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Medicines for the Brain

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

June 2025

NASDAQ: CRVO

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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 the Company, including, but not limited to: the therapeutic potential of neflamapimod; the anticipated timing and achievement of clinical and development milestones, potential discussions with regulatory authorities related to the Initial and Extension phases and clinical development of and approval process for neflamapimod; any other expected or implied benefits or results, including that any future clinical results observed with respect to neflamapimod in the Initial and Extension phases will be replicated in later studies; the design, costs and timing of the initiation of any phase 3 study or other additional clinical trials evaluating neflamapimod in DLB, including as a result of the Company's need to acquire sufficient funding therefor. Terms such as "believes," "estimates," "anticipates," "expects," "plans," "aims," "seeks," "intends," "may," "might," "could," "might," "will," "should," "approximately," "potential," "target," "project," "contemplate," "predict," "forecast," "continue," or other words that convey uncertainty of future events or outcomes (including the negative of these terms) 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 results of the Company's clinical trials, including RewinD-LB; the likelihood and timing of any regulatory approval of neflamapimod or the nature of any feedback the Company may receive from the FDA; the ability to implement business plans, forecasts, and other expectations in the future; general economic, political, business, industry, and market conditions, inflationary pressures, and geopolitical conflicts; and the other factors discussed under the heading "Risk Factors" in the Company's 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 press release speak only as of March 10, 2025 (or such earlier date as may be identified). The Company does not undertake any obligation to update such forward-looking statements to reflect events or circumstances after the date of this press release, except to the extent required by law.

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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

Rongve et al, Int J Geriatric Psychiatry, 2014

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

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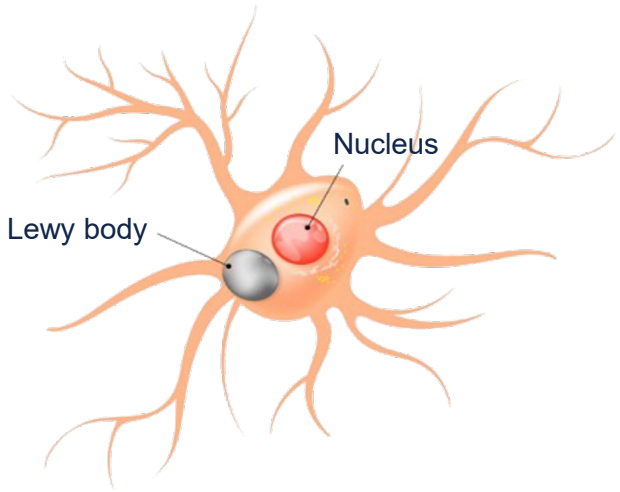
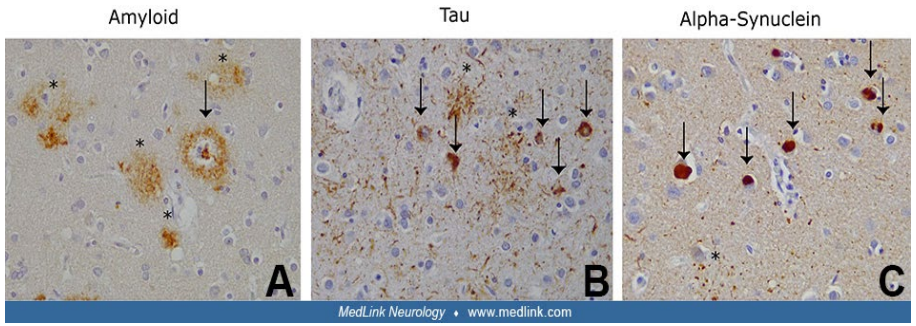
New Insights Underscore Potential to Develop Disease-Modifying Medicines for DLB





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**

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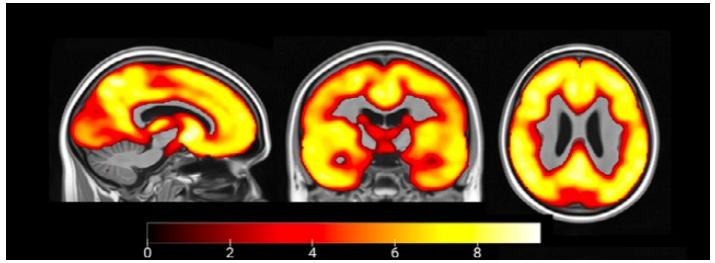
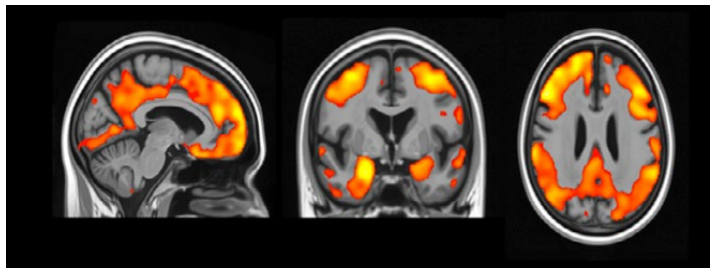
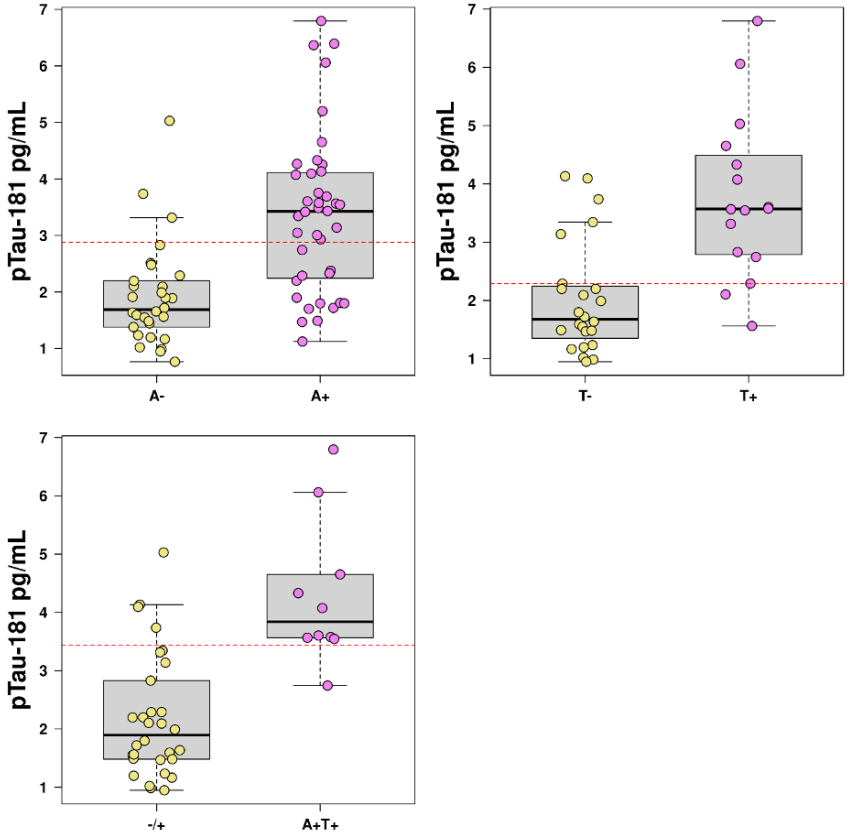
Plasma Levels of Phosphorylated Tau Can Identify and Exclude Patients with AD Co-Pathology in Clinical Trials

Amyloid PET Scan



Tau PET Scan





Diaz-Galvan et al, Alzheimer's & Dementia, 2023

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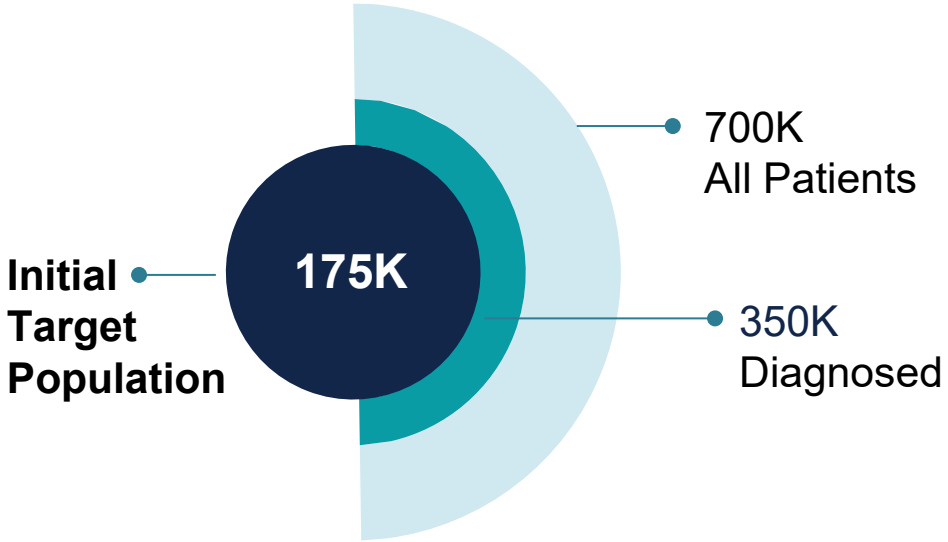
DLB Without Alzheimer's Disease Related Co-Pathology is a Rare and Valuable Commercial Opportunity

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

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Neflamapimod: Targeting Neuroinflammation Driven Synaptic Dysfunction

- **Oral small molecule inhibitor of alpha isoform of p38 MAP kinase (p38α 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-1β 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**

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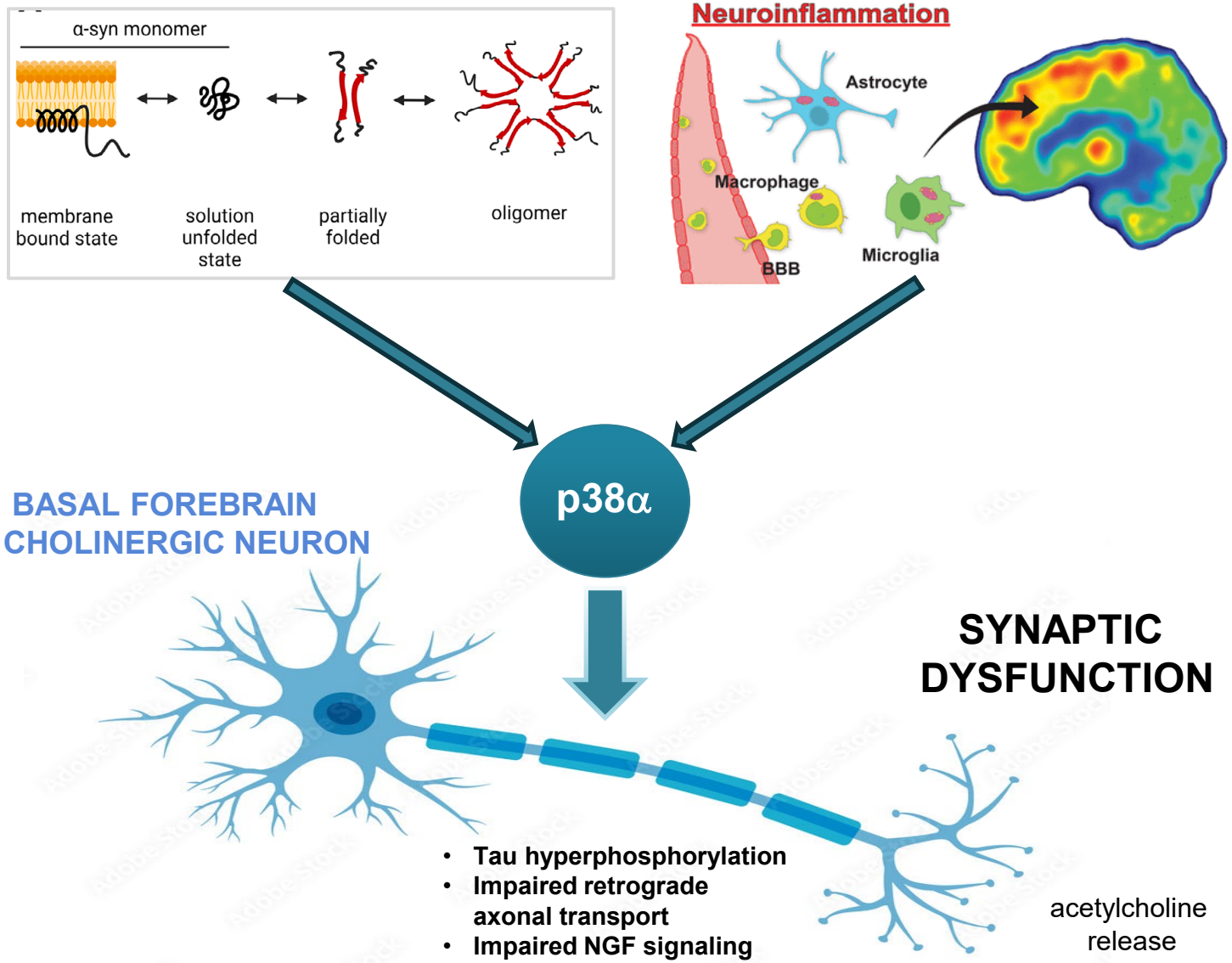
Scientific Rationale for Targeting P38α for DLB

- **P38α is a highly validated target for neurodegeneration, with major roles in[1,2]:**
  - Neuroinflammatory response[3,4]
  - Tau hyper-phosphorylation[5,6]
  - Axonal transport impairment[7]

- **DLB specific rationale, with P38α mediating:**
  - Neuroinflammation induced basal forebrain cholinergic dysfunction[8-10]
  - Rab5 mediated dysfunction and degeneration of cholinergic neurons[11,12]
  - Neurotoxicity of α-synuclein[13,14]



References: 1. Asih, 2020 2. Son I, 2023 3. Prieto, 2015 4. Yang , 2023 5. Stefanoska , 2022 6. Yeganeh, 2025 7. Gibbs, 2018 8. Scali 2003 9. Ehrlich, 2012 10. Gamage, 2023 11. Jiang, 2022 12. Alam & Nixon, 2023. 13. Borland, 2022 14. Yang, 2025

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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:

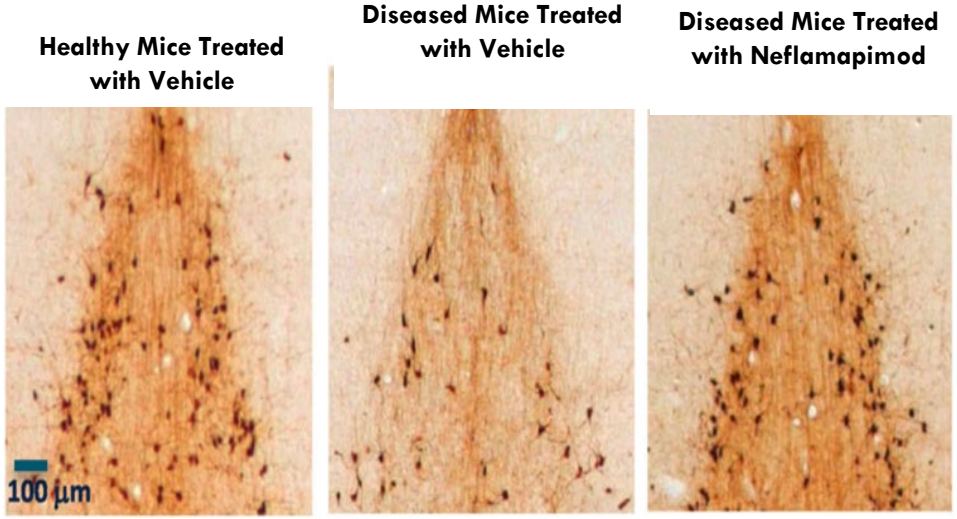
- ✓ Reduced Rab5 activity and tau phosphorylation
- ✓ Reversed loss of cholinergic (ChaT+) neurons in the basal forebrain; and
- ✓ Normalized performance in behavioral tests of cholinergic function[2]

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

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

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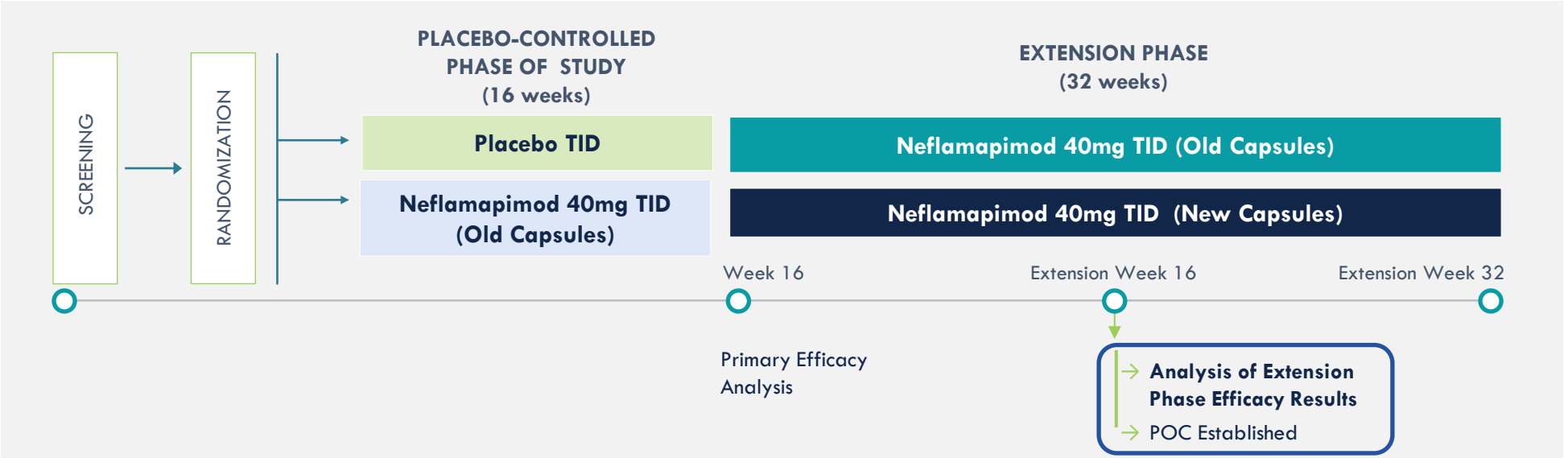
RewinD-LB Phase 2b Study in DLB: Design and Conduct

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.

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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

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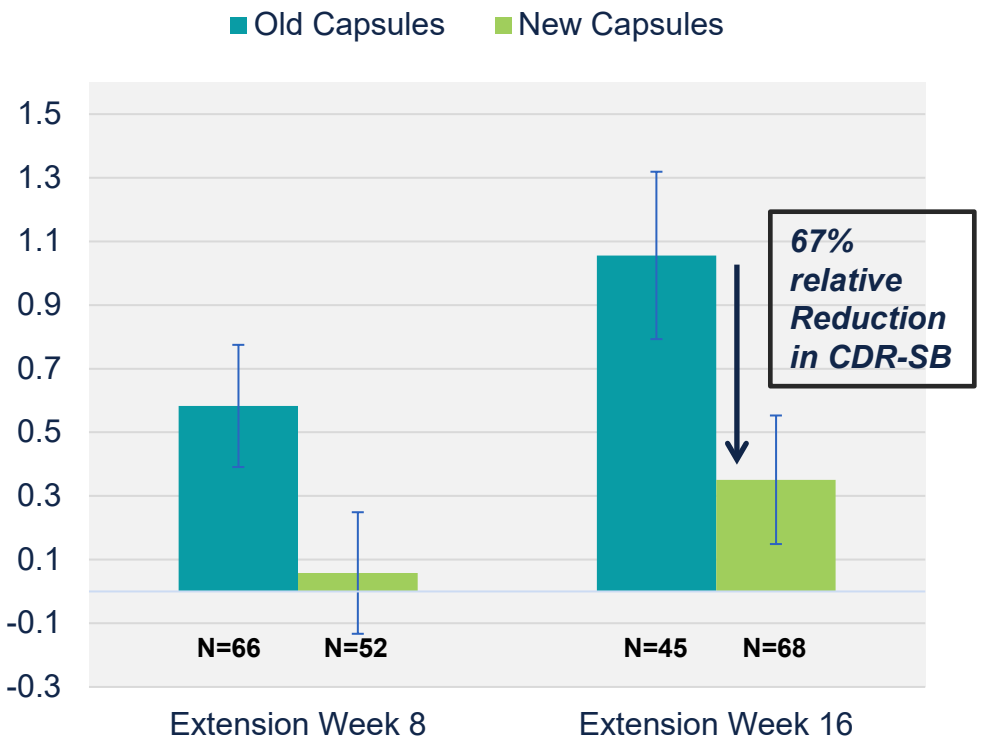
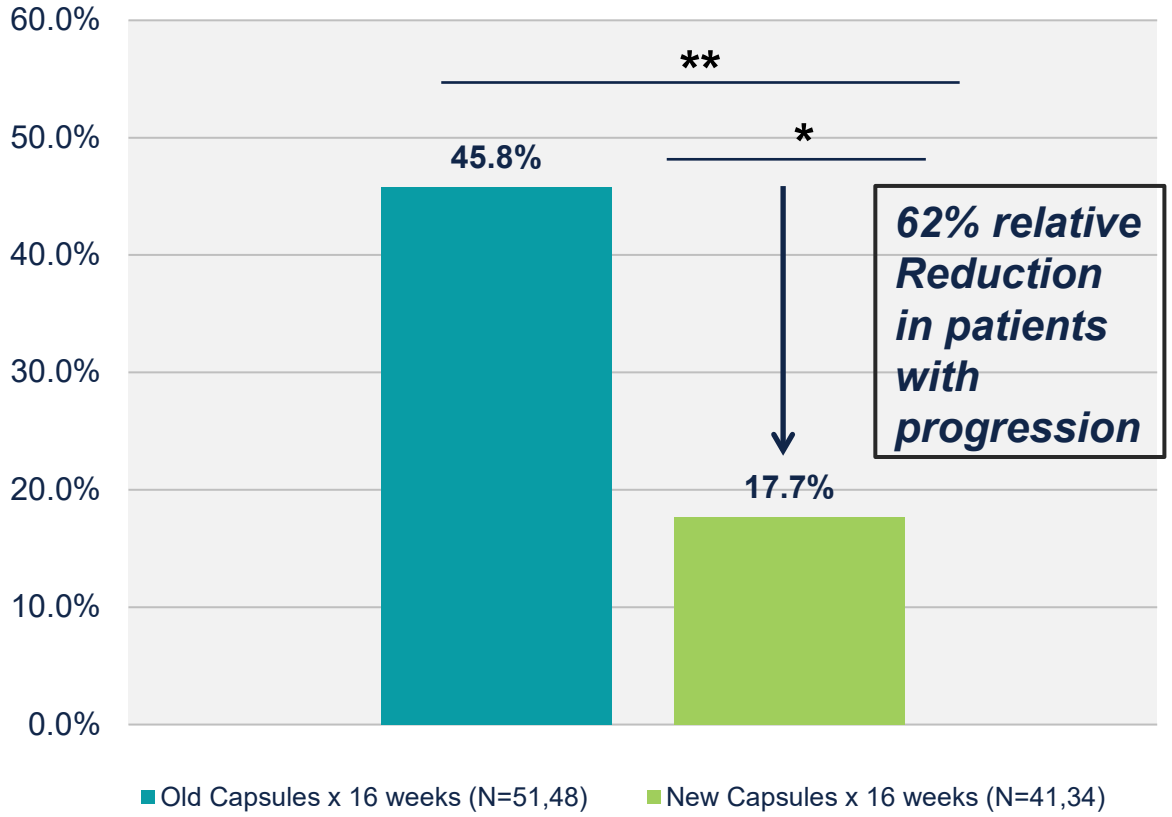
Significant Impact on Clinical Worsening in CDR-SB In DLB Patients Without AD Co-Pathology (ptau181 < 2.2 pg/mL)

RewinD-LB

Mean Increase (Worsening) in CDR-SB



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



*p<0.05 **p=.001

Primary Analysis[1]: Average Difference* Over 16 Weeks

-0.81 (95% CI: -1.23, -0.39)	p<0.001

[1]Linear 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)\

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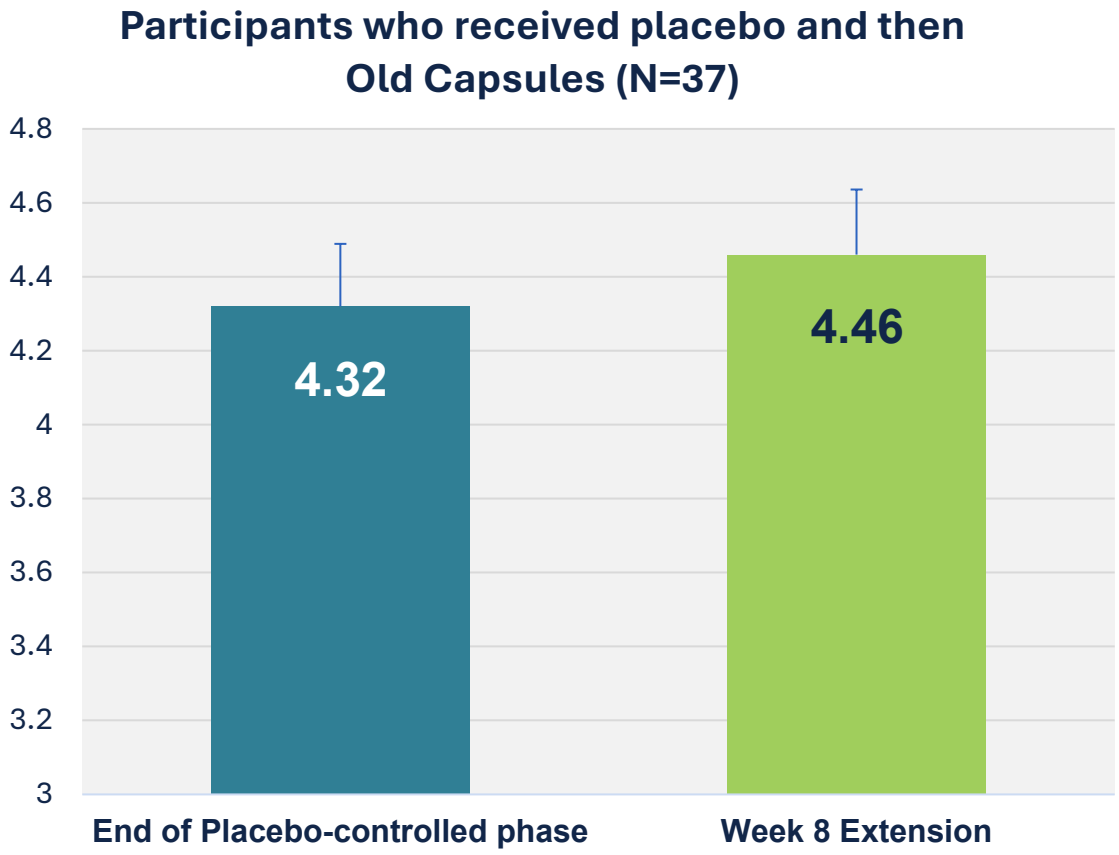
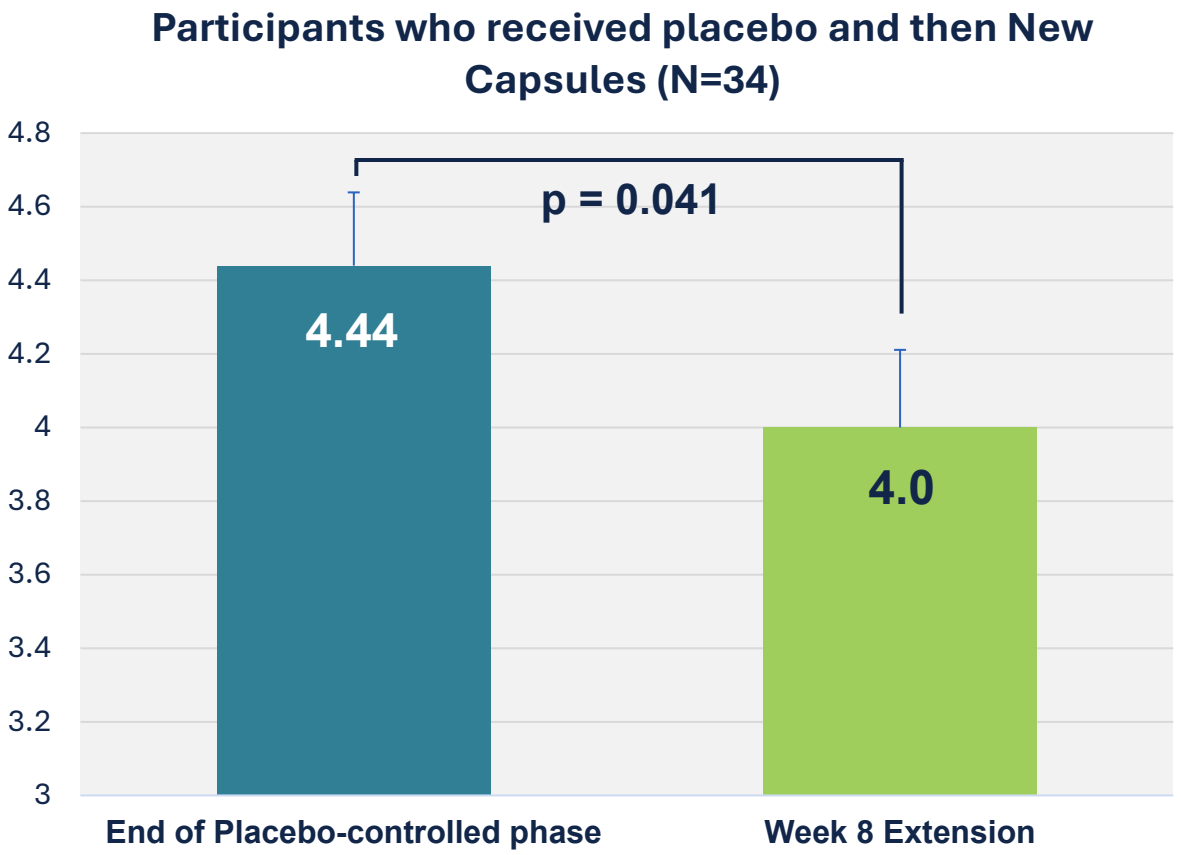
ADCS-CGIC Within-participant Comparison in Participants Who Received Placebo in Initial Phase Also Demonstrates Clinical Significance





Phase 2b Safety and Tolerability Summary

Neflamapimod 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 neflamapimod

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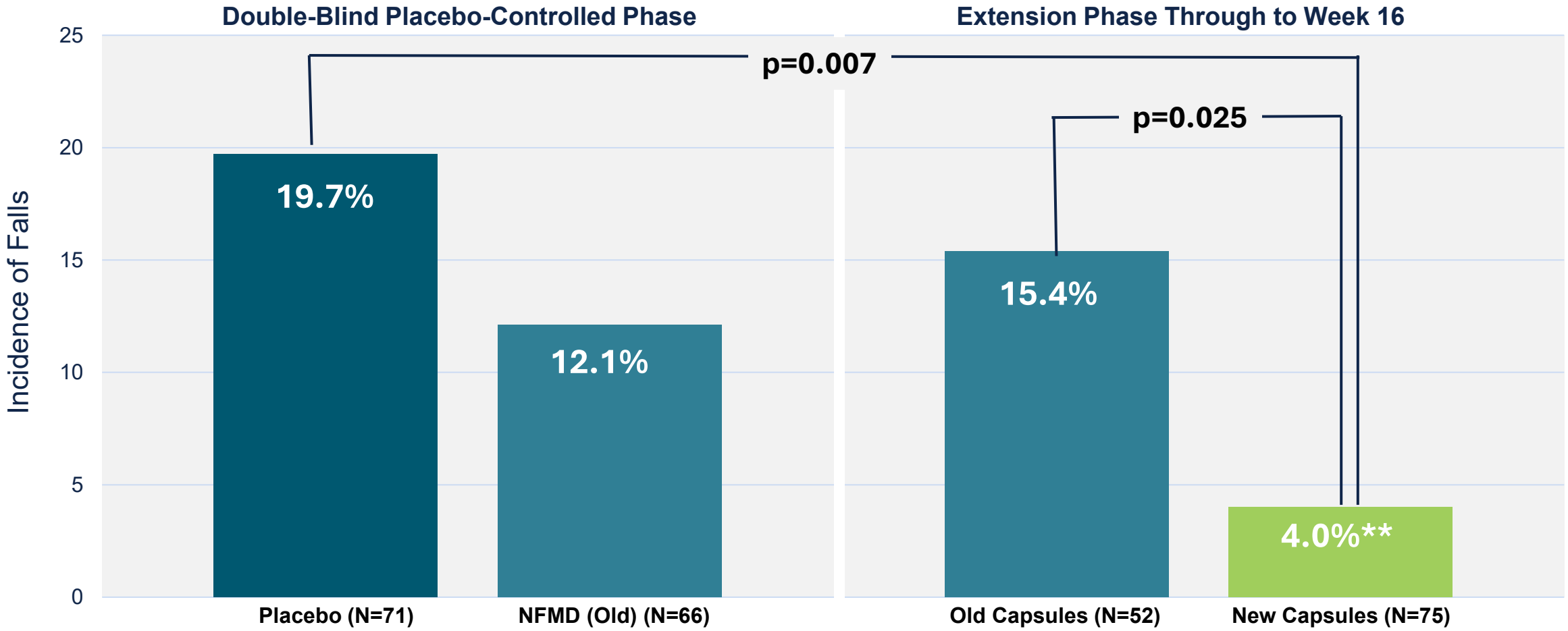
Incidence of Falls Significantly Reduced in Participants with DLB without AD Co-Pathology (Screening Plasma ptau181 < 2.2 pg/mL)



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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**

Projected design based on prior discussions with FDA. Final design, including sizing, will be based on meeting with FDA after completion of Extension Phase of RewinD-LB. Initiation subject to sufficient funding.

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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

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