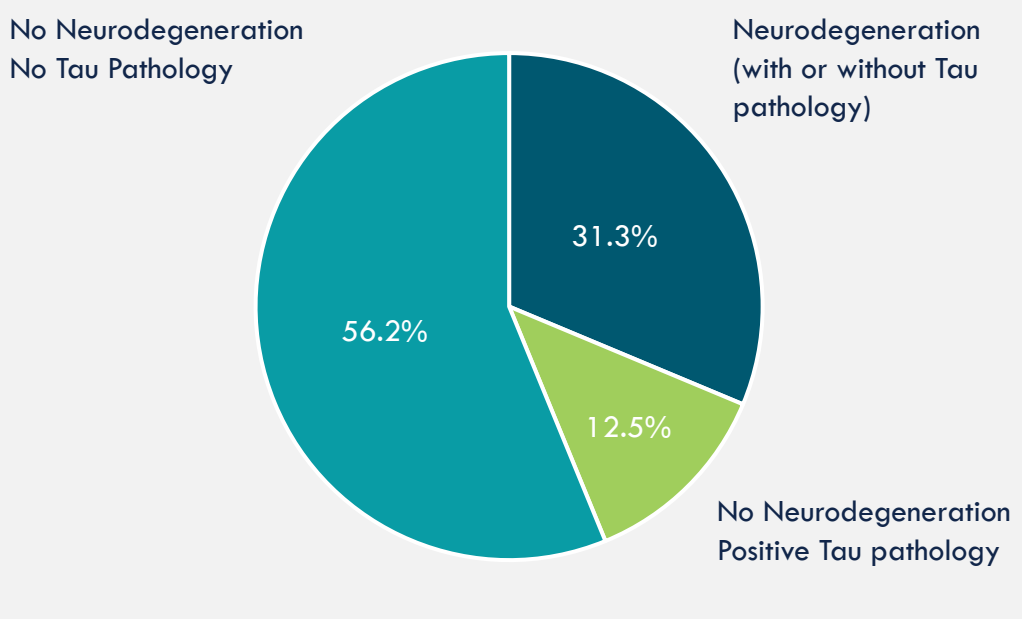
DLB is Associated with Significantly Less Neurodegeneration, Compared to AD

Presence of Neurodegenerative Marker Elevation in CSF (Cerebrospinal Fluid)

Alzheimer's Disease (n=133)



Dementia with Lewy Bodies (n=109)



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

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Therapeutic Opportunity in Dementia with Lewy Bodies (DLB)

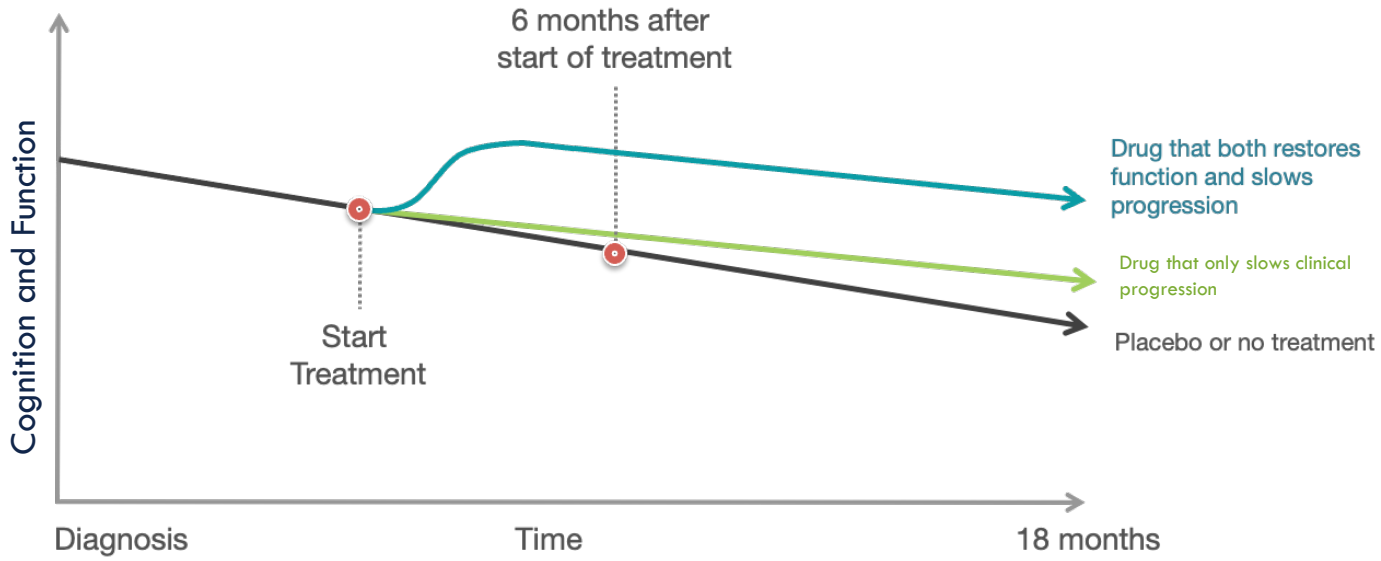
Drug mechanism targets the primary pathology in DLB: basal forebrain cholinergic system

Early-stage DLB 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 of progression (**restore function**) in the near term, as well 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



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)

Advanced disease, with significant neuronal loss in hippocampus

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

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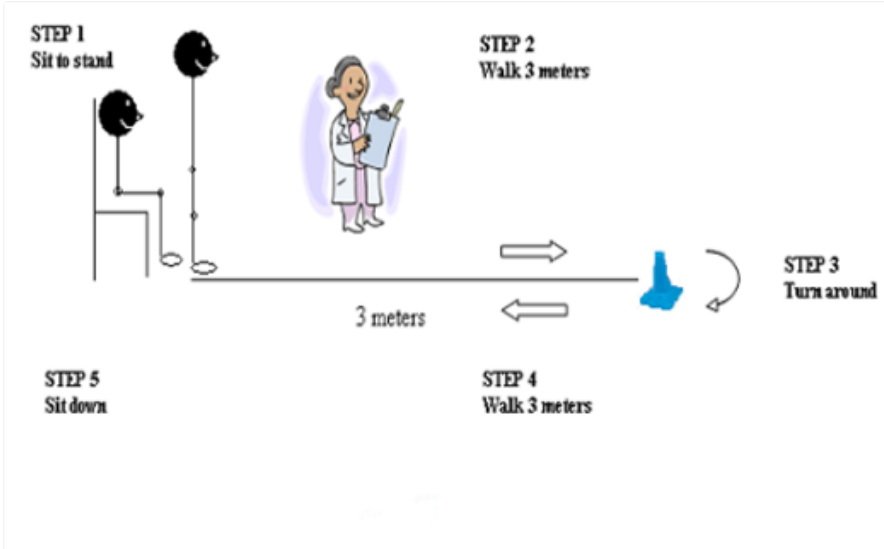
Phase 2a Clinical ("AscenD-LB) Study Major Outcome Measures

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)*:

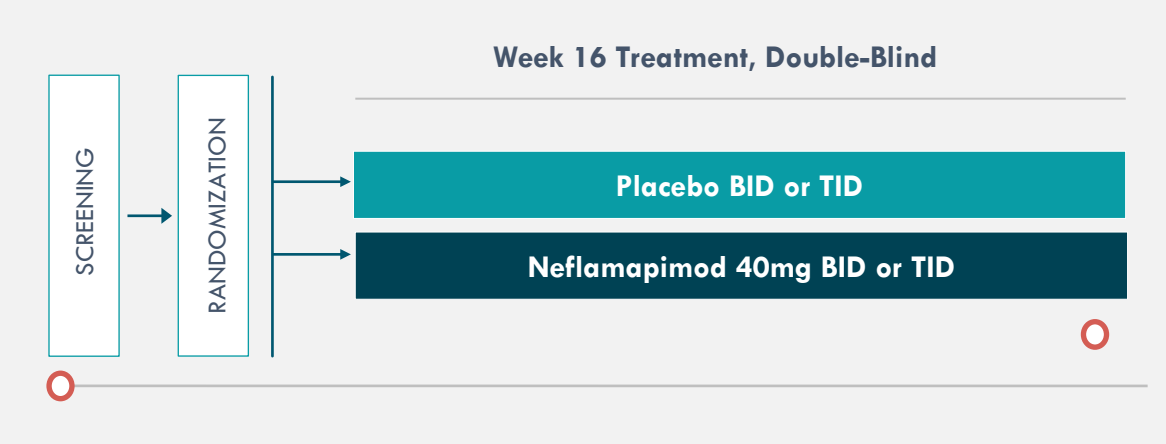
- Detection
- Identification
- One Card Learning
- One Back
- Letter Fluency Test
- Category Fluency Test

*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

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

RESULTS[2]

In the intention-to-treat analysis (including both BID and TID treated patients) neflamapimod significantly improved:

- Dementia Severity (assessed by CDR-SB, p=0.023 vs. placebo)
- Gait (assessed by TUG, p=0.044 vs. placebo).

In a secondary analysis, at the higher (40mg TID) of two dose levels, neflamapimod significantly improved cognitive testing results:

- Assessed by by full NTB (p=0.049 vs. placebo)
- Assessed by tests of Attention alone (p=0.023 vs. placebo).

Well-tolerated, with no treatment-related discontinuations.

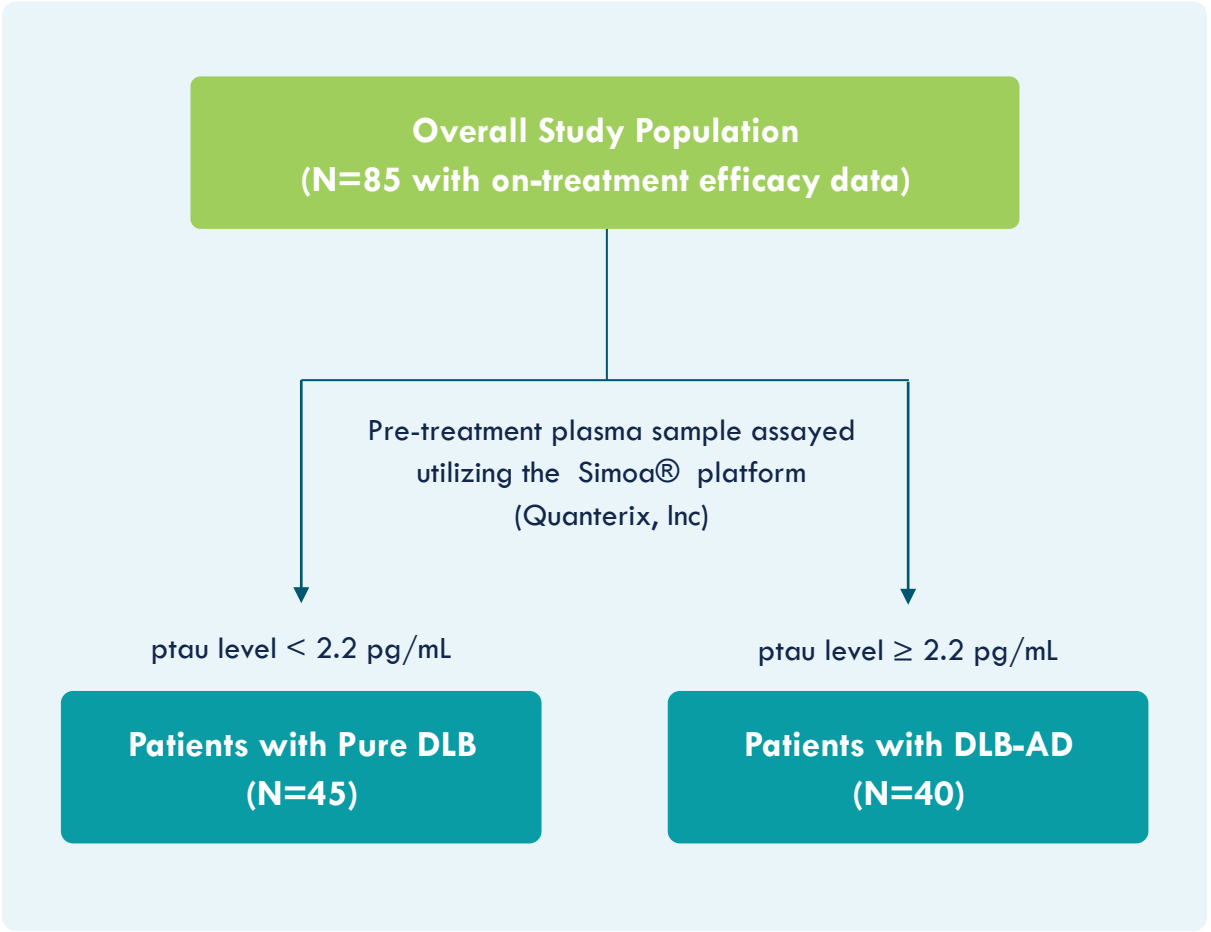
OUTCOME MEASURES

DLB-specific Neuropsychological Test Battery (NTB, six-test cognitive test battery)
Dementia Severity, assessed by CDR-SB
Motor Function, assessed by Timed Up and Go (TUG) test

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 abnormal or normal plasma ptau181 levels

- In original protocol, randomization was to be stratified by screening plasma AD-biomarker status. With no assay available at the time, this could not be done, and baseline plasma sample were stored for future analysis.
- In 2021, scientific publication[1] identified plasma levels of phosphorylated tau could accurately identify those patients with DLB who had brain amyloid plaque (by CSF) and/or tau pathology (by PET scan),
- Efficacy results in AscenD-LB were then analyzed after stratification for abnormal or normal levels of plasma tau phosphorylated at position 181 ("ptau181")
  - Cut-off 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



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

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

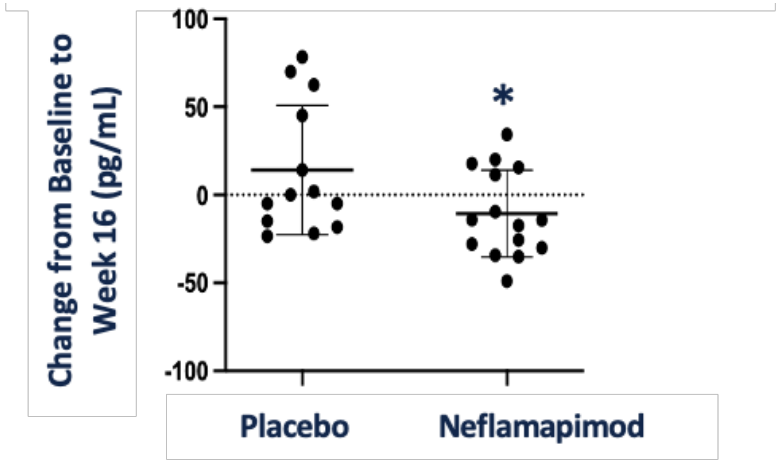
	Overall Study Population				Patients With Pure DLB (Plasma ptau181 < cutoff)			
	N= NFMD TID, Placebo	Difference[1] (95% CI)	p-value	Cohen's d Effect size	N= NFMD TID, Placebo	Difference[1] (95% CI)	p-value	Cohen's d Effect size
NTB	19,37	+0.17 (0.00,0.35)	0.049	0.47	11,19	+0.21 (-0.07,0.49)	0.13	0.56
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 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; 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

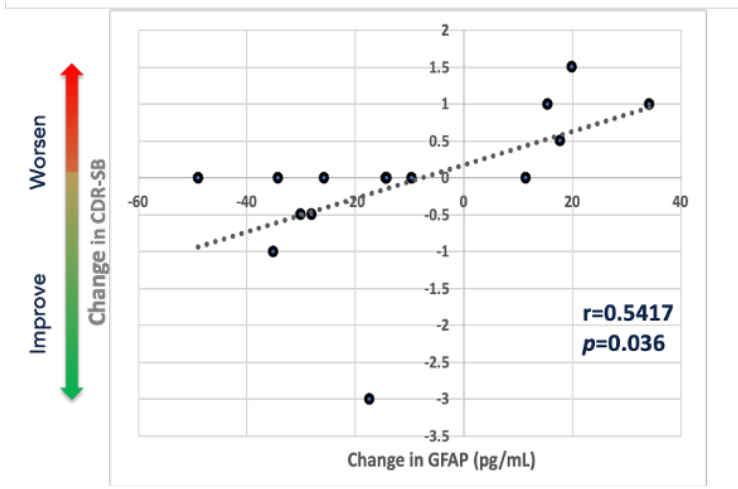
Plasma Biomarker Effect Further Supports Neflamapimod is Clinically Efficacious in Pure DLB

Change on-treatment 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 vs. placebo . **In pure DLB patients, neflamapimod led to significant improvement compared to placebo in the change in GFAP from baseline to week 16**

Change in plasma GFAP is Correlated to the Clinical Outcome (Change in CDR-SB from Baseline to Week 16)

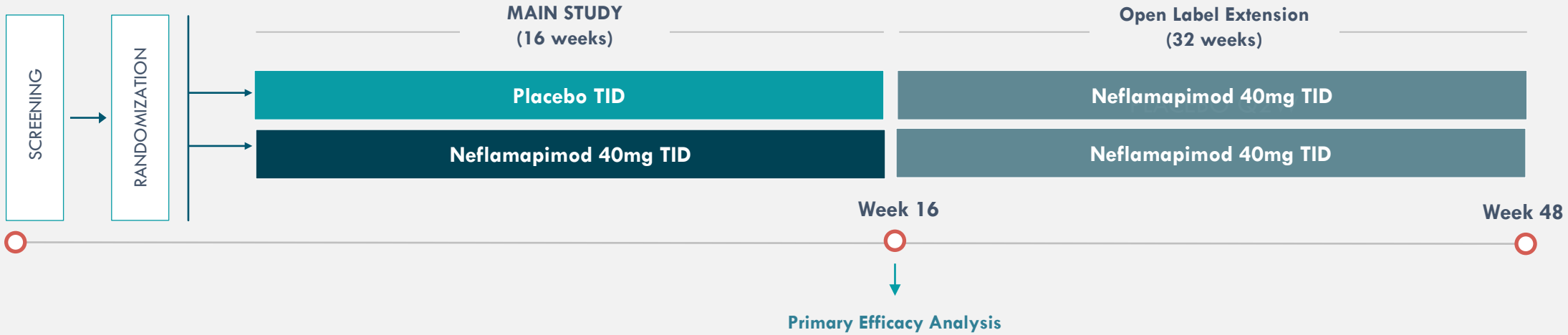


Increased GFAP associated with worsening CDR-SB, reduction in GFAP associated with improvement on CDR-SB among neflamapimod recipients with pure DLB (r=-.54, p=0.036). The correlation was not seen in placebo- recipients (r=0.31, p=NS) **Neflamapimod treatment effects on GFAP correlated with clinical outcome assessed by CDR-SB**

Plasma glial fibrillary acidic protein (GFAP) can differentiate MCI due to Lewy bodies from healthy controls (Hamilton et al, 2023)

Includes BID and TID treated patients in all analyses

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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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

- ✓ Completed private placement for aggregate gross proceeds of up to $149.4M from leading healthcare investors
- ❑ Complete enrollment in Phase 2b DLB study (2Q)
- ❑ Report data from placebo-controlled portion of Phase 2b DLB study (4Q)

1. Plasma ptau181 stratified results.

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 expected in 4Q24; 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

April 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 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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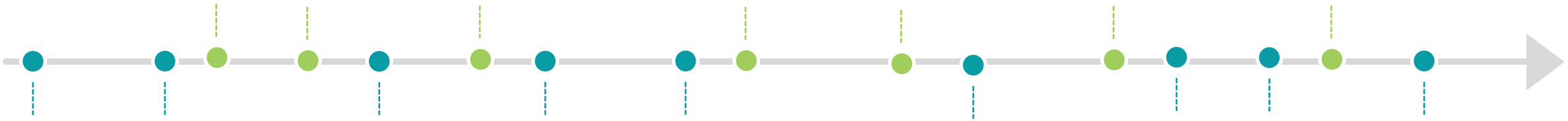
Published Translational Research has Played Major Role in Understanding Neflamapimod's Potential as a Disease-modifying Drug for DLB



July 2019 – August 2020
Conduct of Phase 2a Clinical Study

October 2020:
Presentation of first results of phase 2a study at CTAD

2020-2021:
Multiple publications showing that gait dysfunction in LBD is related to cholinergic system

June 2021:
Full Ts2 mouse data demonstrating neflamapimod treats cholinergic dysfunction and degeneration, and restores function available

May 2021:
Publication that plasma ptau can identify patients with AD co-pathology in DLB

August 2021:
Measurement of ptau181 levels in plasma of pre-treatment samples of phase 2a clinical study

Oct 2021, Feb 2022:
Separate publications demonstrating cholinergic degeneration is primary pathology in DLB (i.e, neurodegenerative process is initiated in the basal forebrain

Nov 2021:
At CTAD, presentation of ITT analysis showing effect on CDR-SB and TUG. Also, first presentation of ptau181 stratified analysis.

2021 - 2023:
Multiple studies correlating plasma ptau levels to cognitive decline and extent of neurodegeneration in both AD and DLB

September 2022:
Publication of preclinical data and primary analysis of phase 2a clinical study in *Nature Communications*, that together demonstrates neflamapimod has positive effect on cholinergic degeneration and dysfunction

2021 - 2022:
Multiple studies correlating basal forebrain atrophy by MRI to cognitive decline and pathology at autopsy in both AD and DLB

Oct-Nov 2022:
Analysis of MRII images of a previously conducted study in Early AD indicates neflamapimod appears to increase basal forebrain volume and its functional connectivity

2022 - 2024:
Additional studies confirming utility of plasma ptau181 to identify tau pathology in patients with DLB

October 2023:
Publication of ptau181 stratified analysis in the journal *Neurology*

July 2023/Jan 2024:
Separate publications indicate GFAP may be plasma biomarker of the underlying disease process in pure DLB

November 2023-March 2024:
Analysis of GFAP levels in plasma from phase 2a study demonstrates positive effect of neflamapimod on this biomarker. Presented at AD/PD meeting in March '24

Disease Understanding Event

Neflamapimod Data Event

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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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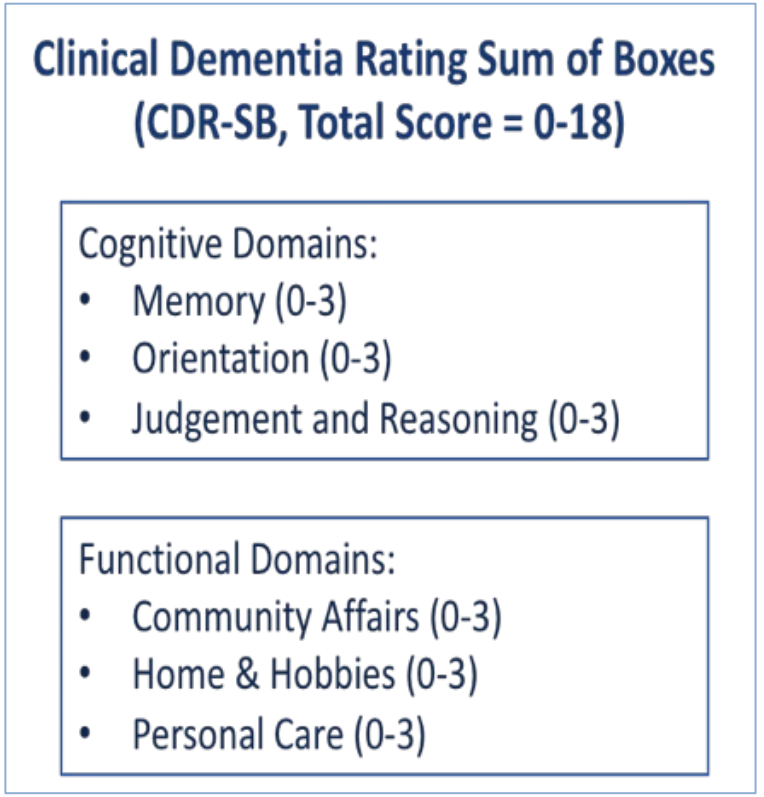
Performance of Clinical Endpoints in Phase 2a

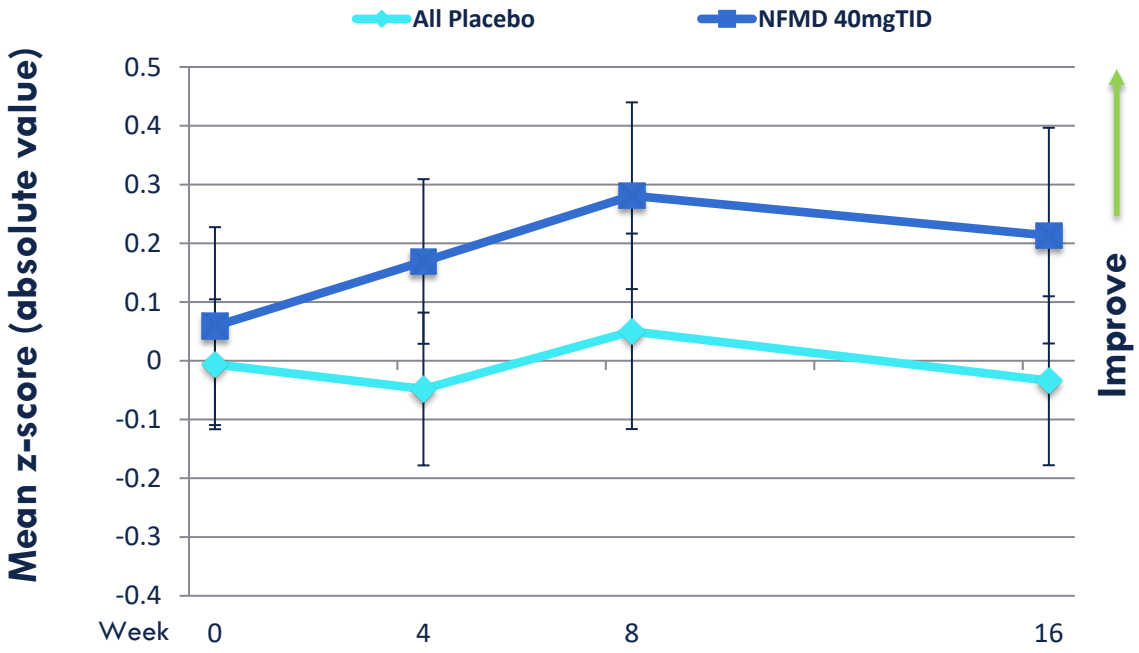
- Clinical endpoints that can detect effects on both cognition and function (specifically, CDR-SB and TUG) performed better in DLB with respect to detecting improvement over placebo than endpoints purely focused on evaluating cognition
- Performance of Neuropsychological Test Battery (NTB, six-test cognitive 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



1. McKeith, *Neurology*, 2017)

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

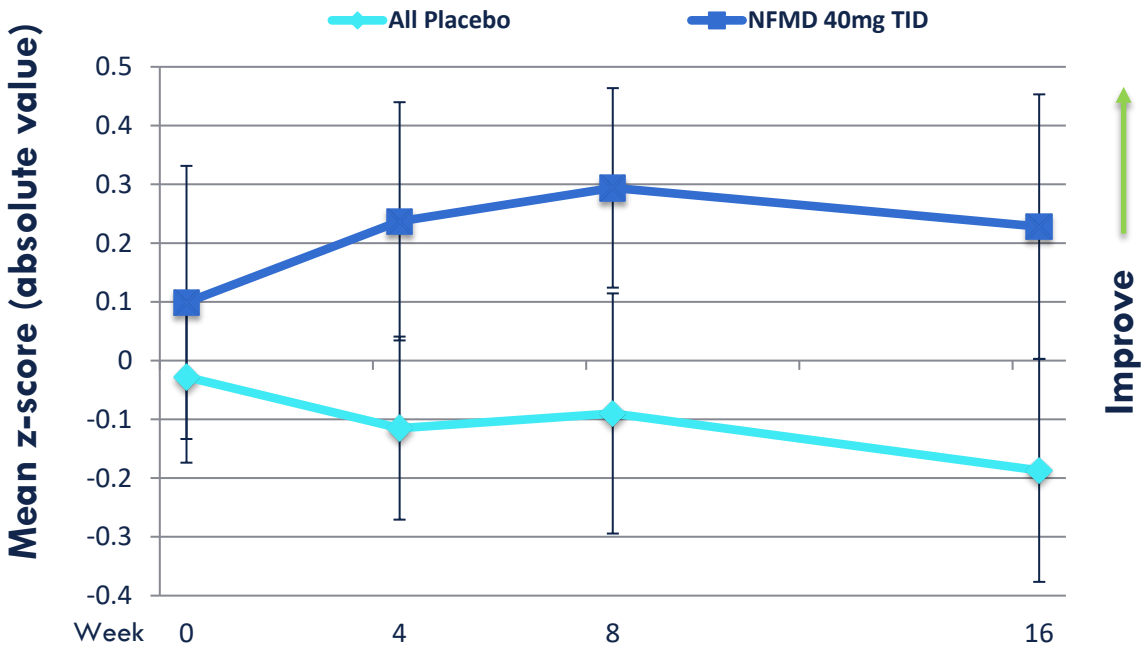
Neuropsychological Test Battery (NTB) Composite



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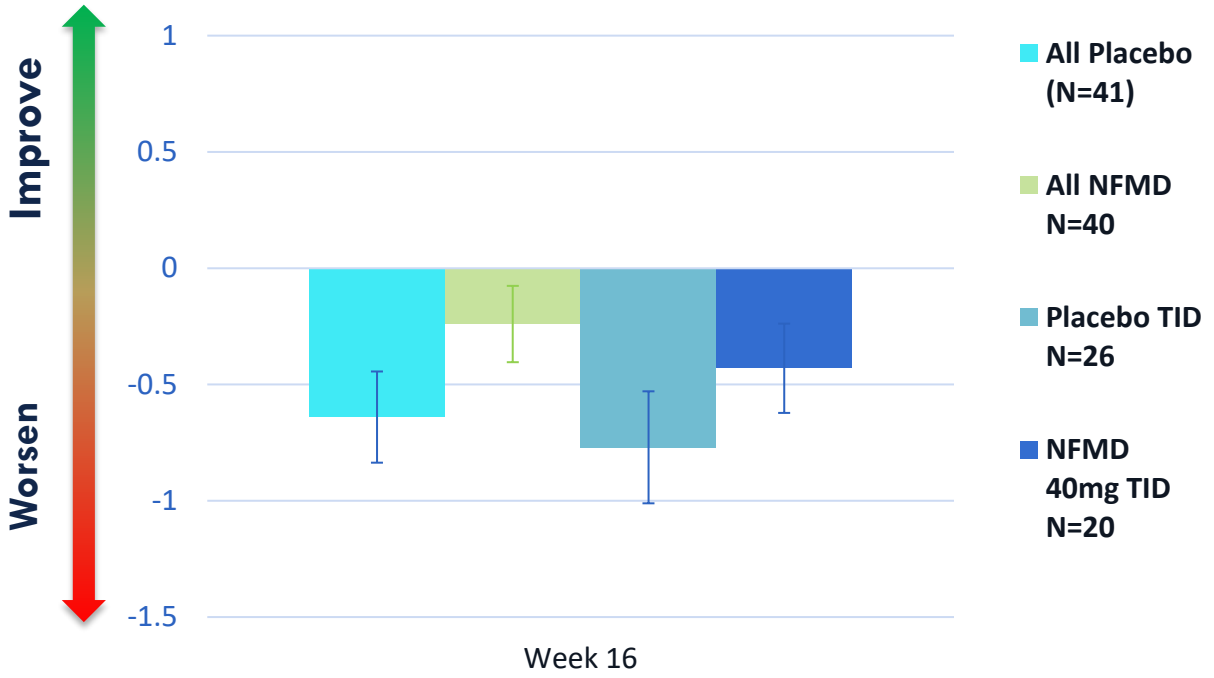
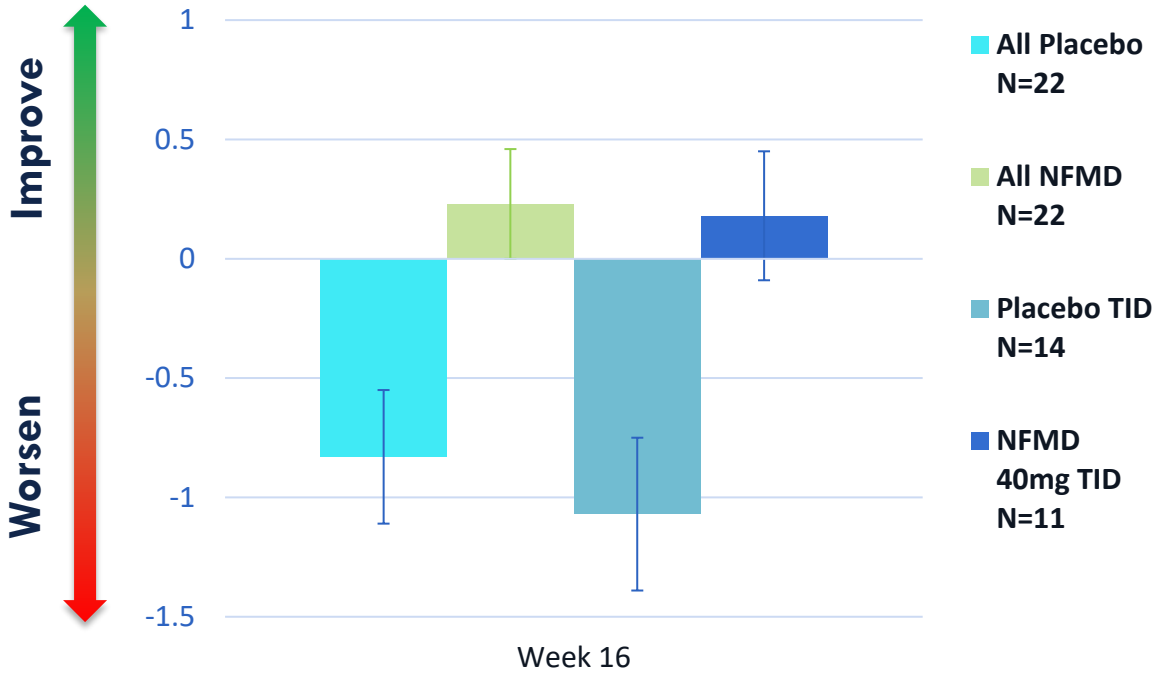
Neflamapimod Treatment in Patients with DLB Demonstrated Substantial Effect on Change from Baseline in CDR-SB in Phase 2a

Overall Patient Population



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



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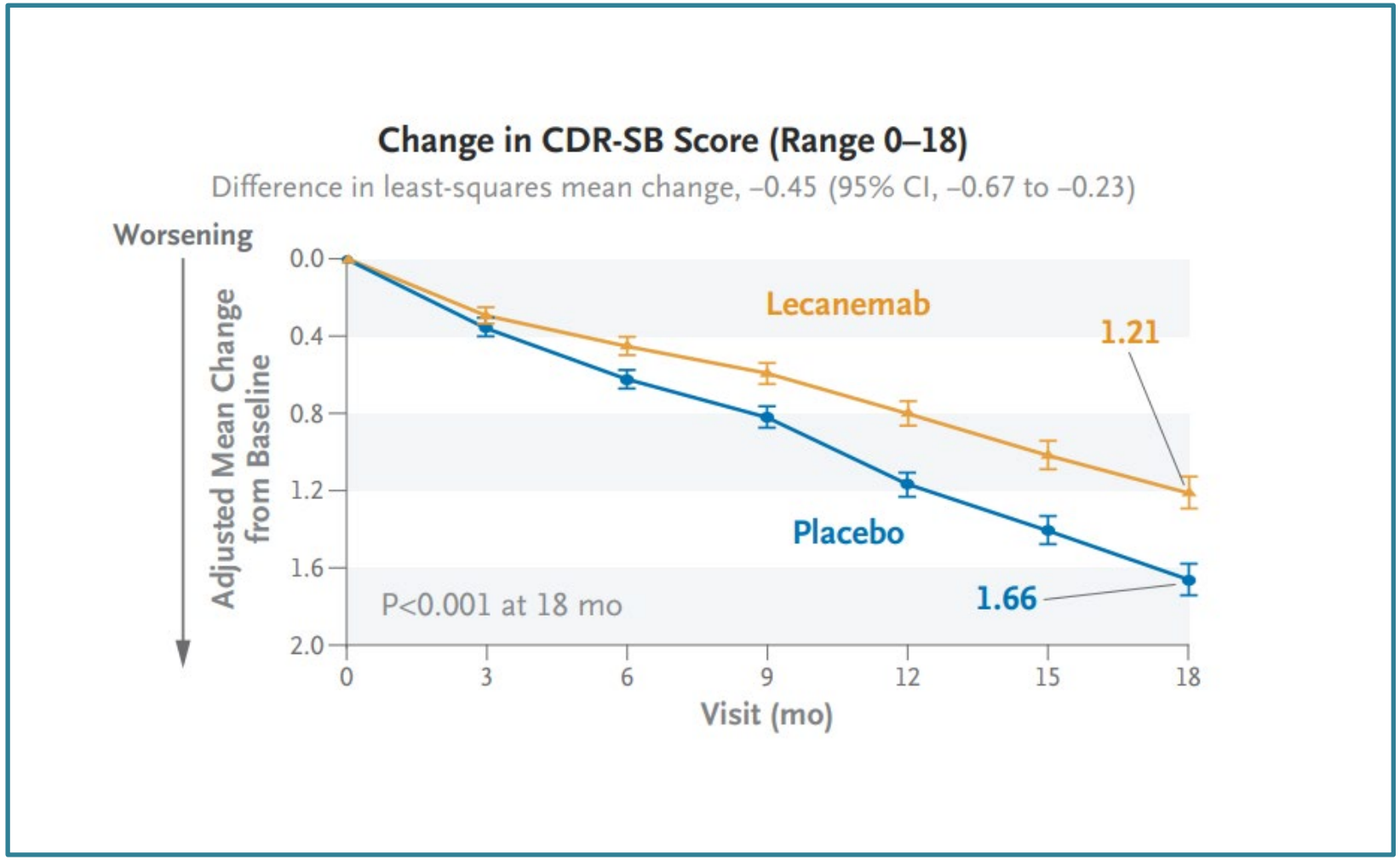
Lecanemab Effects on CDR-SB in Phase 3 Trial for Patients with Early AD



van Dyck CH et al. *New England Journal of Medicine*, 2023
DOI: 10.1056/NEJMoa2212948

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International Shopping List Test

12 words associated with grocery shopping provided verbally, and subject asked to recall ask many words as possible

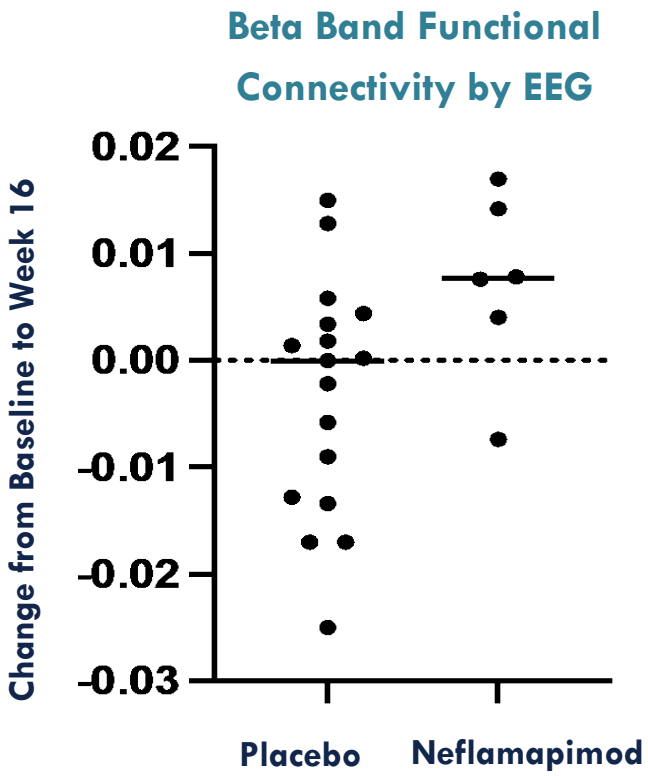
- **Total Score (0-36):** Combined score of three consecutive trials immediately following provision of words.
- **Delayed Recall Score (0-12):** Number of words recalled when subject is asked 20-25 minutes after initial trials to recall as many of the words originally provided.
- **Recognition Scores (0-12):** Number of true positives correctly identified when presented with the original 12 words (true positives) and 12 words not originally presented (false positives).

Potential DLB-Specific EEG Effect of Neflamapimod Treatment Identified in Phase 2a

Task-free, eyes-closed EEG recordings were to be performed at Baseline and Week 16. Due to restrictions on clinical research activities imposed by COVID-19, week 16 EEG assessments were available in approximately one-third the patients

Despite limited numbers, neflamapimod was demonstrated to significantly improve, vs. placebo, Functional Connectivity (AeCC) in the beta band (13-30 Hz)

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



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

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

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

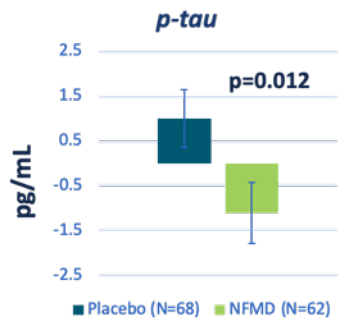
161 patients with CSF-biomarker (Ab42, ptau181) confirmed AD randomized to neflamapimod 40mg BID or placebo for 24 weeks

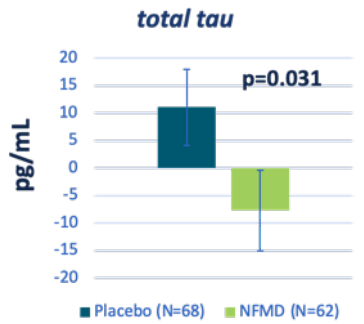
Significant effect vs. placebo on CSF markers of disease progression (ptau, total tau)

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

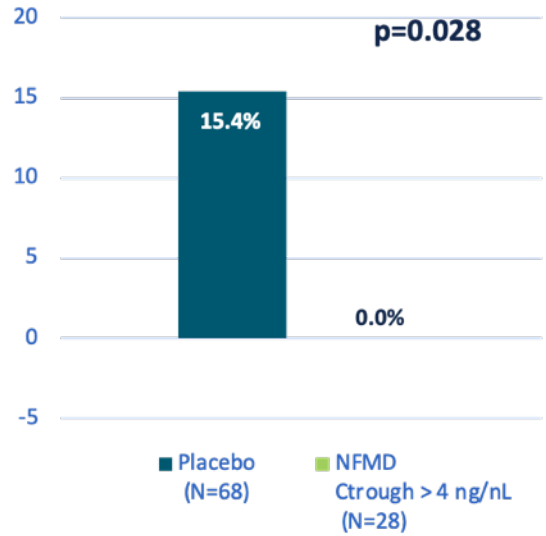
Suggests 40mg TID or 80mg BID would slow disease progression

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

Roadmap to Success: Planned Phase 3 Study

AscenD-LB

91-patient, 16-week placebo-controlled study

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
- ✓ Significant positive effects on EEG and plasma GFAP
- ✓ Results most prominent in patients with pure DLB

RewinD-LB

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

Phase 3 Study Design

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