Medicines for the Brain

RewinD-LB

Week 16 Results from Extension Phase

March 2025

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 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 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.

Today's Agenda

1. Overview of Phase 2b RewinD-LB Study in Dementia with Lewy Bodies (DLB)
2. 16-Week Results from the RewinD-LB Extension Phase
3. Summary of Today's Results & Next Steps
4. Q&A

RewinD-LB Study Overview

Designed to replicate Phase 2a study results, thereby demonstrating proof-of-concept for neflamapimod as a potential treatment for dementia with Lewy bodies (DLB)

- 16-week double-blind, placebo-controlled (40mg TID or placebo, 1:1) initial phase (Initial phase), followed by 32 weeks of open-label treatment with neflamapimod (Extension phase)
- Primary endpoint: change in Clinical Dementia Rating Sum-of-boxes (CDR-SB)
- Excluded patients with concomitant Alzheimer's disease related pathology, as assessed by plasma ptau181

Results of Initial phase of study presented at ILBDC*:

- No discernible differences between neflamapimod 40mg TID and placebo treatment groups during the Initial phase of the clinical study
- Measured trough plasma drug concentrations during this phase were similar to those seen with a lower dose of 40mg BID in earlier studies, a potential explanation for why these results were discordant from prior Phase 2a study in DLB
- Analyses to date suggest the lower–than-expected bioavailability during Initial phase was related to the age of the capsules utilized during this phase of the study

With the introduction of a newer batch of capsules in the ongoing Extension phase of the study, mean trough plasma drug concentration achieved the targeted threshold

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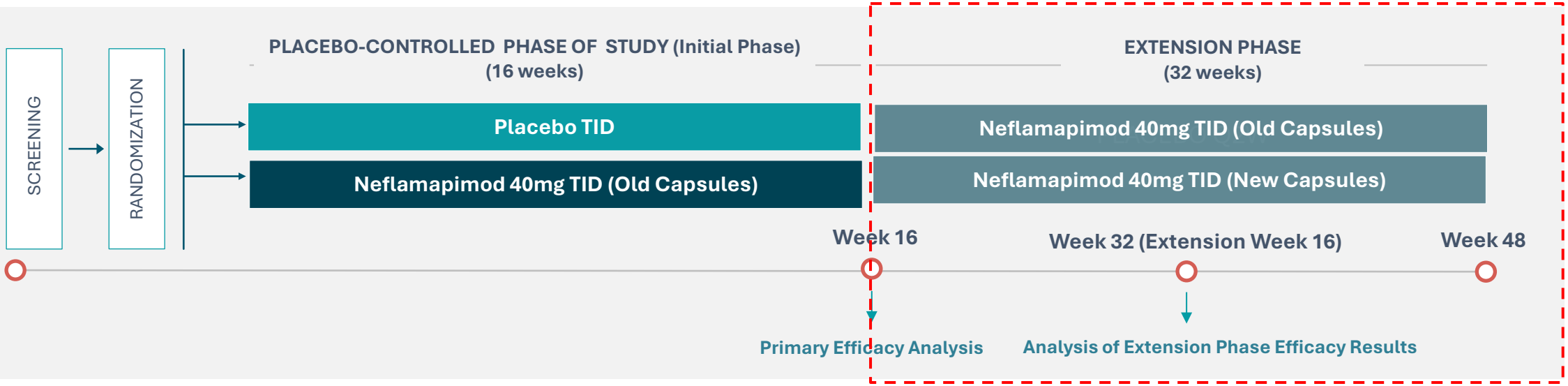
*International Lewy Body Dementia Conference, Amsterdam, NL, 29-31 January 2025

Week 16 Extension Phase Analysis



PARTICIPANTS

Dementia with Lewy bodies (DLB) by consensus criteria

Global CDR score of 0.5 or 1.0

Absence of AD co-pathology, as defined by screening ptau181 < 2.4 pg/mL

COMPARISONS

Outcomes during treatment in the Extension with old capsules vs. treatment with new capsules

Comparison in participants treated with new capsules during Extension with outcomes with placebo administration during Initial phase

CLINICAL OUTCOME MEASURES

- Primary: Clinical Dementia Rating Sum of Boxes (CDR-SB)
- Secondary:
  - Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (ADCS-CGIC)
  - Timed Up and Go (TUG) test
  - Neuropsychological Test Battery (NTB)

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Overview of Batch of Capsules in RewinD-LB Study

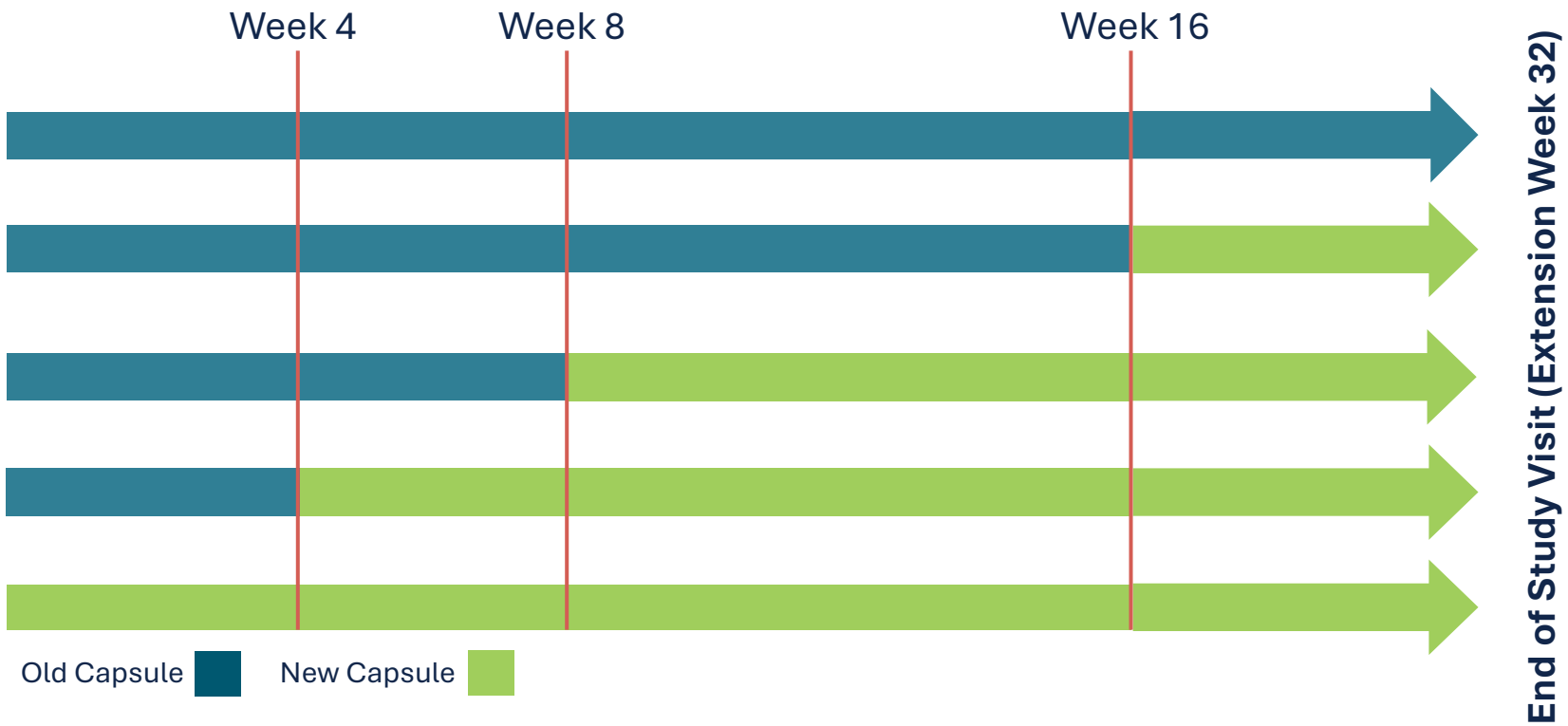
	Old Capsules	New Capsules
Use in RewinD-LB	Placebo-controlled (“Initial”) phase and in Extension	Extension only
Production Date	October 2020 (Age of 3 to 4 years during period of utilization in RewinD-LB)	March 2023 (Age < 2 years during first 16 weeks of Extension)
In Vitro Properties	Lower dissolution kinetics	Expected dissolution kinetics
Mean Trough Plasma Drug Concentration during RewinD-LB	3.9 ng/mL, which is similar to that seen with 40mg BID in prior studies	Attained targeted threshold of 5 ng/mL

Manufacturing processes were identical between both the old and new capsules

Dosing Groups in Extension Phase of RewinD-LB Study

		Number of Participants
"Old Capsules" N=55	Group 1	20
	Group 2	35
"New Capsules" N=94	Group 3	26
	Group 4	22
	Group 5	46
	Total	149

Study Visits During First 16 Weeks of Extension Phase



Extension Week 16 Completion Rate	
Old Capsules (Groups 1-2)	87.3%
New Capsules (Groups 3-5)	91.5%

Note: Participants were all aware that they were receiving neflamapimod in the Extension phase (*i.e.* treatment was "open label"), but neither they nor study site personnel were aware if they were receiving old or new capsules

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Baseline Characteristics (All Extension Phase Participants)

	Old Capsules: Groups 1 and 2 (N=55)	New Capsules: Groups 3, 4 and 5 (N=94)
Age	**70.6** (6.38)	**71.5** (6.10)
Male (Number, %)	**48** (87.3%)	**80** (85.1%)
Mini Mental Status Examination (MMSE)	**23.8** (3.69)	**23.4** (4.82)
CDR-SB	**4.13** (1.94)	**4.25** (1.72)
Core Clinical Criteria (Number, %):		
Cognitive fluctuations	**32** (58.2%)	**77** (81.9%)
Visual Hallucinations	**26** (47.3%)	**54** (57.4%)
REM sleep behavioral disorder	**46** (83.6%)	**69** (73.4%)
Parkinsonism	**46** (83.6%)	**85** (90.4%)
Background Therapy (Number, %)		
AChEI alone*	**36** (65.4%)	**59** (62.8%)
AChEI + Memantine or Mem alone	**9** (16.4%)	**16** (17.0%)
No background therapy**	**10** (18.2%)	**19** (20.2%)
Number (%) with ptau181 > 2.2 pg/mL[1] and < 2.4 pg/mL at screening	**3** (5.5%)	**19** (20.2%)

Except where noted, mean (SD) is shown

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[1] Cut-off utilized in phase 2a study analysis to identify participants with AD co-pathology

Primary Outcome Measure: Change in CDR-SB

- **“Gold standard” for evaluating severity and progression of dementia**
- **Primary endpoint for many Phase 3 clinical studies in early Alzheimer’s Disease (AD)**
- **Best performer for evaluating treatment effects in the Phase 2a study of neflamapimod in DLB**

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

Cognitive Domains:

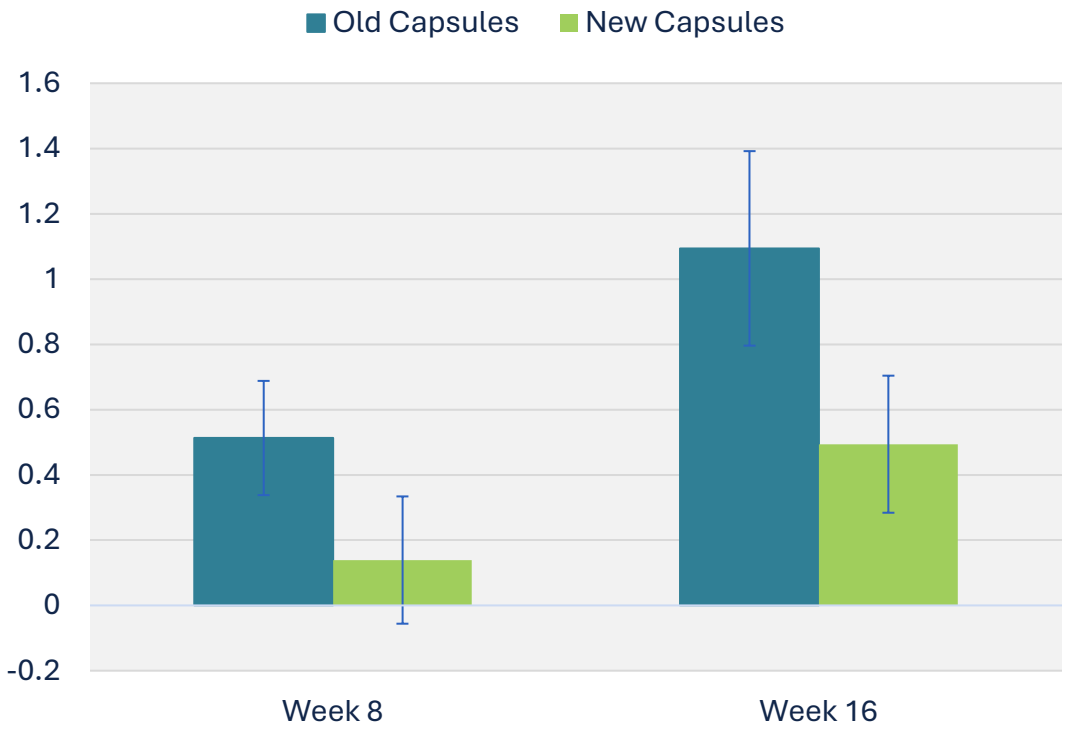
- Memory (0-3)
- Orientation (0-3)
- Judgement and Reasoning (0-3)

Functional Domains:

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

Mean Change from Baseline in CDR-SB in First 16 Weeks of Extension

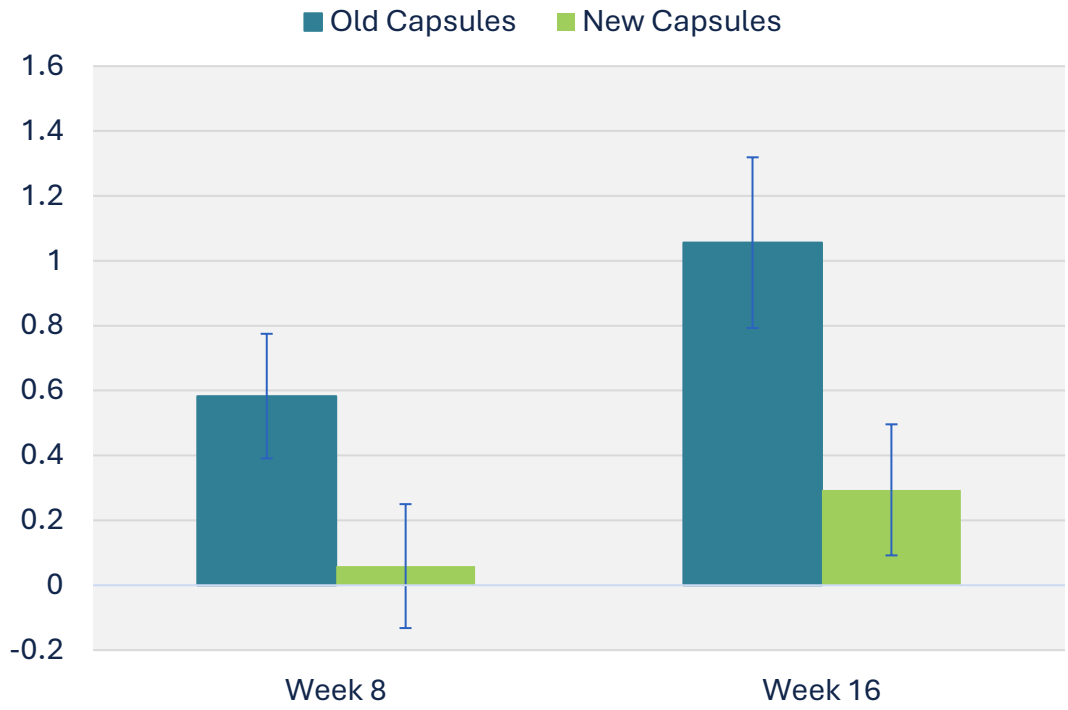
All Participants



p<0.001 for New vs. Old Capsules (MMRM analysis)

Number of Participants		
Old Capsules	75	48
New Capsules	62	84

Participants with Screening ptau181 < 2.2 pg/mL



p<0.001 for New vs. Old Capsules (MMRM analysis)

Number of Participants		
Old Capsules	66	45
New Capsules	52	67

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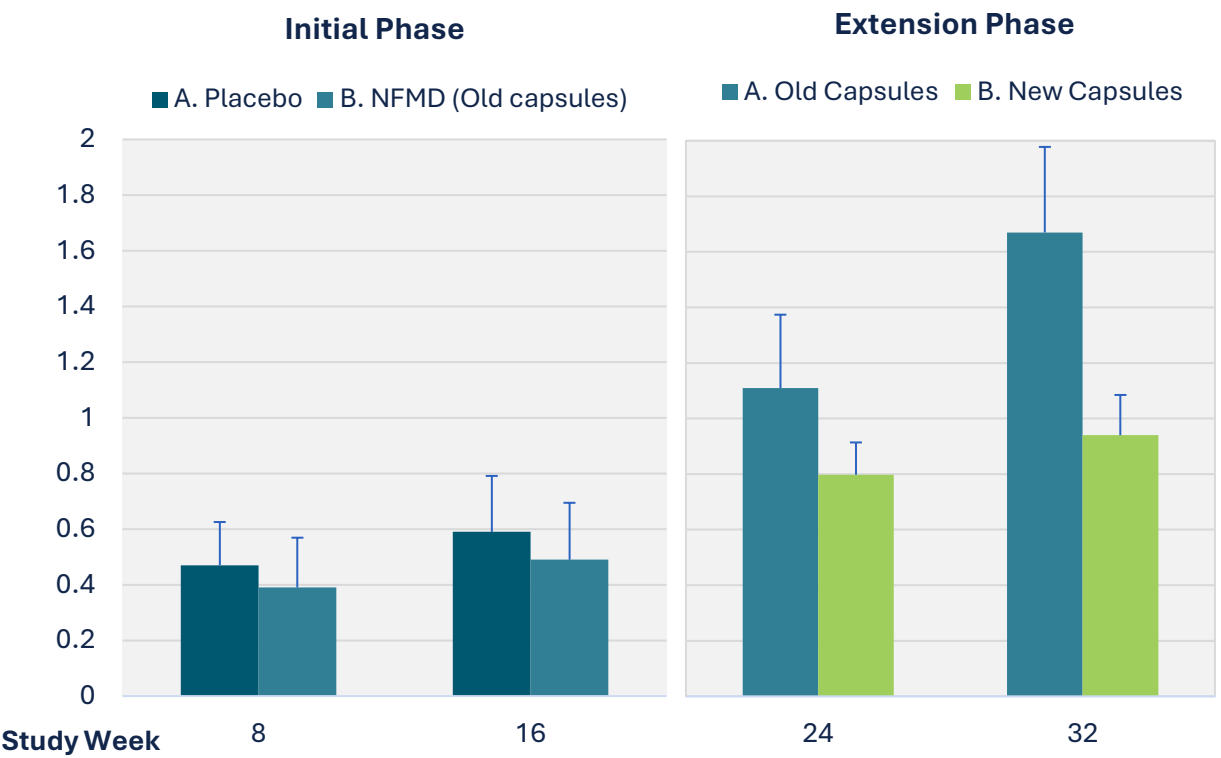
Error bars represent standard error of the mean

Mean Change in CDR-SB from Baseline to Week 32 (Week 16 of Extension)

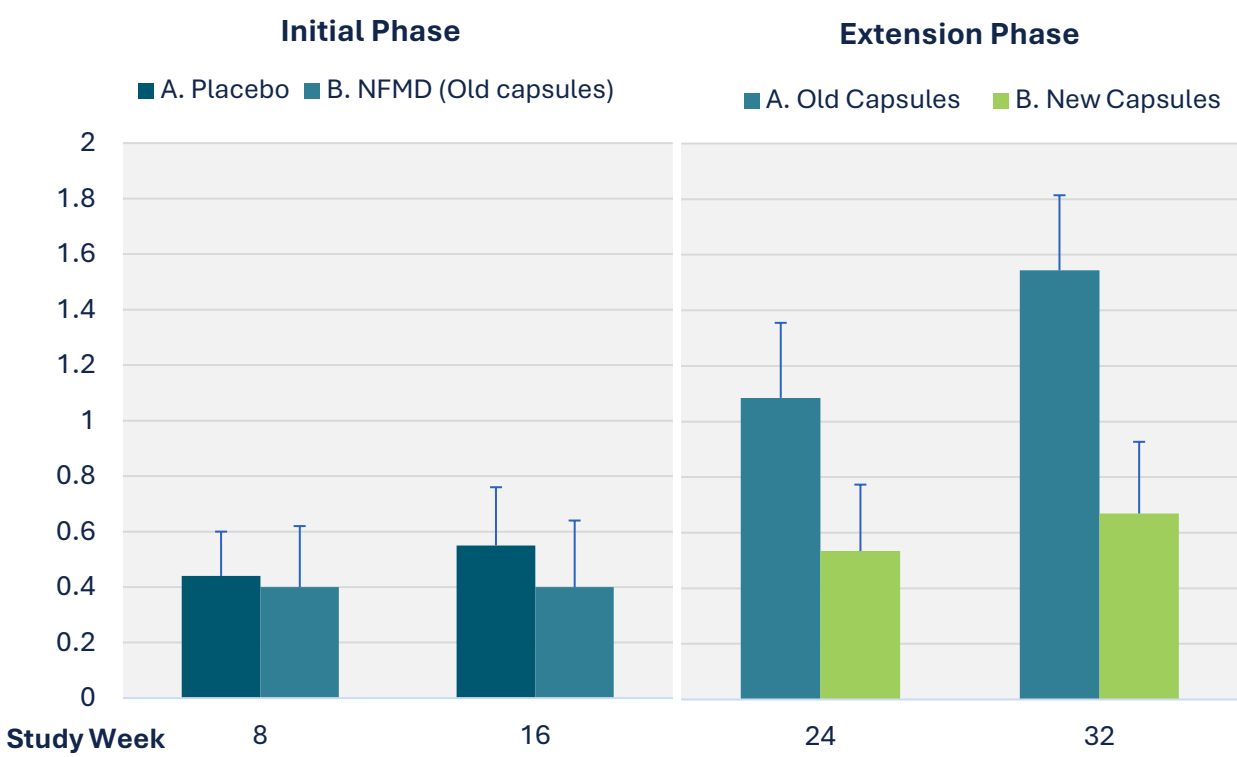
All Participants



P=0.003 for New Capsules vs. placebo (MMRM analysis)

Number of Participants				
	Week 8	Week 16	Week 24	Week 32
Group A	78	77	49	48
Group B	77	74	89	84

Participants with Screening ptau181 < 2.2 pg/mL



p<0.001 for New Capsules vs. placebo (MMRM analysis)

Number of Participants				
	Week 8	Week 16	Week 24	Week 32
Group A	66	67	47	45
Group B	62	62	73	68

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Error bars represent standard error of the mean

New Capsules Improves Outcome on CDR-SB

Analysis of Change in CDR-SB during First 16 Weeks of Extension in New vs. Old Capsules

	Mean (95% CI) Difference* between New and Old Capsules	P-Value
All Participants	-0.73 (-1.14, -0.32)	p<0.001
Participants with screening ptau181 < 2.2 pg/mL	-0.81 (-1.23, -0.39)	p<0.001

Analysis of Change in CDR-SB During First 32 Weeks of Study (includes Initial phase + First 16 weeks of Extension)

	Old Capsules		New Capsules	
	Mean Difference* to Placebo (95% CI)	P-Value	Mean Difference* to Placebo (95% CI)	P-Value
All Participants	0.00 (-0.28, 0.29)	0.97	-0.45 (-0.78, -0.15)	p=0.003
Participants with screening ptau181 < 2.2 pg/mL	-0.06 (-0.36, 0.23)	0.67	-0.57 (-0.88, -0.25)	p<0.001

Linear Mixed-Effects Model for Repeated Measures (MMRM) with baseline CDR-SB, Sex, Age and MMSE as covariates
*Negative indicates improvement

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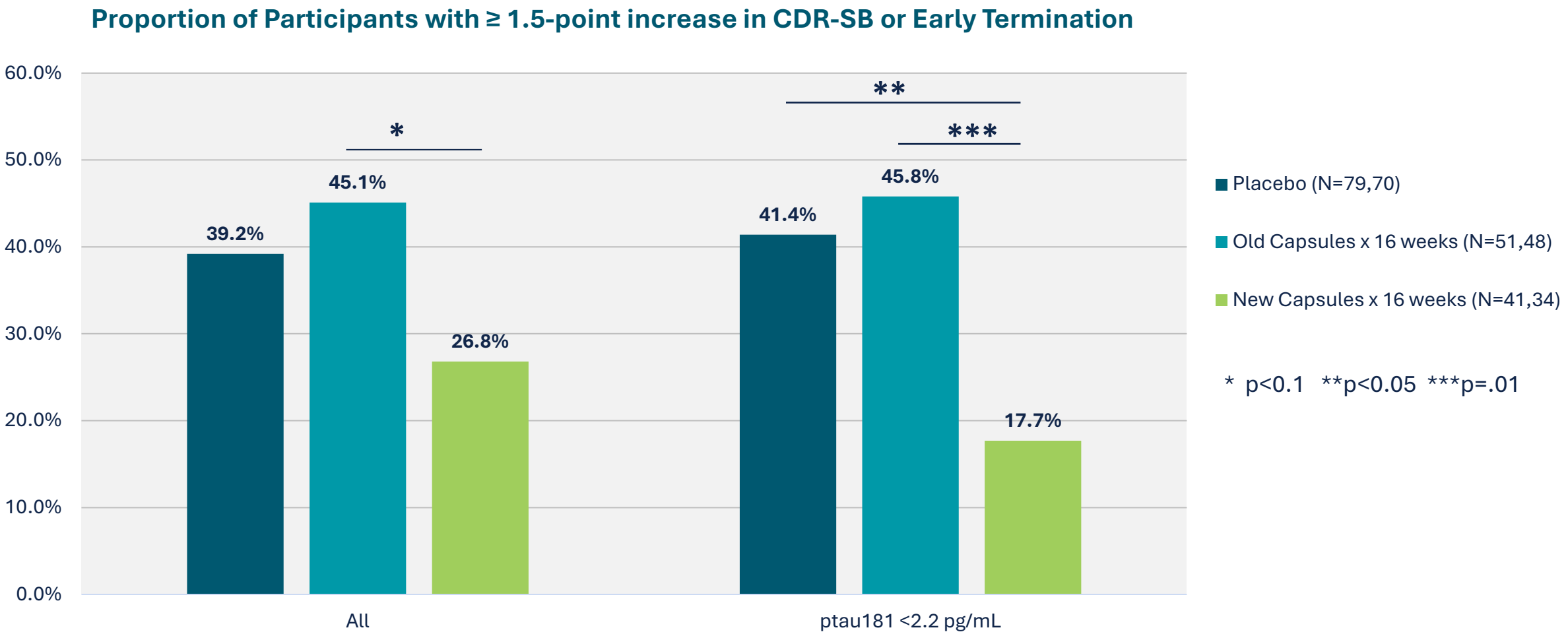
CI – confidence interval

Progression Over 16 Weeks



Placebo is during 16-week Initial phase of the study; Old and New Capsules during first 16 weeks of the Extension

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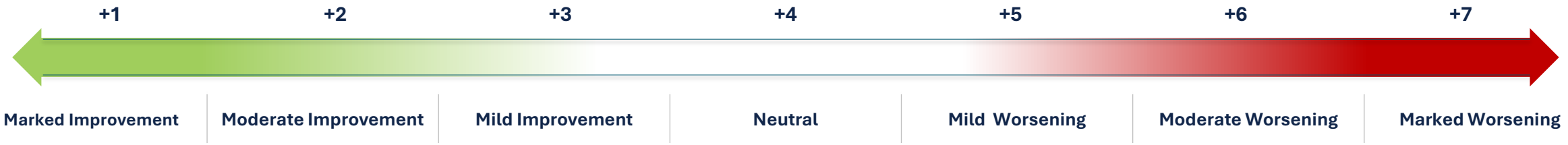
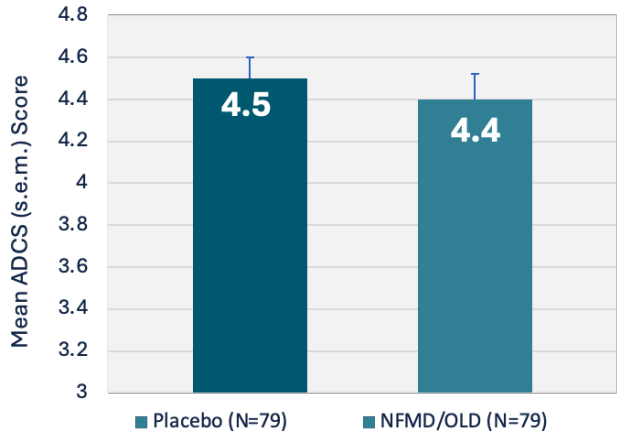
Secondary Endpoint: Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (ADCS-CGIC)



Calculate Group Means from Individual Scores

Interpretation of Group Mean Scores		
<4.0	4.0	>4.0
Improvement	No Change	Worsening

Results in Initial Phase of the Study



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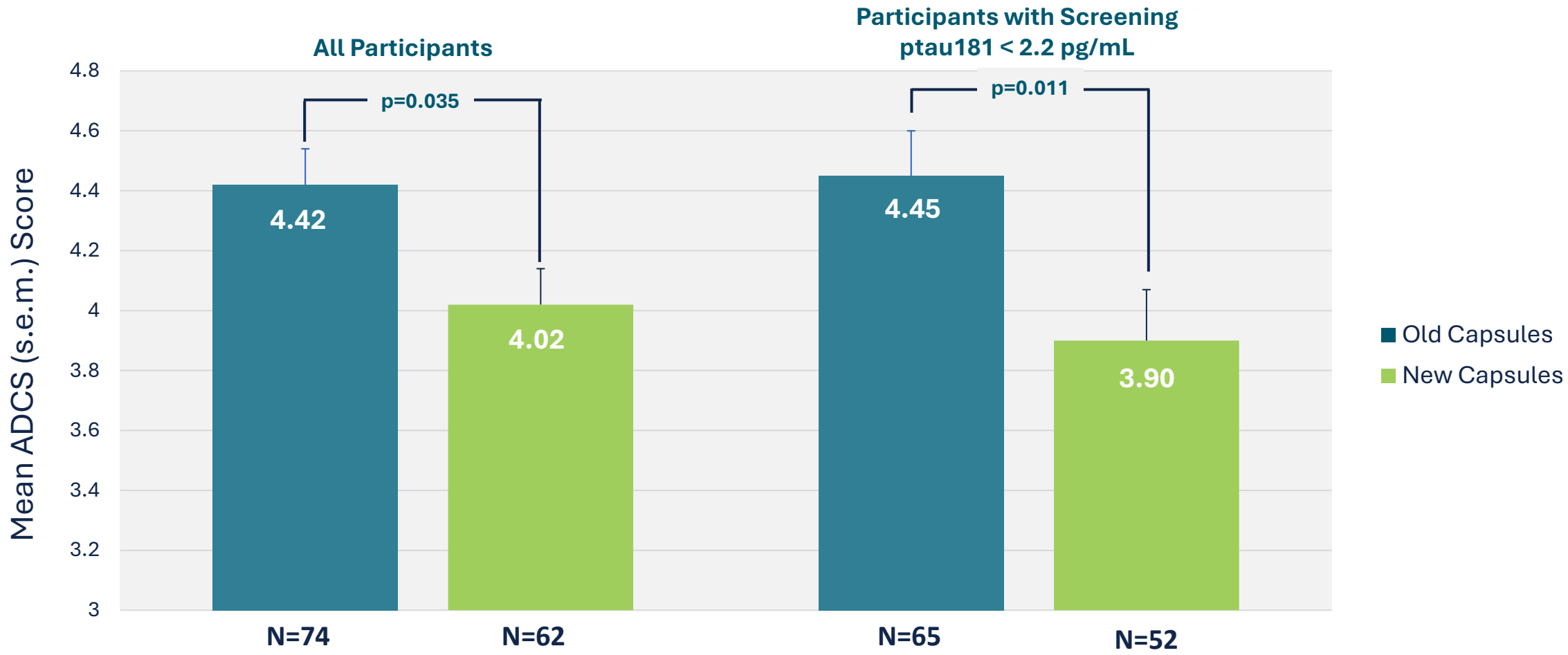
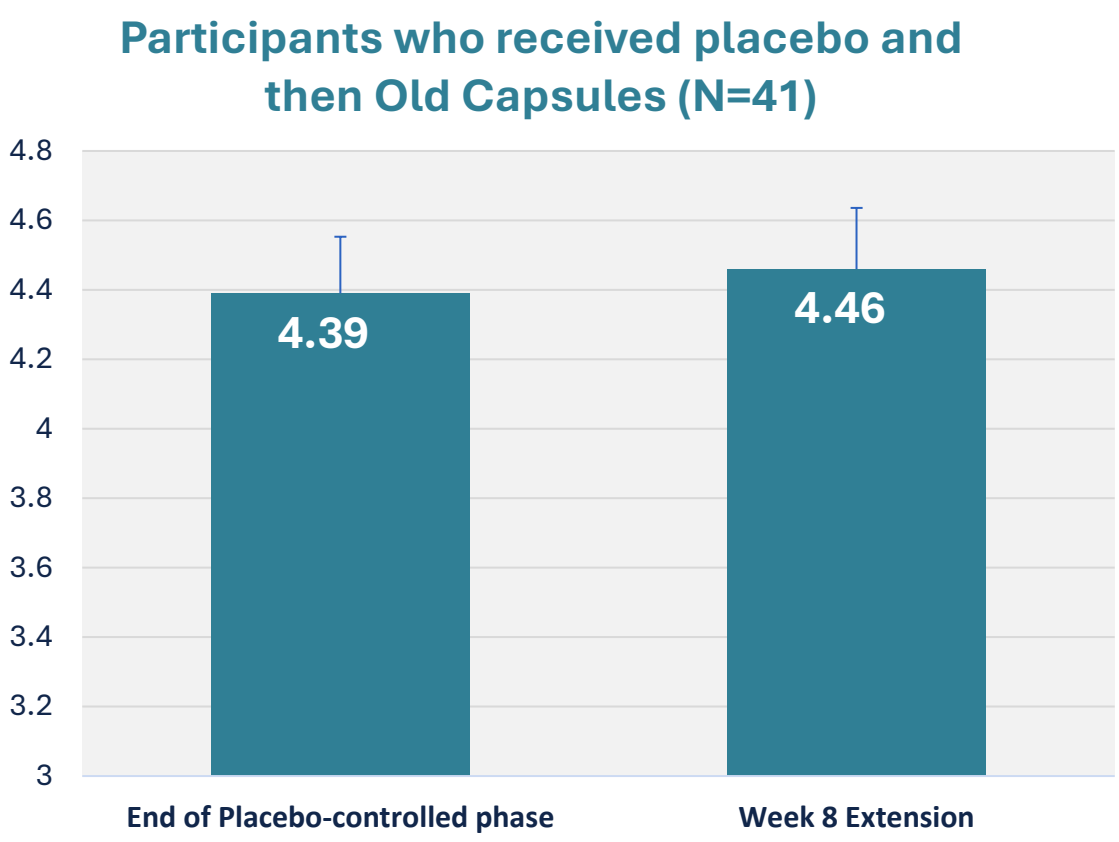
ADCS-CGIC by Capsule Form Administered during Extension Phase

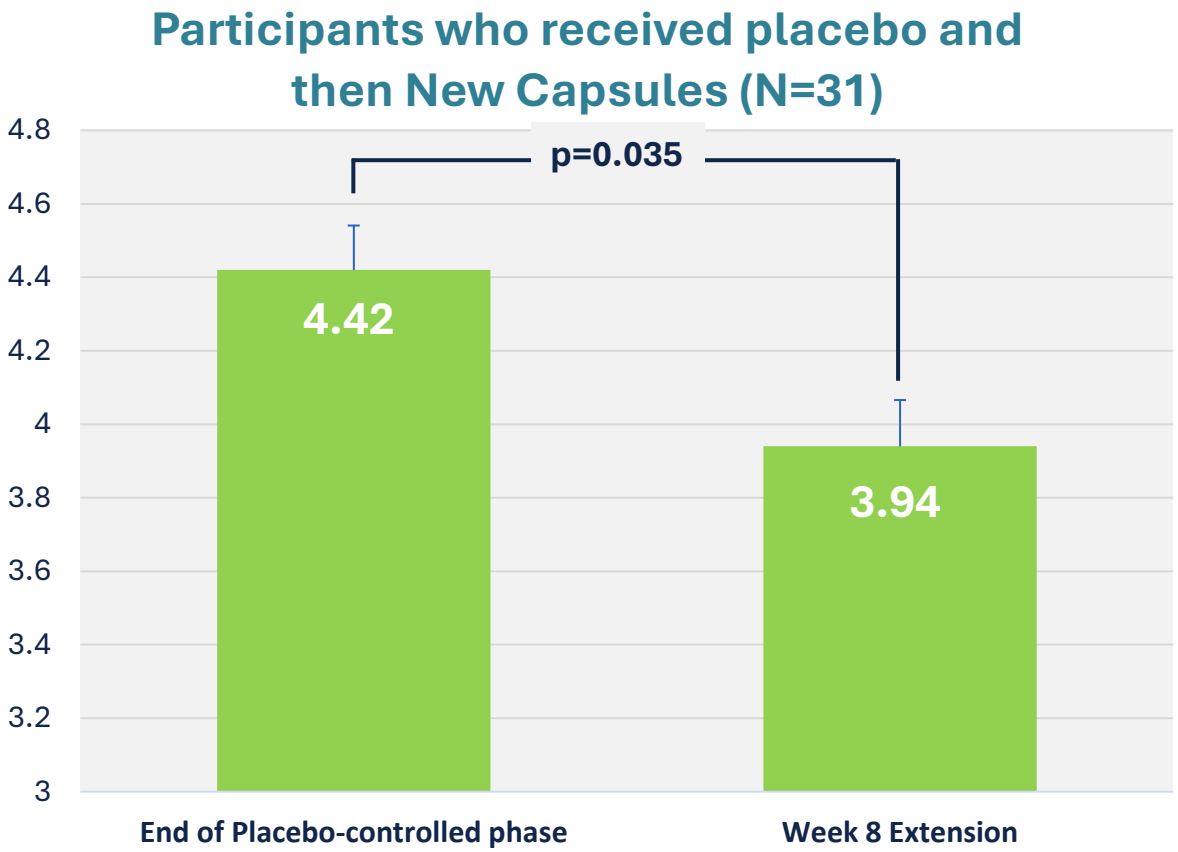


CGIC Administered at Week 8 of the Extension

Error bars represent standard error of the mean

ADCS-CGIC: Within-participant Comparison in Participants Who Received Placebo in Initial Phase

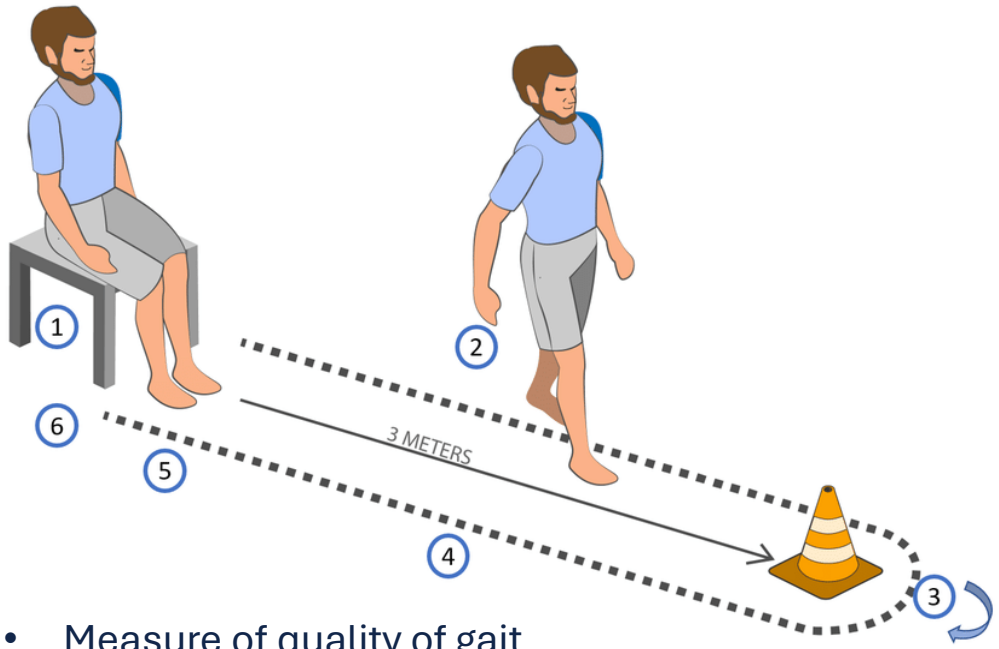




Error bars represent standard error of the mean

Secondary Endpoints: Function Specific Endpoints

Timed Up and Go Test (TUG)



- Measure of quality of gait
- Correlates with risk of falls
- In DLB, outcome on TUG thought to be driven by cognitive control of motor function

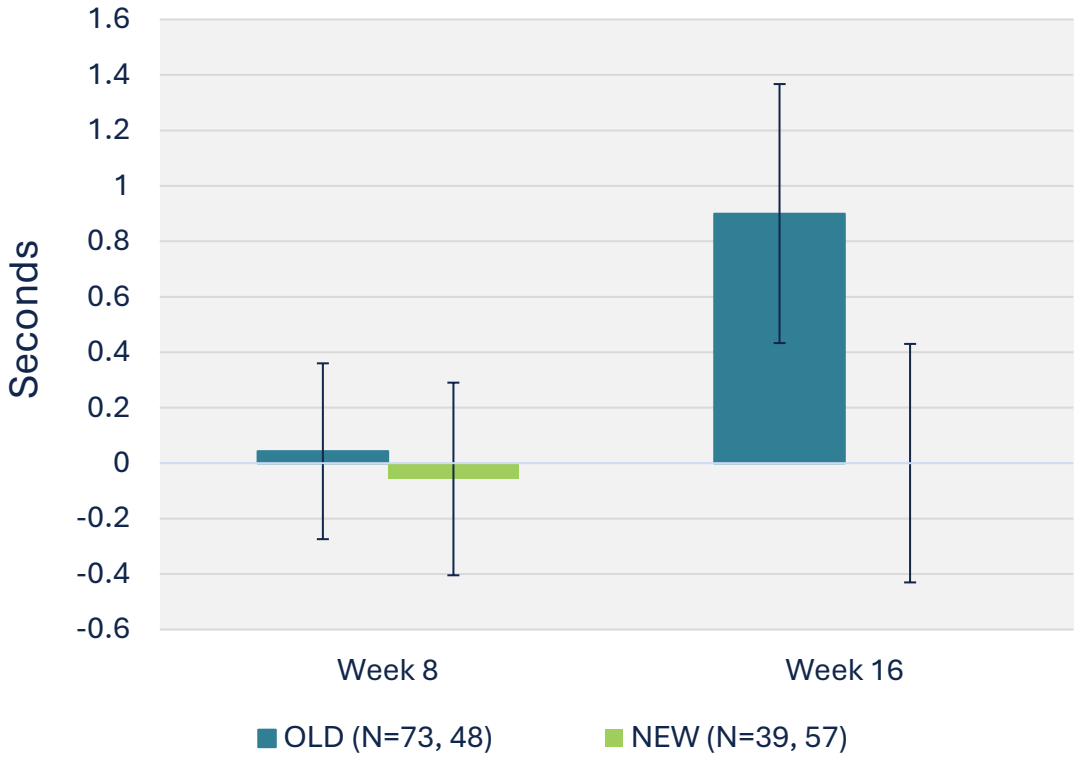
Neuropsychological Test Battery (NTB)

- Detection
- Identification
- One Card Learning
- One Back

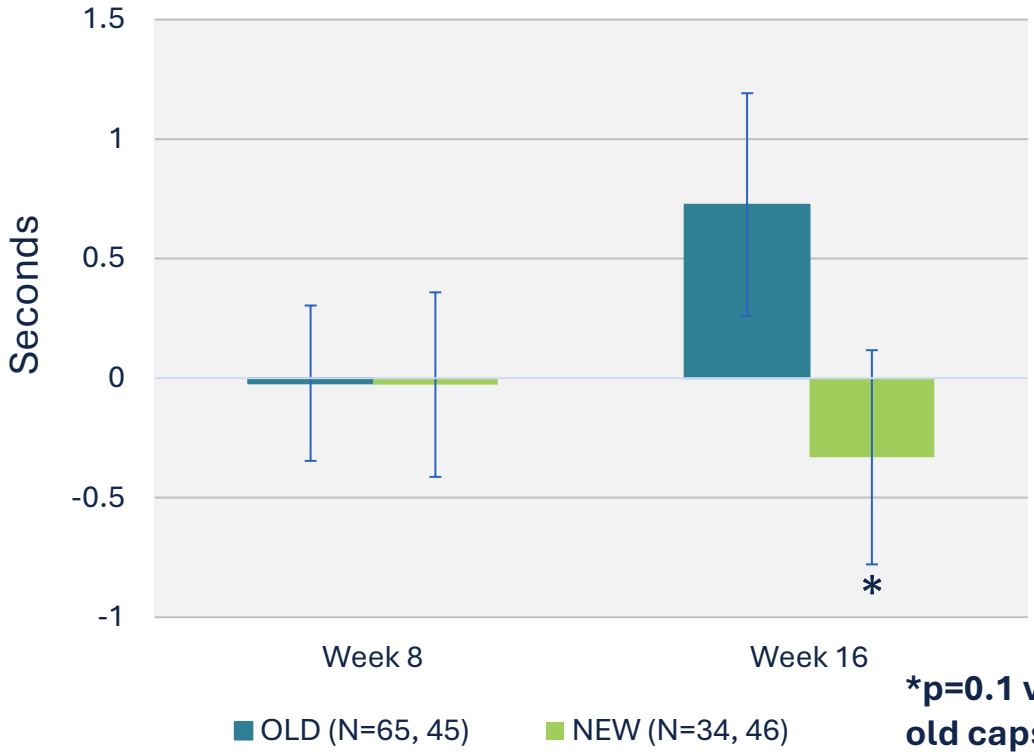
- Study-specific cognitive test battery designed to assess attention, executive function and visual learning
- Results of the four tests combined into single z-score
- Compared to CDR-SB and TUG, NTB performed less well to detect treatment effects in Phase 2a study of neflamapimod in DLB

Mean Change from Baseline in Timed Up and Go (TUG) during first 16 weeks of Extension

All Participants



Participants with Screening ptau181 < 2.2 pg/mL

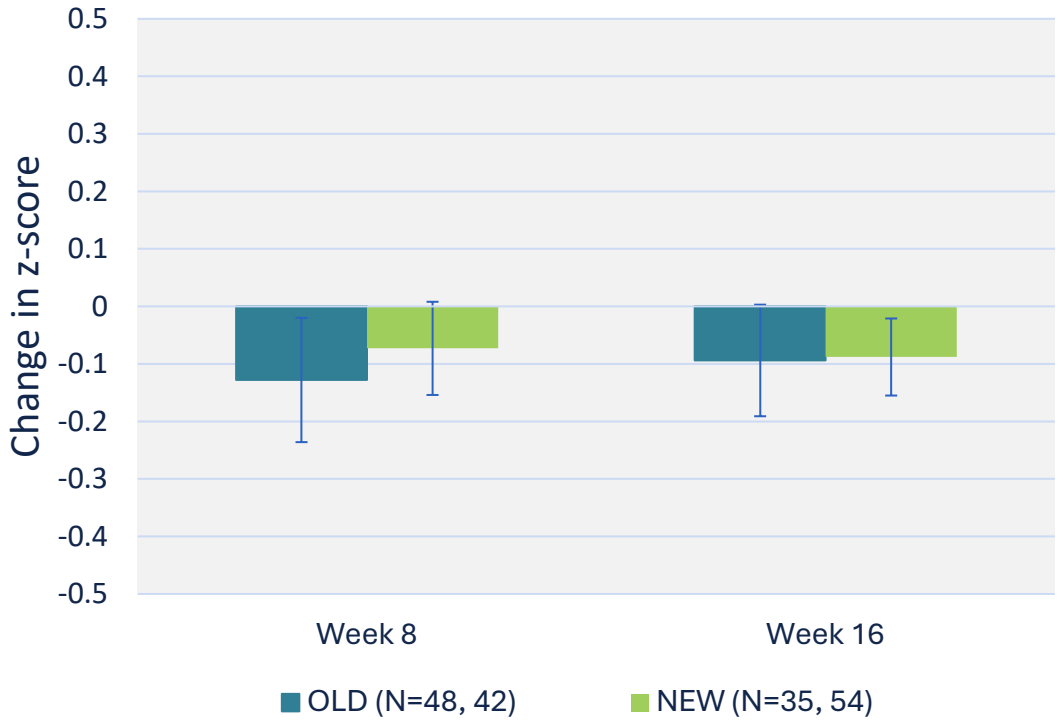


***p=0.1 vs. old capsule**

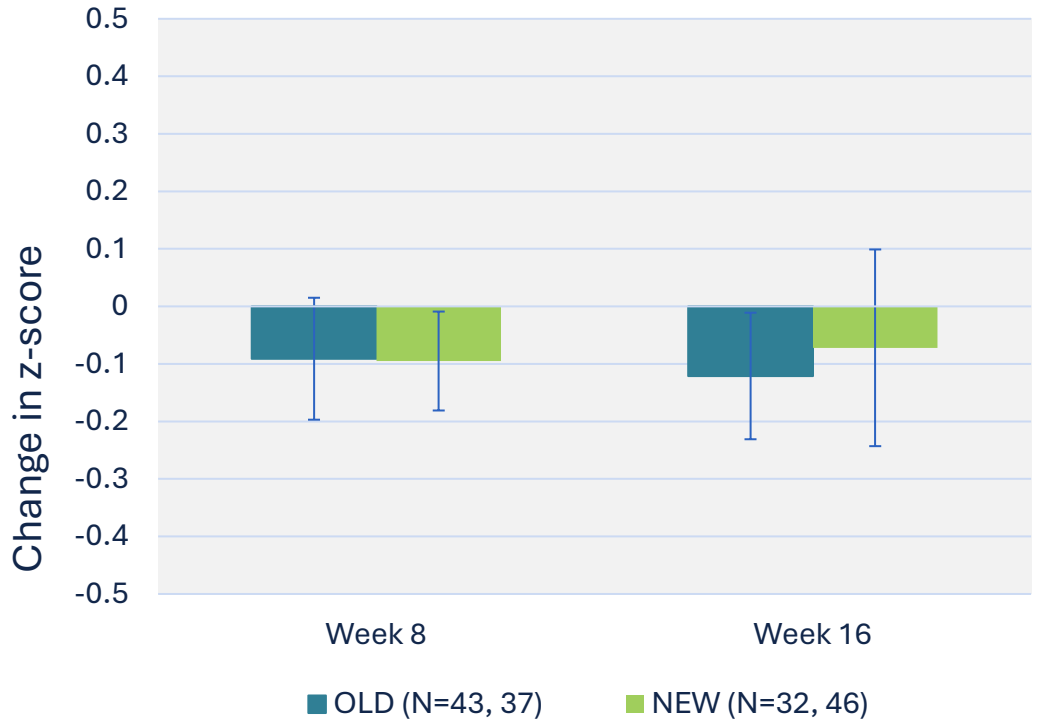
Error bars represent standard error of the mean

Mean Change from Baseline in Neuropsychological Test Battery (NTB) during first 16 weeks of Extension

All Participants



Participants with Screening ptau181 < 2.2 pg/mL



Consistent with low levels (and lower levels in prior Phase 2a study) of deficits at baseline in the cognitive tests utilized in the study (CTAD, 2025)

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Error bars represent standard error of the mean

Safety: Treatment Discontinuations in Extension Phase Up to Week 16

	Old Capsules: Groups 1 and 2 (N=55)	New Capsules: Groups 3, 4 and 5 (N=94)
Early Discontinuation of Treatment	**4 withdrawal by participant** (1 each at weeks 2 and 4, 2 at week 8) **2 adverse event** (both at week 2) **1 physician decision** (at week 4)	**6 withdrawal by participant** (3 each at weeks 4 and 8) **2 adverse event** (1 each at weeks 4 and 8)
Adverse Events Leading to Discontinuation	**Stomachache** (week 2) **Gastritis and worsening palpitations** (week 2)	**Confusion** (week 4) **Fatigue** (week 8)

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Note: Week refers to study week during Extension

Treatment Emergent Adverse Events (TEAE)
Seen At Incidence >2% During First 16 Weeks of Extension

	OLD CAPSULES: GROUPS 1 & 2 (N=55)	NEW CAPSULES: GROUPS 3, 4 AND 5 (N=94)	TOTAL (N=149)
Falls	8 (14.5%)	7 (7.4%)	15 (10.1%)
COVID-19	2 (3.6%)	5 (5.3%)	7 (4.7%)
Headache	1 (1.8%)	5 (5.3%)	6 (4.0%)
Urinary Tract Infection	5 (9.1%)	3 (3.2%)	8 (5.4%)
Diarrhea	4 (7.3%)	3 (3.2%)	7 (4.7%)
Skin Laceration	1 (1.8%)	3 (3.2%)	4 (2.7%)
Hallucination	5 (9.1%)	2 (2.1%)	7 (4.7%)
Fatigue	3 (5.5%)	2 (2.1%)	5 (3.4%)
Confusional State	3 (5.5%)	2 (2.1%)	5 (3.4%)
Arthralgia	2 (3.6%)	1 (1.1%)	3 (2.0%)
Dizziness	3 (5.5%)	1 (1.1%)	4 (2.7%)
AST Increased	3 (5.5%)	1 (1.1%)	4 (2.7%)
ALT Increased	3 (5.5%)	0 (0%)	3 (2.7%)

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NOTE – Ordered by highest % in New Capsule group, followed by % in Old Capsule group

TEAE Seen At Incidence >2% During First 16 Weeks of Extension in Participants with Screening ptau181 < 2.2 pg/mL

	OLD CAPSULES: GROUPS 1 & 2 (N=52)	NEW CAPSULES: GROUPS 3, 4 AND 5 (N=75)	TOTAL (N=127)
Headache	1 (1.9%)	5 (6.7%)	6 (4.7%)
COVID-19	2 (3.8%)	4 (5.3%)	6 (4.7%)
Falls	8 (15.4%)	3 (4.0%)*	11 (8.7%)
Urinary Tract Infection	5 (9.6%)	3 (4.0%)	8 (6.3%)
Hallucination	5 (9.6%)	2 (2.7%)	7 (5.5%)
Diarrhea	3 (5.8%)	2 (2.7%)	5 (3.9%)
Fatigue	3 (5.8%)	2 (2.7%)	5 (3.9%)
Confusional State	3 (5.8%)	2 (2.7%)	5 (3.9%)
Skin Laceration	1 (1.9%)	2 (2.7%)	3 (2.4%)
Dizziness	3 (5.8%)	1 (1.3%)	4 (3.1%)
Arthralgia	2 (3.8%)	1 (1.3%)	3 (2.4%)
AST Increased	3 (5.8%)	0 (0%)	3 (2.4%)
ALT Increased	3 (5.8%)	0 (0%)	3 (2.4%)

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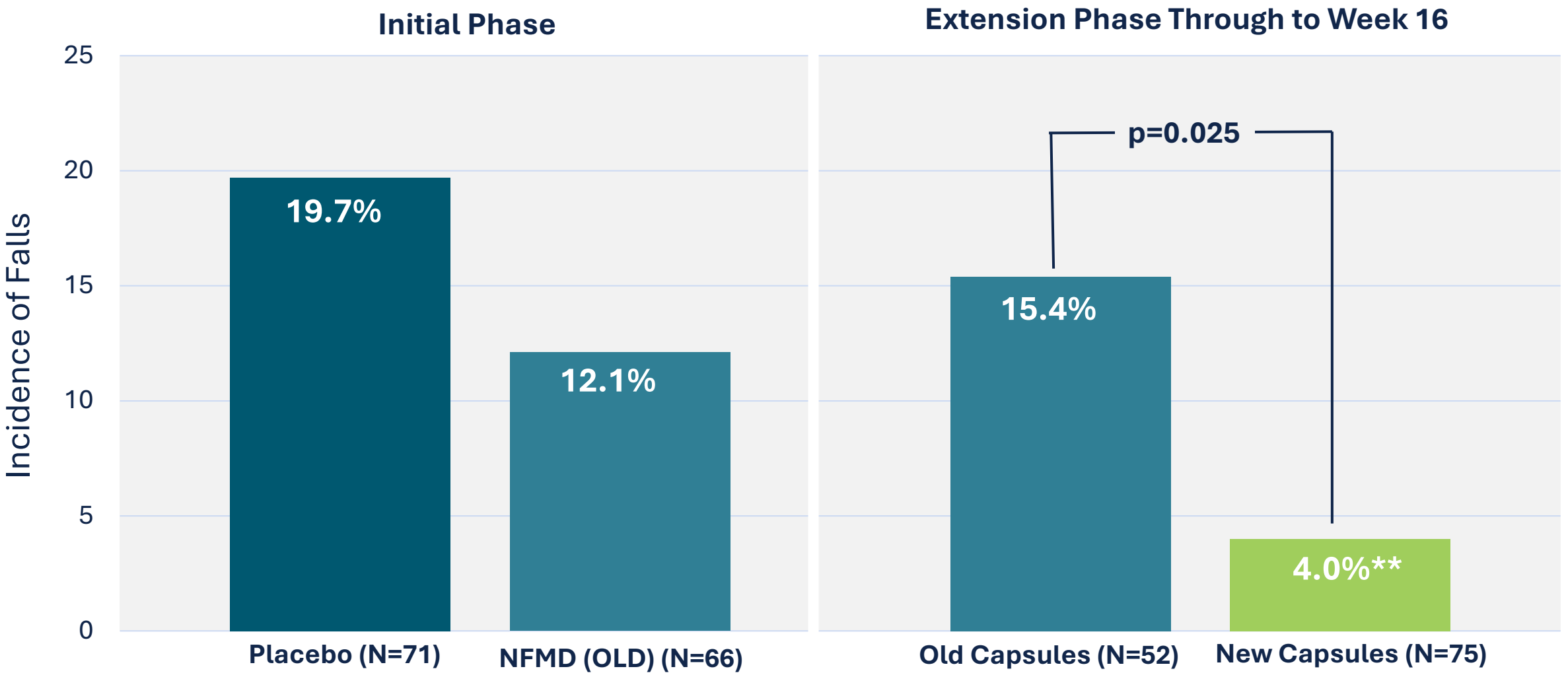
NOTE – Ordered by highest % in New Capsule group, followed by % in Old Capsule group

*p=0.025 vs. incidence with old capsules

Incidence of Falls in Participants with Screening ptau181 < 2.2 pg/mL During First 16 Weeks of Extension



**p=0.007 vs. placebo

New Capsule Performance Met Expectations of 40mg TID Neflamapimod

	Old Capsules	New Capsules
Production Date	October 2020 (Age of 3 to 4 years during period of utilization in RewinD-LB)	March 2023 (Age < 2 years during first 16 weeks of Extension)
In Vitro Properties	Lower dissolution kinetics	Expected dissolution kinetics
Mean Trough Plasma Drug Concentration during RewinD-LB	3.9 ng/mL, which is similar to that seen with 40mg BID	Attained targeted threshold of 5 ng/mL
Clinical Outcomes during RewinD-LB	No discernible difference to placebo on clinical outcome measures	Improvement on CDR-SB and CGIC compared to old capsules, as well as compared to placebo

Manufacturing processes were identical between both the Old and New Capsules

Summary of Analyses of Extension Phase Week 16 Results (Week 32 of Overall Study)

Positive effects with New Capsules on multiple clinical endpoints:

- Improvement on primary efficacy endpoint, change in CDR-SB, both vs. Old Capsules ($p<0.001$) during first 16 weeks of the Extension and vs. placebo ($p=0.003$) utilizing all data in the study through to week 32 (includes Initial phase and first 16 weeks of the Extension)
- Improvement on ADCS-CGIC in comparison to Old Capsules ($p=0.035$) during the Extension and in a within-participant comparison to placebo treatment during Initial phase ($p=0.035$)
- Trend towards improvement in TUG vs. Old Capsules at week 16 of Extension; no discernible effects on NTB
- Greater positive clinical effect in participants with levels of screening ptau181 < 2.2 pg/mL

Old and New Capsules have similar overall safety/tolerability profile

- Lower incidence of falls during the Extension with the New Capsules ($p=0.025$ vs. Old Capsules and $p=0.007$ vs. placebo in participants with screening ptau181 < 2.2 pg/mL)

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Next Steps in DLB

- **Present RewinD-LB Data at Scientific Conferences Throughout 2025:**
  - AD-PD 2025, Vienna, AT, April 1-5: presentation of Extension Week 16 Results
  - Alzheimer's Association International Conference (AAIC) 2025, Toronto, CA, July 27-31: plan to submit
  - American Neurologic Association (ANA), Baltimore MD, Sep 13-16: presentation at Special Interest Group, Neurodegenerative Diseases Therapeutics
  - Clinical Trials in Alzheimer's Disease (CTAD), San Diego, CA, USA Dec 1-4: plan to submit
- **Meet with FDA after week 32 Extension (week 48 study overall) data are available to finalize proposed Phase 3 design**

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Q&A