



CERVOMED

Medicines for the Brain

The Opportunity in Dementia with Lewy Bodies (DLB) for Neflamapimod

June 2025

NASDAQ: CRVO

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What is the average time from diagnosis of DLB to requiring nursing home care?

A. 2 years

B. 4 years

C. 6 years

D. 8 years

Dementia with Lewy Bodies (DLB) is a High-Value, Untapped Opportunity



DLB represents a large, accessible patient population with no approved treatments to date

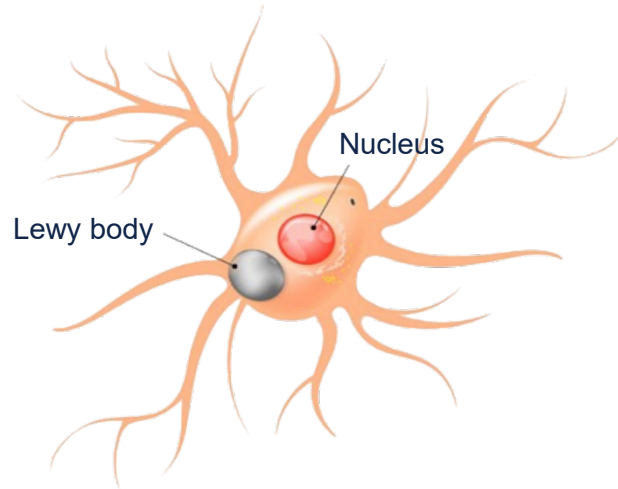


Ongoing research has provided clear insights on the molecular mechanisms of DLB, paving the way for the first effective treatments



DLB is a distinct dementia that progresses rapidly, and provides a straightforward path for pivotal development and approval based on gold standard clinical endpoints

New Insights Underscore Potential to Develop Disease-Modifying Medicines for DLB

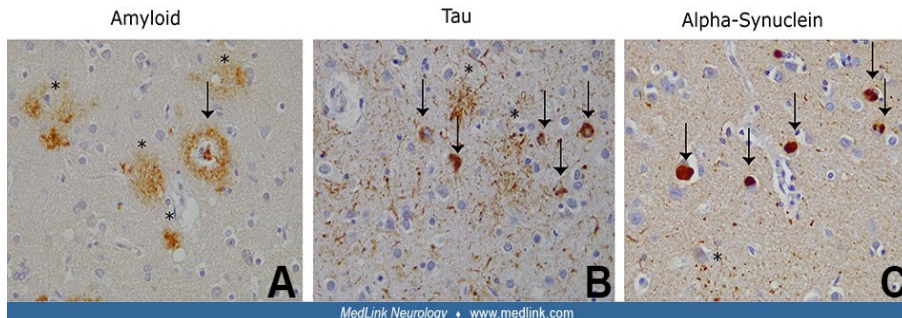


DLB is a Distinct Dementia

- DLB associated with abnormal deposits (“Lewy bodies”) within neurons of a protein called alpha-synuclein in the brain.
- About 50% of DLB patients have “pure” DLB
 - Absence of biomarker evidence of Alzheimer’s disease (AD) related co-pathology (amyloid/or tau)
 - Limited neuronal death and loss, particularly in the hippocampus
- Major driver of clinical progression in pure DLB is disease in basal forebrain cholinergic system (vs. in the hippocampus for AD)

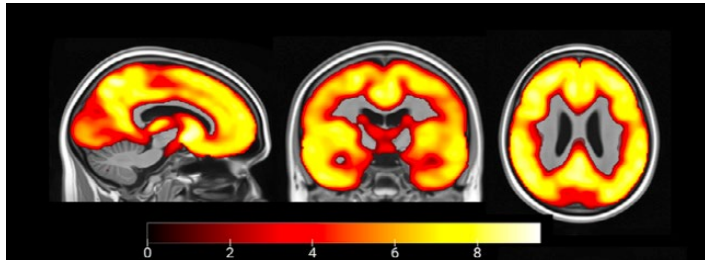
Drug Development Opportunity in Pure DLB

- Rapid clinical progression that in the absence of concomitant AD co-pathology is driven by synaptic dysfunction in the cholinergic system, rather than neuronal loss
- Therapy that effectively treats synaptic dysfunction can lead to significant clinical effects in pure DLB that can be demonstrated in 3-6 months duration clinical trials

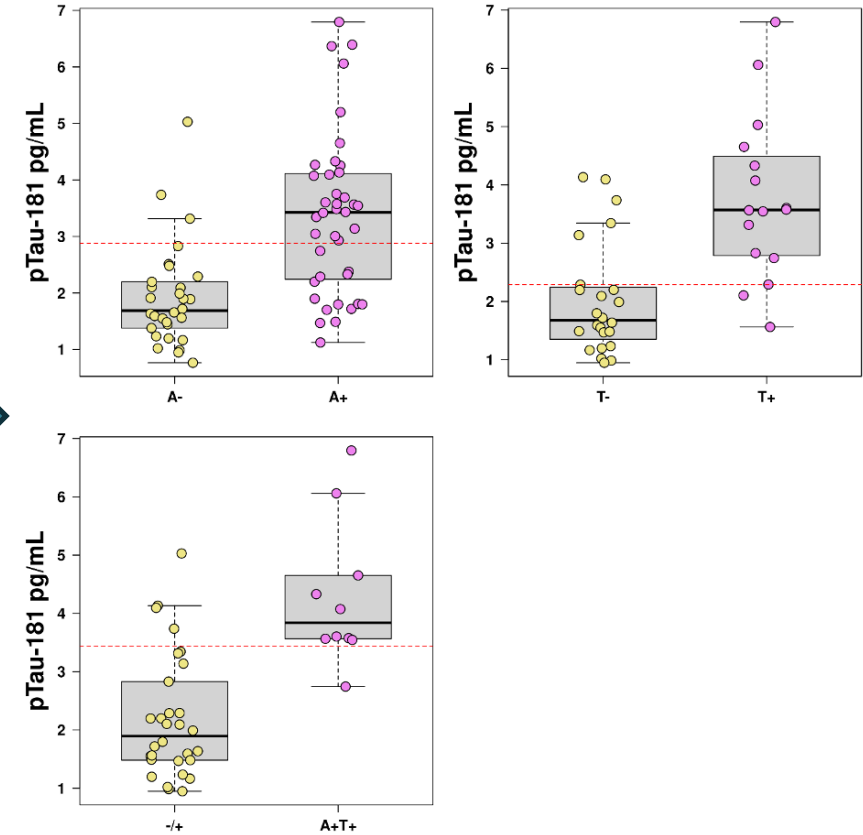
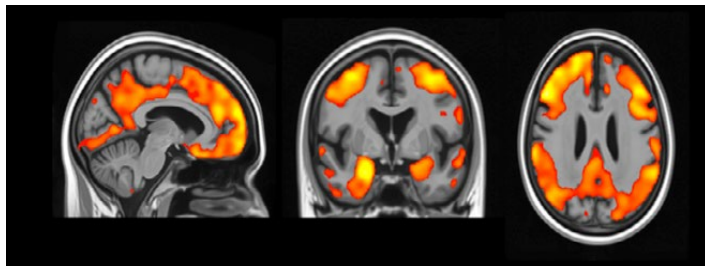


Plasma Levels of Phosphorylated Tau Can Identify and Exclude Patients with AD Co-Pathology in Clinical Trials

Amyloid PET Scan

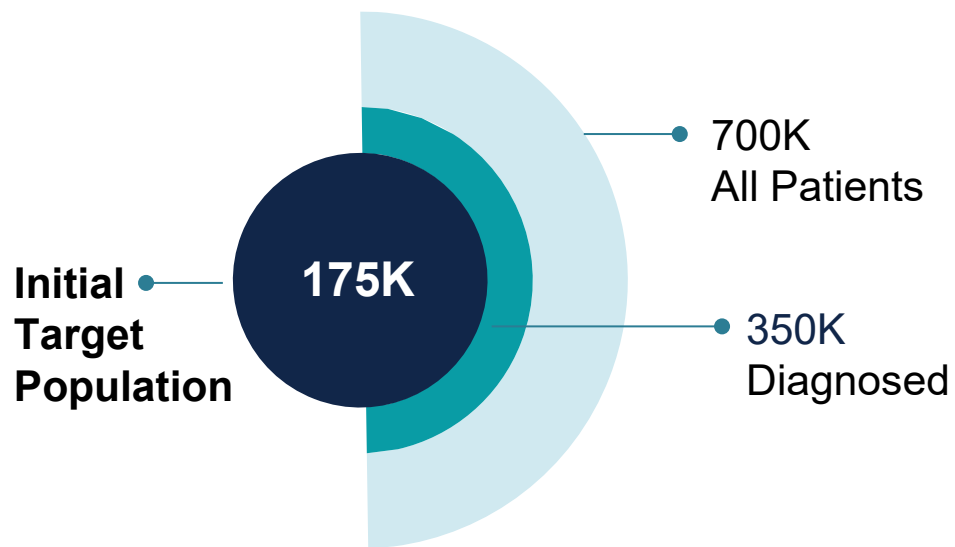


Tau PET Scan



DLB Without Alzheimer's Disease Related Co-Pathology is a Rare and Valuable Commercial Opportunity

Multi-Billion Dollar US Market Opportunity



- 175,000 US patients with DLB, no AD co-pathology, and under medical care
- DLB is a specialty disease with high unmet medical need

Treatment Landscape

- Acetylcholinesterase inhibitors are the mainstay of treatment
 - Provide transient improvement in cognition, but no improvement in motor function
- There are no therapies that target the underlying disease process
- Patients are generally managed by neurologists



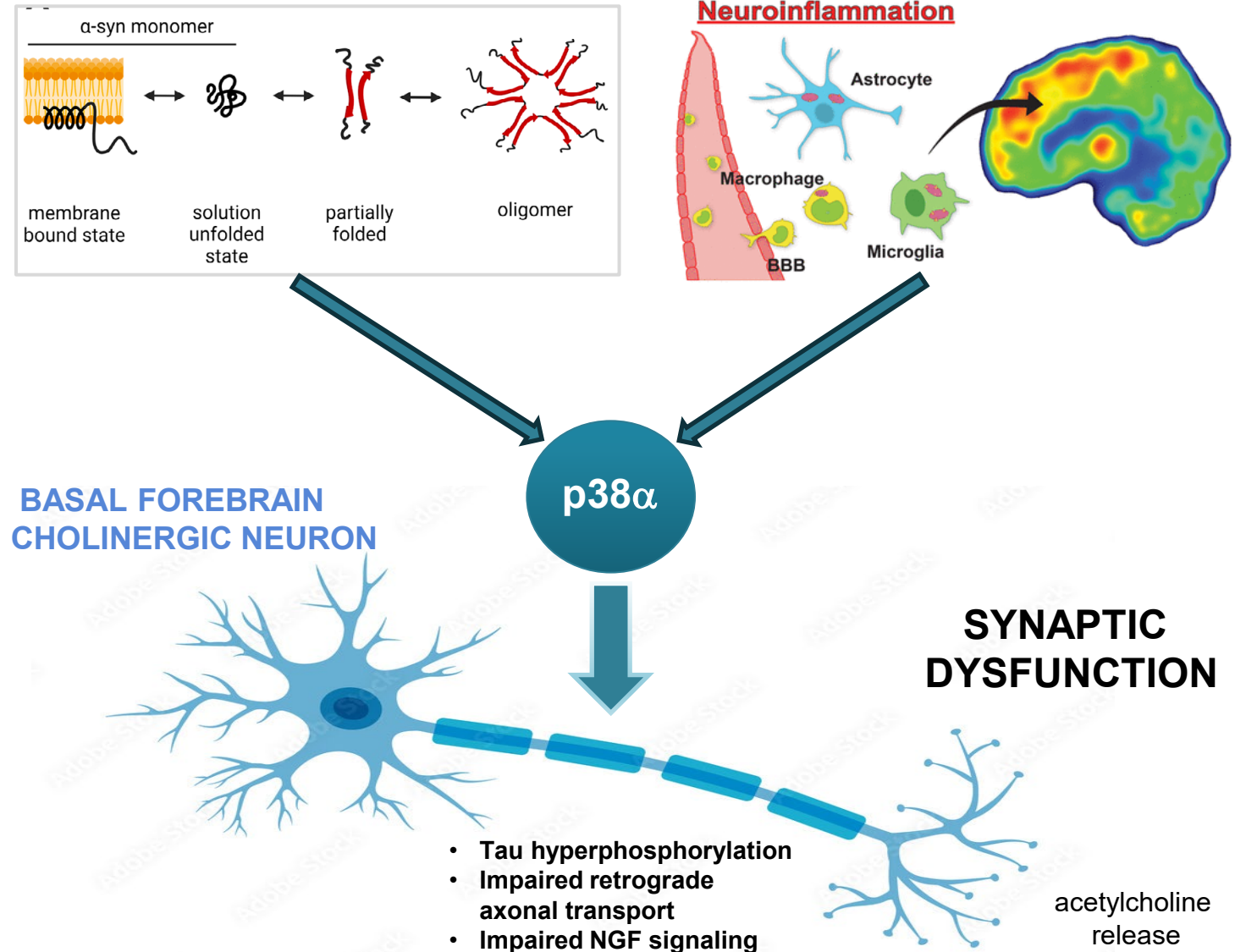
Neflamapimod: Targeting Neuroinflammation Driven Synaptic Dysfunction

- **Oral small molecule inhibitor of alpha isoform of p38 MAP kinase (p38 α kinase)**
 - Potent (<10nM IC50), highly selective
 - Blood-brain-barrier penetrant with brain:plasma ratio of ~2
- **Safety profile well defined**
 - Chronic, repeat dose toxicology studies completed
 - At dose of 40mg TID in humans, 10-fold safety margin to No-adverse effect level in long-term toxicology studies
 - Clinical safety data in >500 volunteers and patients
- **Target engagement demonstrated in phase 2 studies in Alzheimer's disease (AD)**
 - Reduction in CSF levels of IL-8 (marker of IL-1 β signaling)
 - Reduction in CSF levels of phosphorylated tau and total tau
 - Increase in volume of basal forebrain and its functional connectivity by MRI
- **Clinical Proof-of-concept demonstrated in Phase 2b trial in patients with Dementia with Lewy Bodies without AD Co-Pathology**



Scientific Rationale for Targeting P38 α for DLB

- **P38 α is a highly validated target for neurodegeneration, with major roles in^{1,2}:**
 - Neuroinflammatory response^{3,4}
 - Tau hyper-phosphorylation^{5,6}
 - Axonal transport impairment⁷
- **DLB specific rationale, with P38 α mediating:**
 - Neuroinflammation induced basal forebrain cholinergic dysfunction⁸⁻¹⁰
 - Rab5 mediated dysfunction and degeneration of cholinergic neurons^{11,12}
 - Neurotoxicity of α -synuclein^{13,14}



Preclinical and Clinical Results Prior to Phase 2b Clinical Trial

Preclinical

Disease processes in basal forebrain reversed

When administered in mice that develop basal forebrain cholinergic degeneration, neflamapimod:

- ✓ Reduced Rab5 activity and tau phosphorylation
- ✓ Reversed loss of cholinergic (ChaT+) neurons in the basal forebrain; and
- ✓ Normalized performance in behavioral tests of cholinergic function²

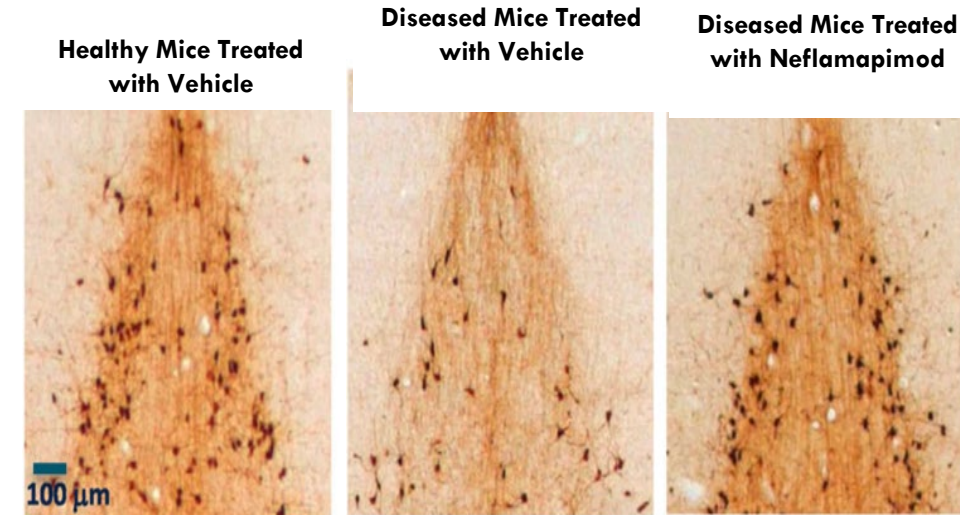
Clinical

Improvement on multiple clinical endpoints in Phase 2a trial

In AscenD-LB, a 91-patient, 16-week, placebo-controlled Phase 2a trial in patients with DLB, neflamapimod:

- ✓ Significantly improved dementia severity (assessed by Clinical Dementia Rating Sum-of-Boxes, CDR-SB, $p=0.023$ vs. placebo)
- ✓ Significantly improved gait (assessed by Timed Up and Go, TUG, $p=0.044$ vs. placebo)
- ✓ Reduced levels of plasma biomarker of neurodegeneration (glial fibrillary acidic protein (GFAP))
- ✓ Results most prominent in patients without AD Co-Pathology (i.e., as measured by levels in blood of phosphorylated tau)

Cholinergic neurons in basal forebrain



Cholinergic neurons identified by staining for choline acetyl transferase expression

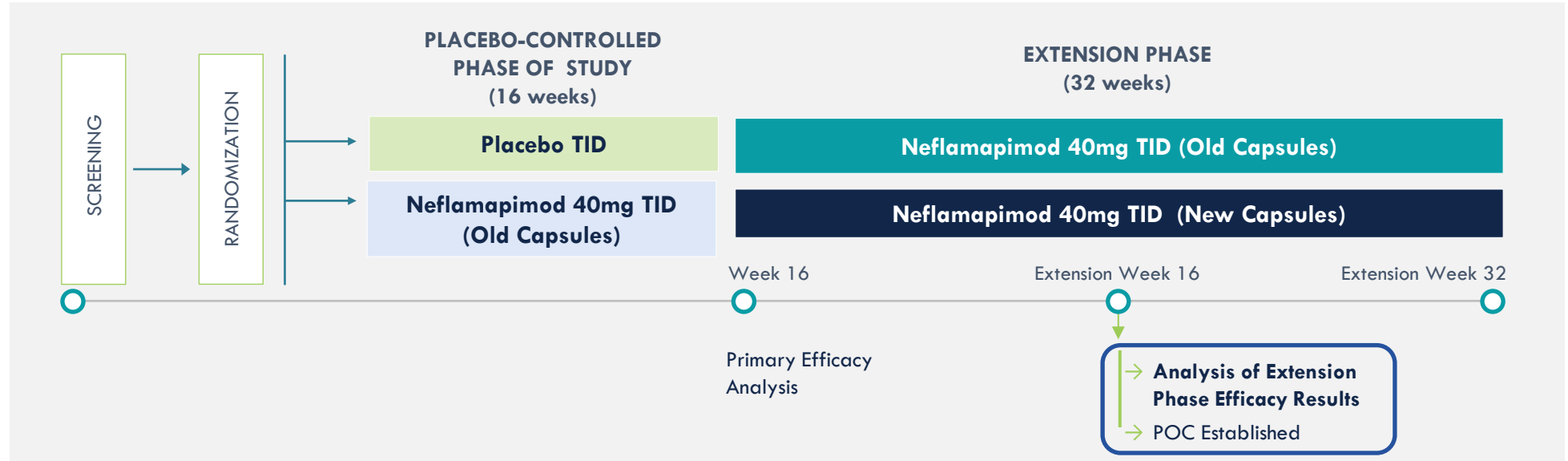
RewinD-LB Phase 2b Study in DLB: Design and Conduct

PATIENTS

- 159 patients with dementia with Lewy bodies by consensus clinical criteria
- CDR global score of 0.5 or 1.0 at baseline
- Without AD Co-Pathology (assessed by plasma phospho-tau)

SELECTED KEY CLINICAL OUTCOME MEASURES

- **Primary:** Clinical Dementia Rating Sum of Boxes (CDR-SB)
- **Secondary:**
 - Clinical Global Impression of Change (CGIC)



Dosing Groups and Comparisons

- Pharmacokinetic measurements in the placebo-controlled phase, in which only Old Capsules were utilized, showed that expected plasma neflamapimod concentrations were not achieved during the first 16 weeks of the study.
- With introduction during the Extension Phase of a new batch of capsules that achieved the targeted plasma drug concentrations, the effects of neflamapimod with New Capsules (N=94; active drug arm) could be compared against outcomes in participants who continued to receive Old Capsules (N=55; control arm).

In Phase 2b, Clear Benefit Seen Across Primary Endpoint and Multiple Other Clinical Endpoints During Extension Phase



CDR-SB

- Global measure of cognition that is commonly used as a primary endpoint in studies of dementia
- Phase 2b results showed a clear and clinically meaningful benefit in CDR-SB for Neflamapimod in DLB ($p < 0.001$ vs. Old Capsules).



ADCS CGIC

- Clinical global impression of change is complementary endpoint that helps to confirm if treatment effects are clinically meaningful.
- Phase 2b showed a rapid and clear improvement in CGIC compared to Old Capsules ($p = 0.03$) or placebo ($p = 0.04$)



Other Endpoints

- In Phase 2b, neflamapimod also showed significant improvements in secondary and exploratory endpoints--including **fluctuations, working memory, and incidence of falls**--demonstrating consistency and breadth of clinical benefit.

Relevant CDR-SB Domain Scores in Early-Stage DLB



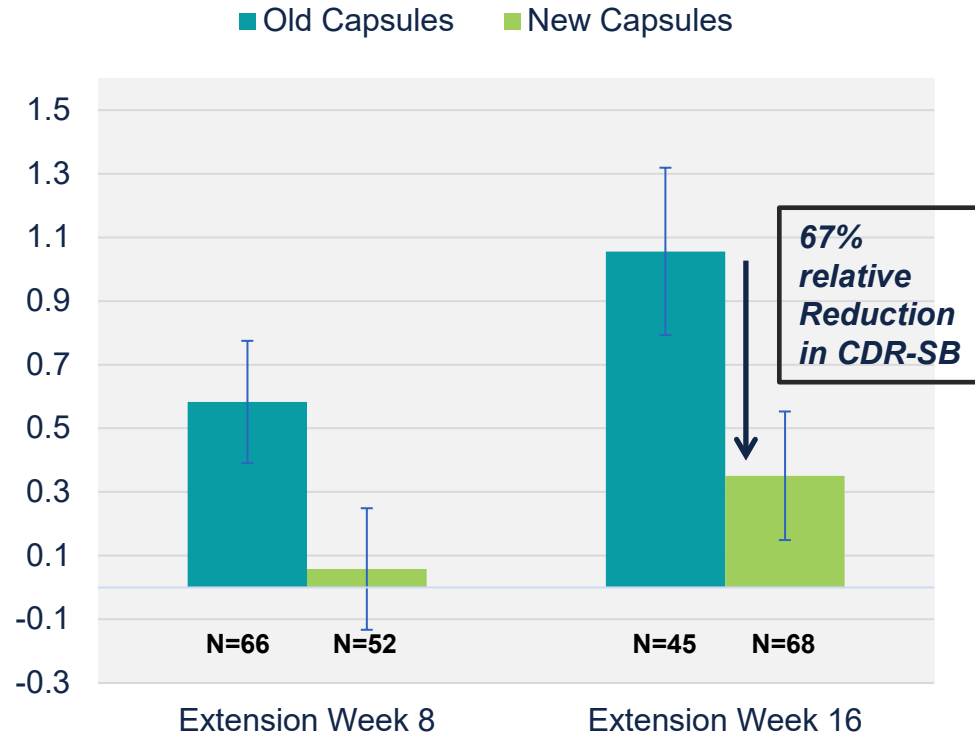
Construct of CDR-SB is such that **≥ 0.5 Change is Inherently Clinically Meaningful**

Score	Judgement & Reasoning	Community Affairs	Home and Hobbies	Personal Care
0.0	Solves everyday problems & handles business & financial affairs well; judgment good in relation to past performance	Independent function at usual level in job, shopping, volunteer and social groups	Life at home, hobbies, and intellectual interests well maintained	Fully capable of self care
0.5	Slight impairment in solving problems, similarities, and differences	Slight impairment in these activities	Life at home, hobbies, and intellectual interests slightly impaired	Fully capable of self care
1.0	Moderate difficulty in handling problems, similarities, and differences; social judgment usually maintained	Unable to function independently at these activities although may still be engaged in some; appears normal to casual inspection	Mild but definite impairment of function at home; more difficult chores abandoned; more complicated hobbies and interests abandoned	Needs prompting

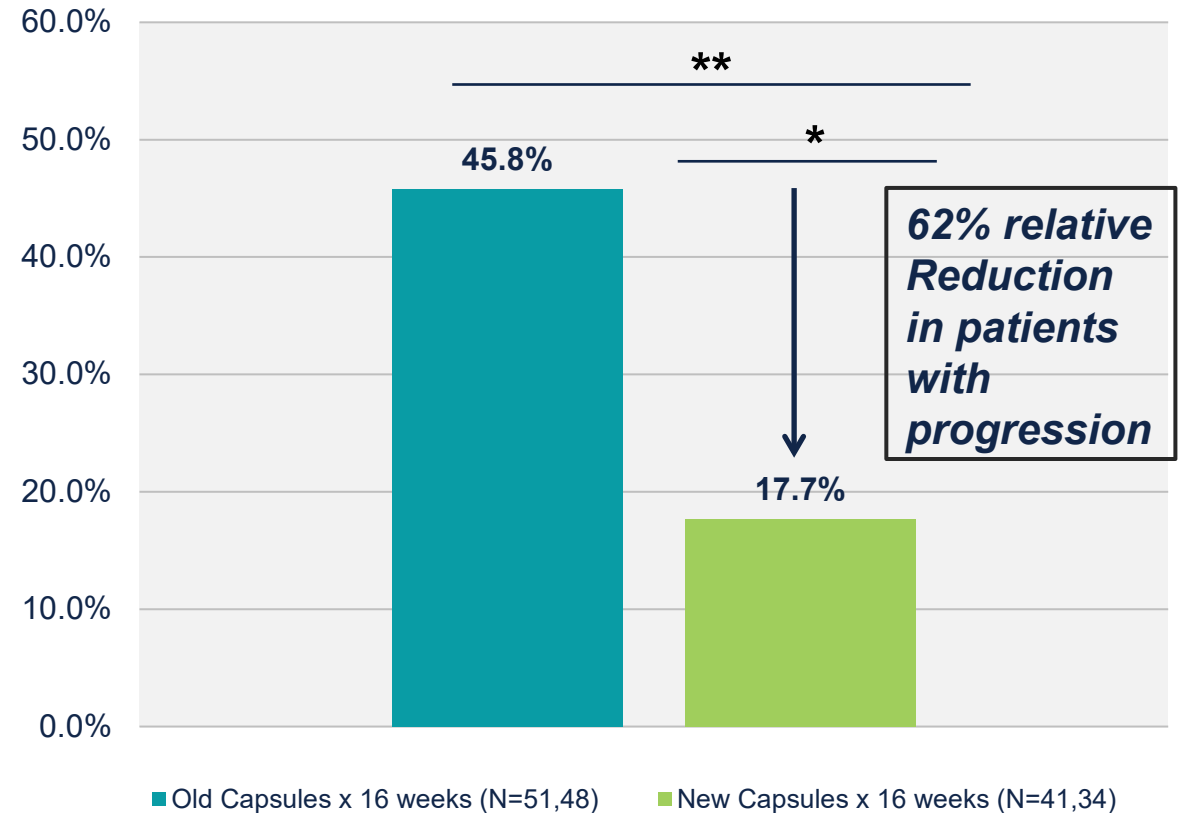
Significant Impact on Clinical Worsening in CDR-SB In DLB Patients Without AD Co-Pathology (ptau181 < 2.2 pg/mL)



Mean Increase (Worsening) in CDR-SB



Proportion with Progression (≥ 1.5-point increase in CDR-SB)



*p<0.05 **p=.001

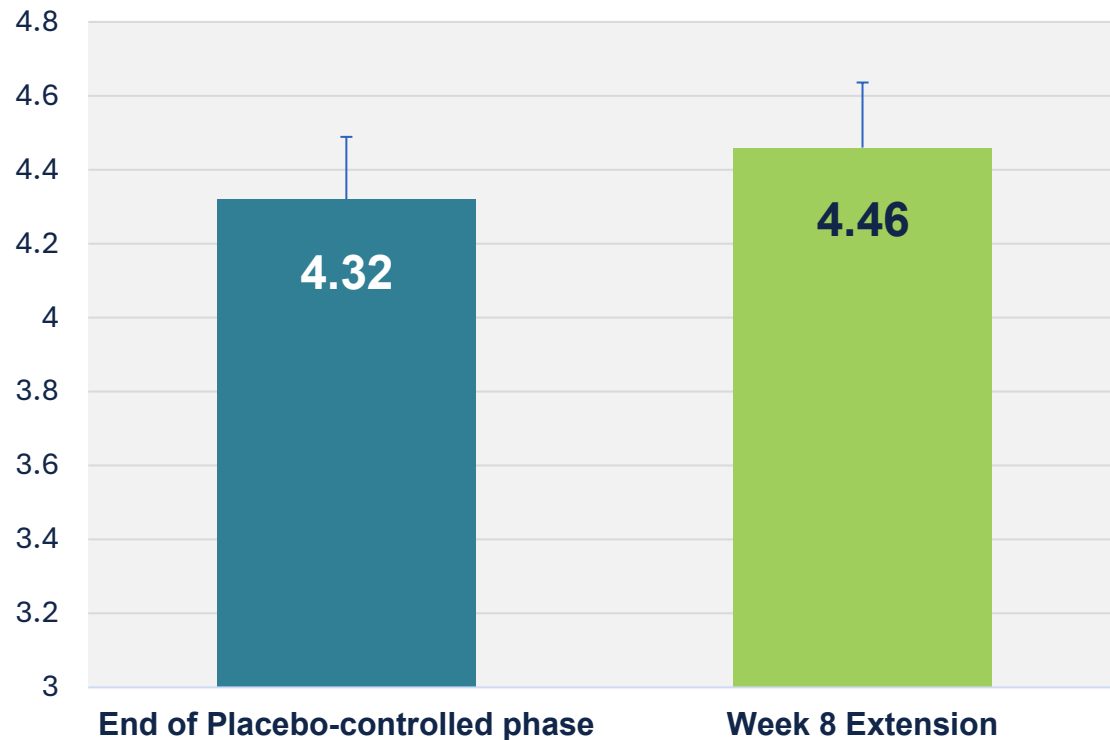
Primary Analysis¹: Average Difference* Over 16 Weeks

-0.81 (95% CI: -1.23, -0.39)	p<0.001
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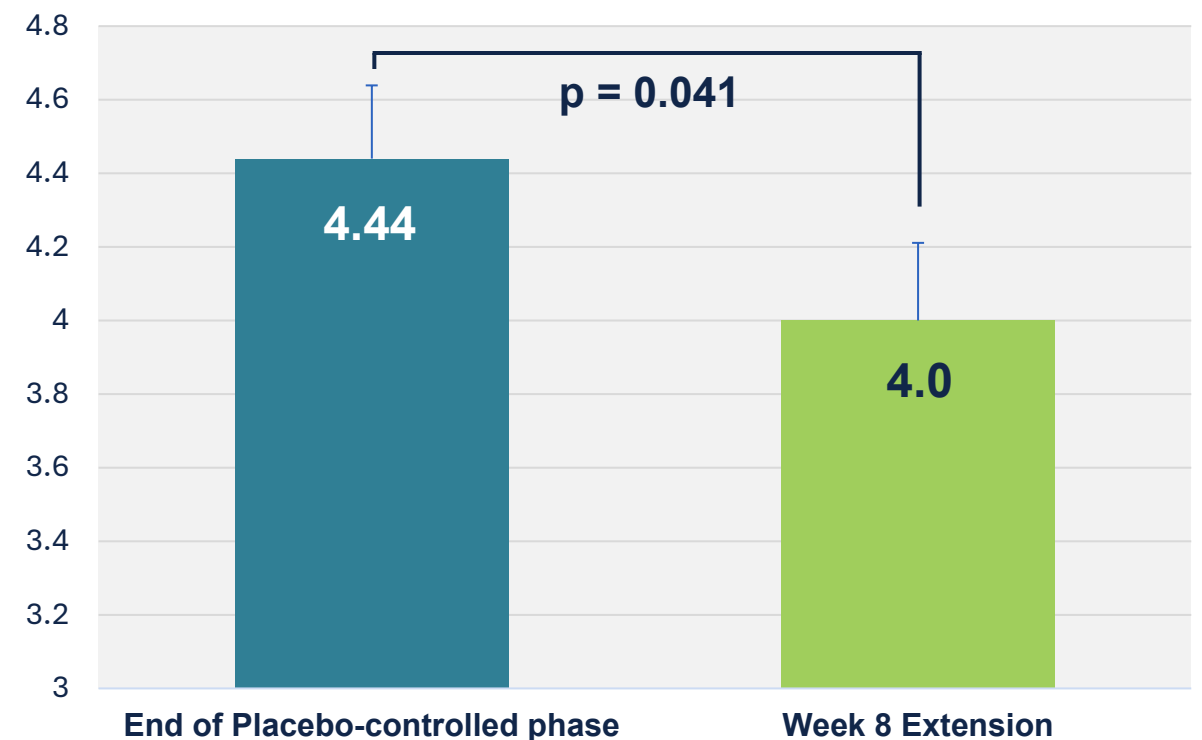
¹Linear Mixed-Effects Model for Repeated Measures (MMRM) with baseline CDR-SB, Sex, Age and MMSE as covariates
 *Negative indicates improvement; greater than 0.5 difference considered clinically significant (Tarawneh & Pankratz, Alz Res Ther, 2024)

ADCS-CGIC Within-participant Comparison in Participants Who Received Placebo in Initial Phase Also Demonstrates Clinical Significance

Participants who received placebo and then Old Capsules (N=37)



Participants who received placebo and then New Capsules (N=34)



Phase 2b Safety and Tolerability Summary



Neftamapimod was well-tolerated, with <4% rate of discontinuation due to adverse events in each of Initial Phase and Extension

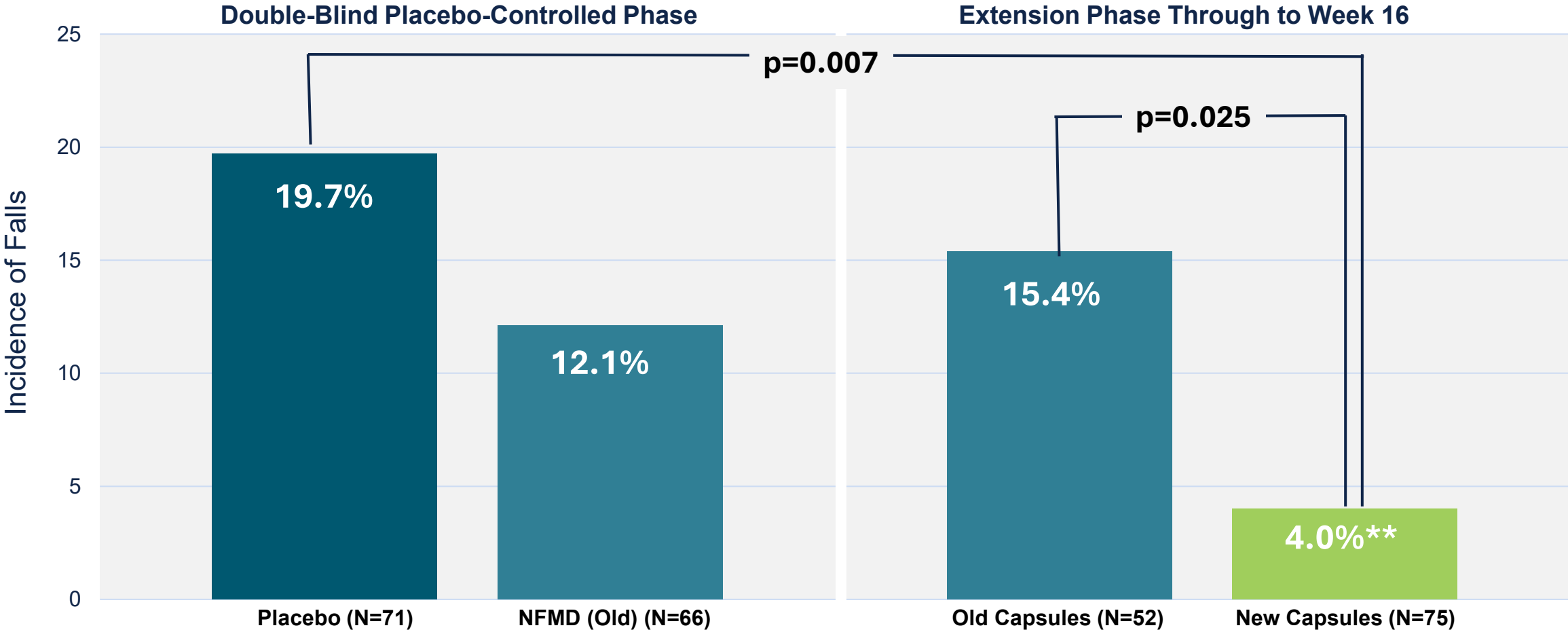


~90% of patients who entered the Extension Phase continued through to Week 16 of the Extension



Adverse events were typically mild, and similar to placebo, with the exception of falls which were significantly lower for patients receiving neftamapimod

Incidence of Falls Significantly Reduced in Participants with DLB without AD Co-Pathology (Screening Plasma ptau181 < 2.2 pg/mL)



Phase 2b Neflamapimod Summary



Neflamapimod has demonstrated proof-of-concept in DLB



Data across clinical endpoints demonstrates that neflamapimod slows the clinical progression of DLB



Cervomed will meet with global regulators to reach agreement on Phase 3 design, following the conclusion of the Extension Phase of the Phase 2b study

Projected Phase 3 Trial Design for Neflamapimod



KEY PARAMETERS

- DLB by consensus criteria and no AD co-pathology by plasma phospho-tau
- Primary Endpoint: CDR-SB
- Approximately 300 patients

- **Plan to initiate in mid-2026 Phase 3 study intended to support registration of neflamapimod**

Neflamapimod is a Substantially Derisked Asset Targeting an Untapped Multi-Billion Dollar Opportunity



DLB clinical progression is rapid; significant clinical effect observable in short-term studies



Phase 2b Positions Neflamapimod for Phase 3 Success

- Phase 3 will replicate patient population and clinical measures
- 24-week treatment duration in Phase 3 (vs. 16 weeks in Phase 2b)



High unmet need in DLB; Fast-Track Designation