CERVOMED

Medicines for the Brain

EFFICACY AND SAFETY RESULTS OF THE REWIND-LB PHASE 2B CLINICAL TRIAL OF NEFLAMAPIMOD IN DEMENTIA WITH LEWY BODIES (DLB)

SN Gomperts[1], JP Taylor[2], LS Honig[3], ND Prins[4], A Gardner[5], K Blackburn[5], JJ Alam[5], JE Galvin[6]

1. Massachusetts General Hospital – Charlestown, MA (United States)
2. Newcastle University – Newcastle Upon Tyne (United Kingdom)
3. Columbia University Irving Medical Center – New York, NY (United States)
4. Brain Research Center – Amsterdam (Netherlands)
5. CervoMed – Boston, MA (United States)
6. Miller School of Medicine – Miami, FL (United States)

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, 2024 filed with the U.S. Securities and Exchange Commission (SEC) on March 17, 2025, 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 April 5, 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.

Disclosures

- Neflamapimod is an investigational drug
- J. Alam, A. Gardner, and K. Blackburn are employees of CervoMed Inc., the company developing neflamapimod
- S.N. Gomperts and J-P Taylor each have acted as a consultant for CervoMed
- The other co-authors have no disclosures to declare

Neflamapimod Background

Pre-Clinical

Through inhibiting p38a, protein kinase mediating cellular response to neuroinflammation, acts on molecular mechanisms underlying cholinergic degeneration:

- Rab5
- Tau

In mice that develop basal forebrain cholinergic degeneration:

- ✓ ↓ Rab5 activity and ↓ tau phosphorylation
- ✓ Reverses loss of cholinergic (ChaT+) neurons in the basal forebrain
- ✓ Normalized performance in behavioral tests of cholinergic function

AscenD-LB

Phase 2a Study in DLB

16-week placebo-controlled study in patients with DLB

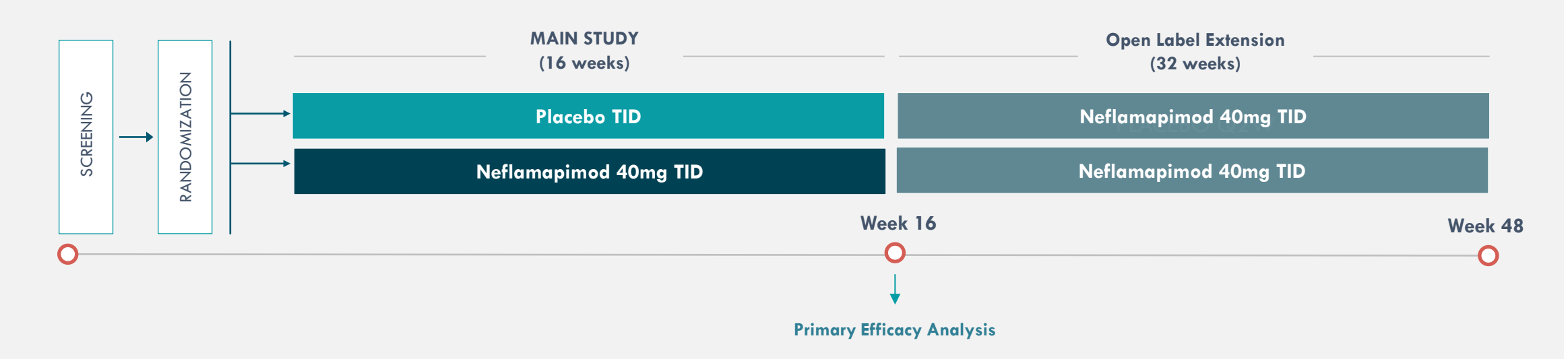
Placebo (N=45) vs. Neflamapimod 40 mg (N=46), BID or TID

Results vs. placebo:

- ✓ Significant improvement on dementia severity (CDR-SB) and mobility (TUG) in full efficacy population analysis (i.e., including BID dose)
- ✓ Significant improvement on cognitive testing at 40mg TID vs. placebo, particularly with respect to attention
- ✓ Results most prominent in patients without elevated plasma ptau181

- **Abbreviations**. CDR-SB: Clinical Dementia Rating Sum of Boxes; TUG: Timed Up and Go test
- References: Prins et al, 2021; Jiang et al, 2022; Alam et al, 2023; Prins et al, JPAD, 2024

RewinD-LB Phase 2b Clinical Trial



PARTICIPANTS

DLB by consensus criteria; Global CDR=0.5 or 1.0

Pre-treatment plasma ptau181 <2.4 pg/ml (i.e., excluding patients with AD co-pathology)

INTERVENTION

159 participants randomized on a blinded basis 1:1 to neflamapimod 40mg capsules or matching placebo capsules, 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

Plasma biomarker: GFAP

RewinD-LB Investigator Sites

USA

A. Burke, Barrow Neurological Institute, Phoenix, AZ
D. Shprecher, Banner Sun Health Research Institute, Sun City, AZ
K. Bradley, Banner Alzheimer's Institute, Tucson, AZ
R. Hess, UCSD, La Jolla, CA
A. Ritter, Hoag Memorial Hospital Presbyterian, Newport Beach, CA
M.L. Purino, SC3 Research Group, Pasadena, CA
S. Sha, Stanford Neuroscience Health Center, Palo Alto, CA
S. Holden, U. of Colorado, Aurora, CO
Y. Torres-Yaghi, Georgetown University, Washington DC
M. Tolea, J. Galvin, U. Of Miami Miller School of Medicine, Boca Raton, FL
L. Pao, JEM Research Institute, Lake Worth, FL
R. Laird, ClinCloud, Viera, FL
A. Ahmed, AdventHealth Neuroscience, Orlando, FL
J. Cahill, Panhandle Research, Pensacola, FL
J.E. Fleisher,Rush University Medical Center, Chicago, IL
R. Pahwa, U. of Kansas Medical Center, Kansas City, KS
A. Traylor, Tandem Clinical Research, Marrero, LA
L.S. Rosenthal, Johns Hopkins, Baltimore, MD
S.N. Gomperts, MGH, Charlestown, MA
B. Boeve, Mayo Clinic, Rochester, MN
D.L. Murman, U. Of Nebraska Medical Center, Omaha, NE

USA, continued

C., Bernick, Cleveland Clinic Foundation, Las Vegas, NV
L. Honig, Columbia, New York, NY
A. Bozoki, U. of North Carolina, Chapel Hill, NC
R. Drake, Neuroscience Research Center, Canton, OH
B. Tousi, Cleveland Clinic, Cleveland, OH
D. Scharre. The Ohio State University, Columbus, OH
M. Mega, Center for Cognitive Health, Portland, OR
J. Toledo Atucha, Houston Methodist Hospital, Houston, TX
E. Czander, Sana Research, Arlington, VA
R.S. Turner, ReCognition Health, Fairfax, VA
M.J. Barrett, Virginia Commonwealth University, Richmond, VA

Netherlands

EGB Vijverberg, N. Prins, Brain Research Center, Amsterdam
P. Dautzenberg, Brain Research Center, Den Bosch
L. Exalto, Brain Research Center, Zwolle

United Kingdom

J. Kane, Queen's University Belfast
L. Chouliaras, U. Of Cambridge
S. Vann Jones, Cornwall Partnership, Exeter
D. Aarsland, King's College London
E. MacSweeny, ReCognition Health, London
R. Weil, University College London, London
A. Byrne, J-P Taylor, U. Of Newcastle, Newcastle upon Tyne
S. Sharif, Southern Health NHS Trust, MARC, Southampton

Results of Placebo-controlled (“Initial”) Phase of RewinD-LB

Presentation at International Lewy Body Dementia Conference, Amsterdam, NL, 29-31 Jan 2025

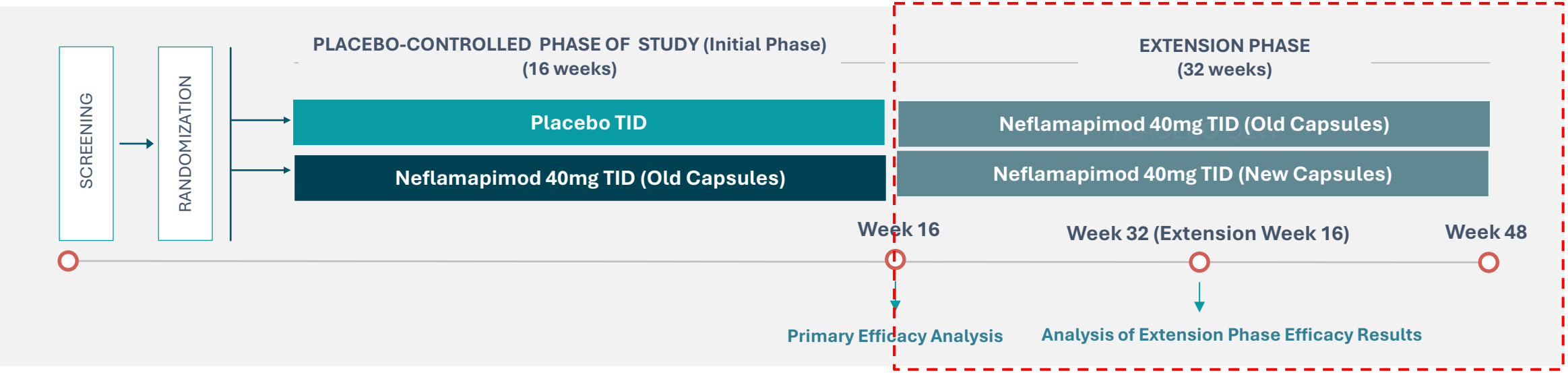
- No discernible differences between neflamapimod 40mg TID and placebo treatment groups during the Initial 16-week phase of the clinical study
- Measured trough plasma drug concentrations during this phase were similar to those seen with a lower dose of 40mg BID in earlier studies, a potential explanation for why these results were discordant from the positive Phase 2a study results
- 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

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

Today's Presentation: 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

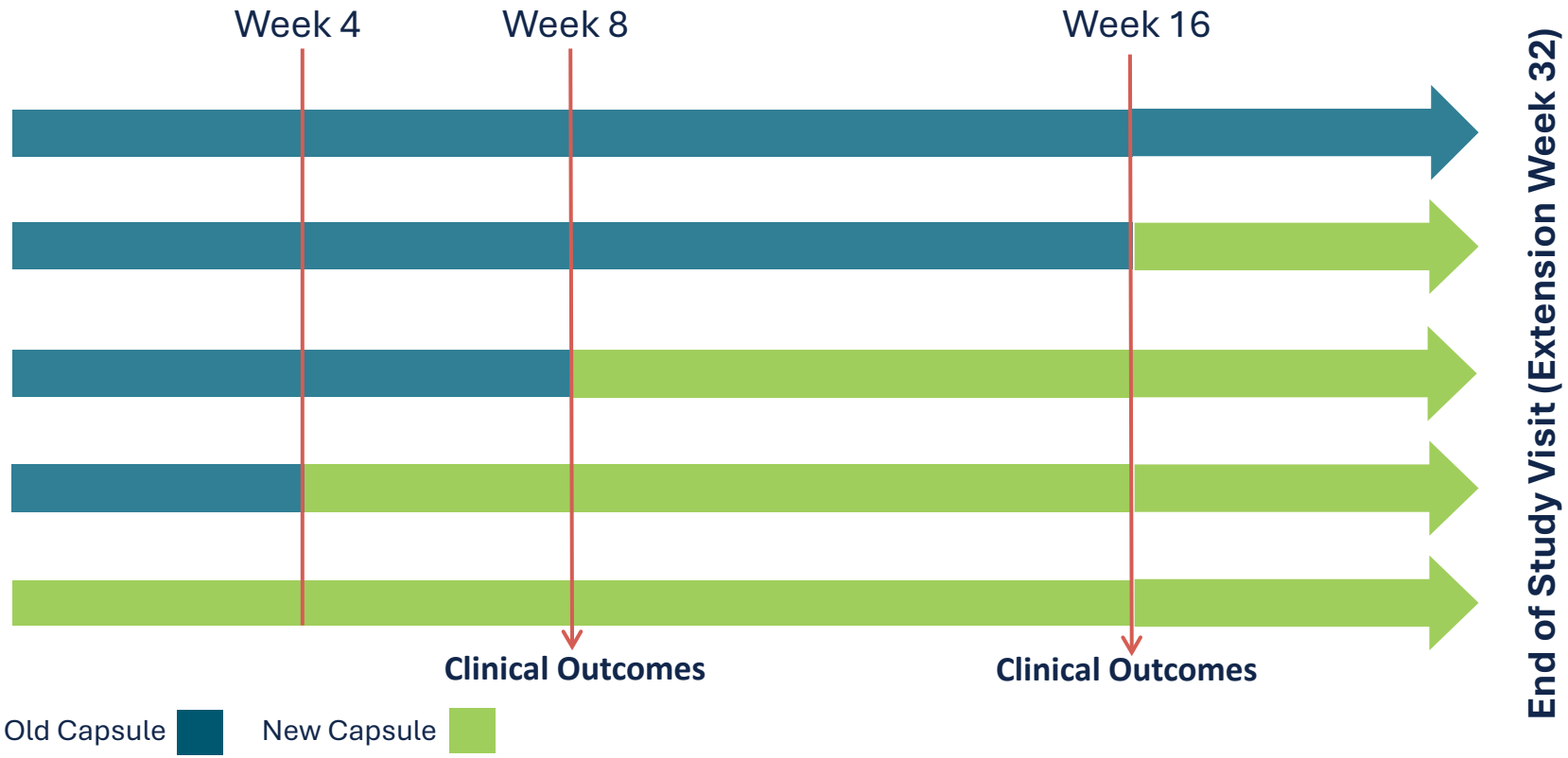
CLINICAL OUTCOME MEASURES

- 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)
- Exploratory:
  - Dementia Cognitive Fluctuation Scale (DFCS)
  - International Shopping List Test (ISLT)
  - Neuropsychiatric Inventory (NPI)
  - Unified Parkinson Disease Rating Scale (UPDRS) Part III (Motor)

Dosing Groups in Extension Phase of RewinD-LB Study

	Number of Participants
Group 1	20
Group 2	35
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

Baseline Characteristics of Extension Phase Participants

	Old Capsules Only During 1st 16 Weeks of Extension (N=55)	New Capsules at Any Time During 1st 16 Weeks of Extension (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)
ISLT Immediate	**13.2** (5.01)	**13.8** (5.05)
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, %)		
Acetyl Cholinesterase Inhibitor (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] at screening	**52** (94.5%)	**75** (79.8%)

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

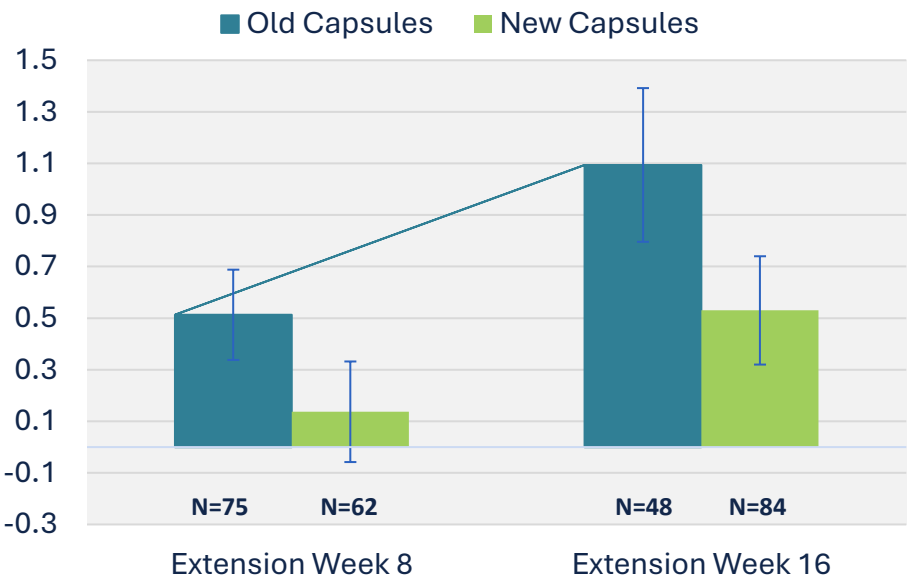
Except where noted, mean (SD) is shown

Analysis Approach

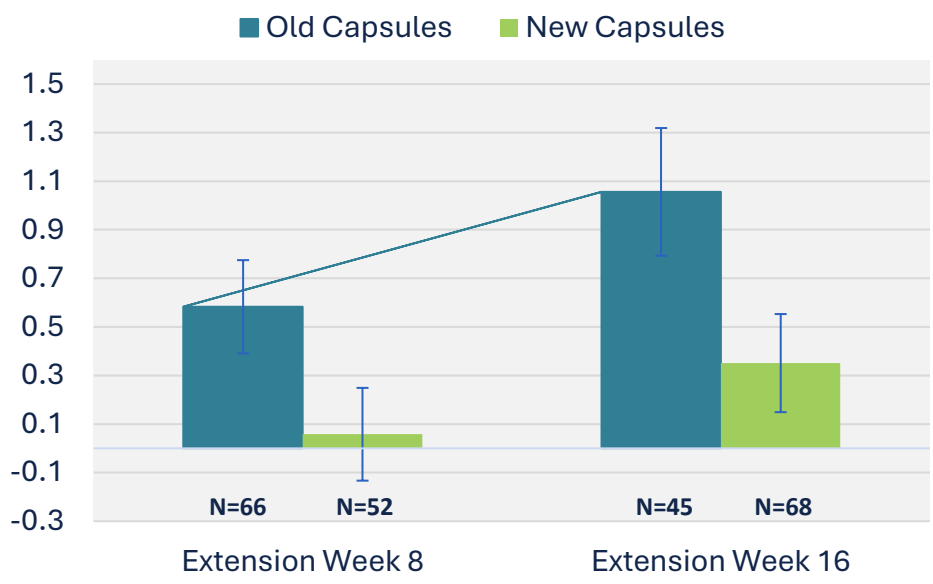
- As per the protocol and statistical analysis (SAP) plan, treatment effects on clinical endpoints evaluated by linear mixed effects model for repeated measures (MMRM) that included all timepoints
  - CGIC, a categorical measure, evaluated by Mann-Whitney statistical test at endpoint
- Main comparison evaluated outcomes in participants receiving New Capsules compared to that in participants receiving Old Capsules during the Extension
  - For the CDR-SB and CGIC, where worsening was noted in placebo recipients, comparisons between New Capsule recipients during the Extension phase and placebo recipients during the Initial phase also evaluated
- To assess likelihood of differences in outcome being due to chance, p-values are reported tor the primary outcome measure and CGIC; 95% confidence intervals for differences between old and new capsules are reported for all other endpoints

Clinically Meaningful Impact on CDR-SB During the Extension

All Participants



Participants with Screening ptau181 < 2.2 pg/mL



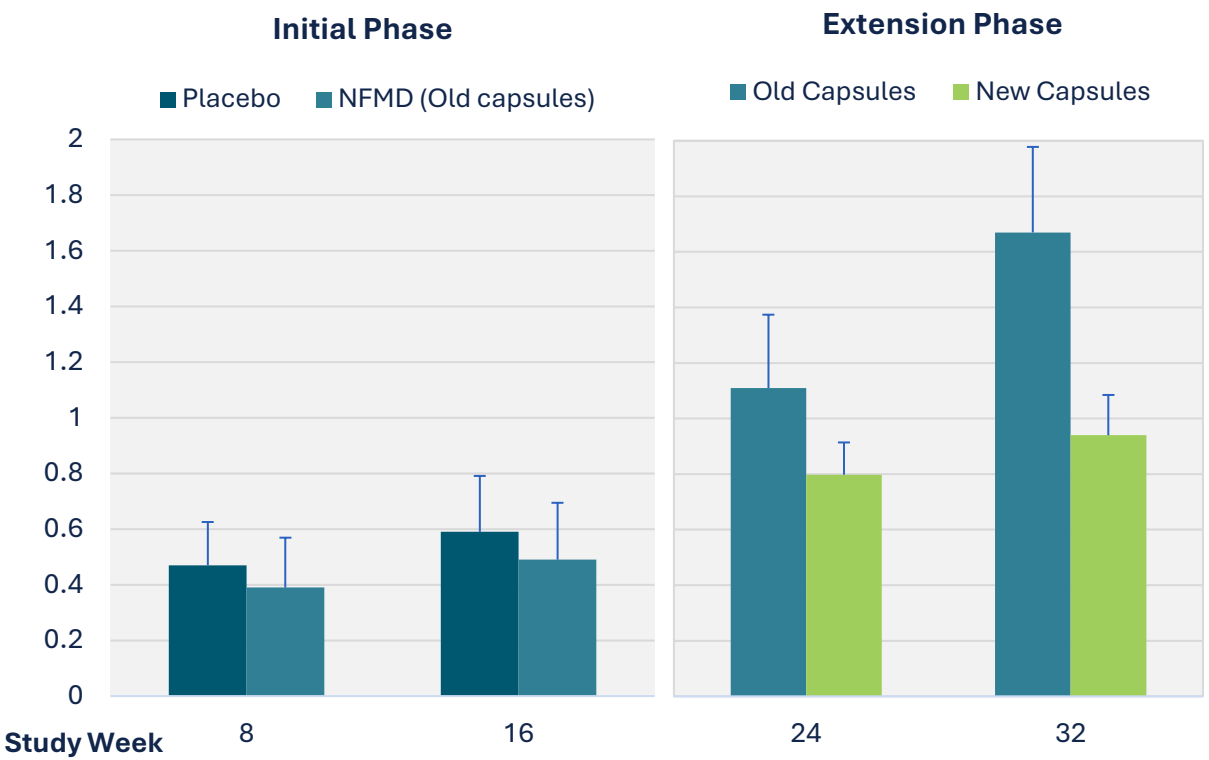
Error bars represent standard error of the mean

	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

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

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

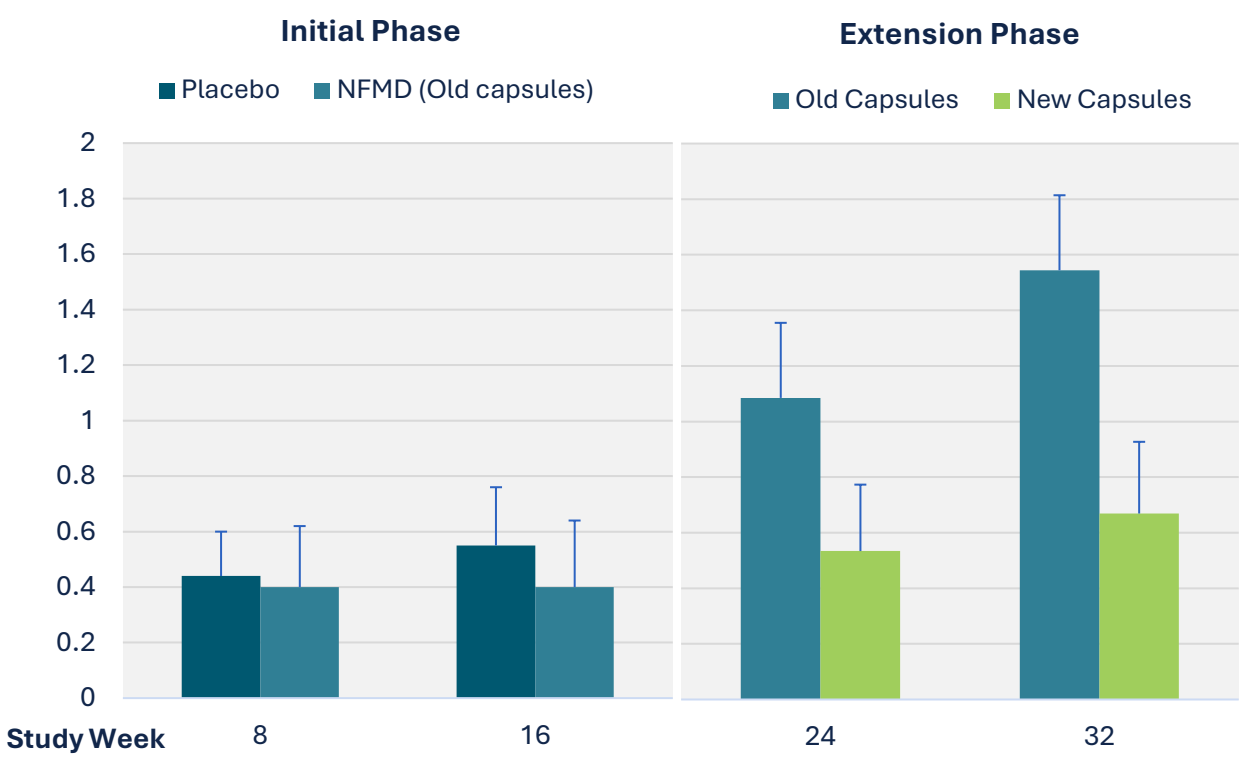
All Participants



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

Number of Participants					
	Week 8	Week 16		Week 24	Week 32
Placebo	78	77	Old Capsules	75	48
NFMD (Old)	77	74	New Capsules	62	84

Participants with Screening ptau181 < 2.2 pg/mL

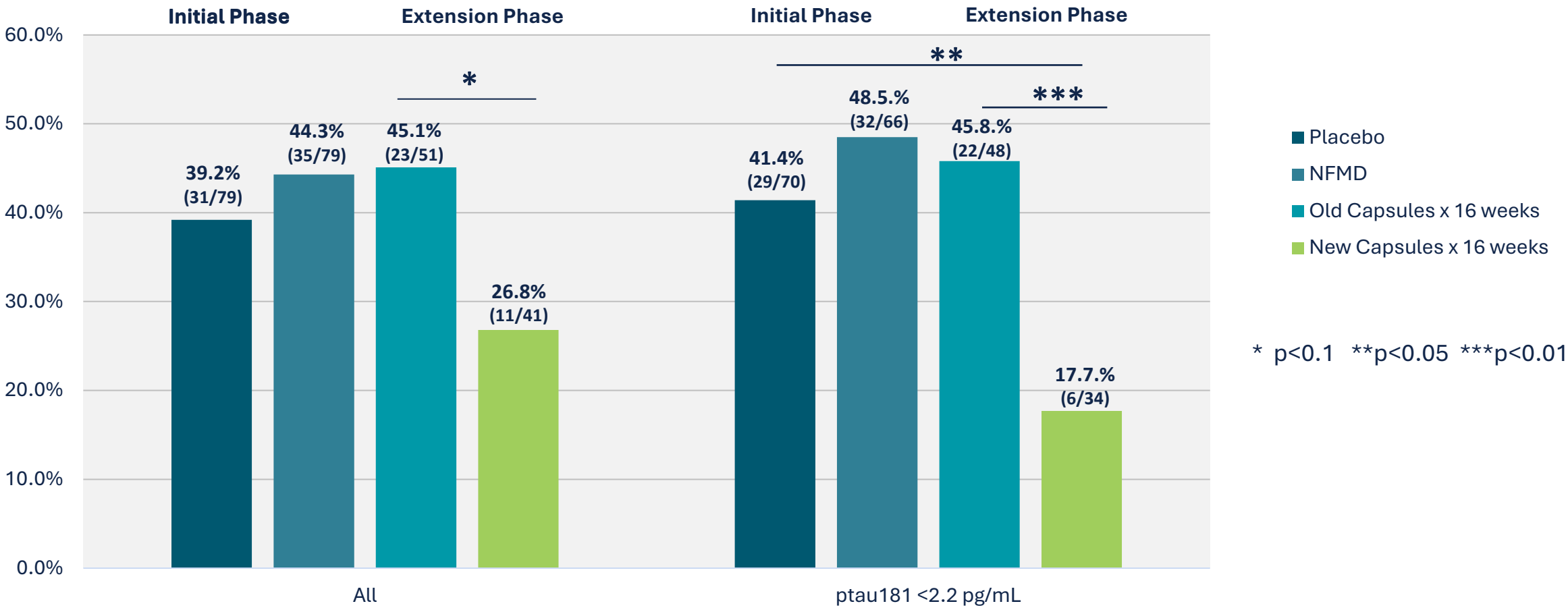


p<0.001 for New Capsules vs. placebo (MMRM analysis)

Number of Participants					
	Week 8	Week 16		Week 24	Week 32
Placebo	66	67	Old Capsules	66	45
NFMD (Old)	62	62	New Capsules	52	68

Clinically Relevant Progression Over 16 Weeks

Percentage of Participants with ≥ 1.5-point increase in CDR-SB over 16 weeks[1]



* p<0.1 **p<0.05 ***p<0.01

Placebo and NFMD (Old) are during 16-week Initial phase of the study; Old and New Capsules during first 16 weeks of the Extension

[1] Early termination considered as a progressor (treatment failure)

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

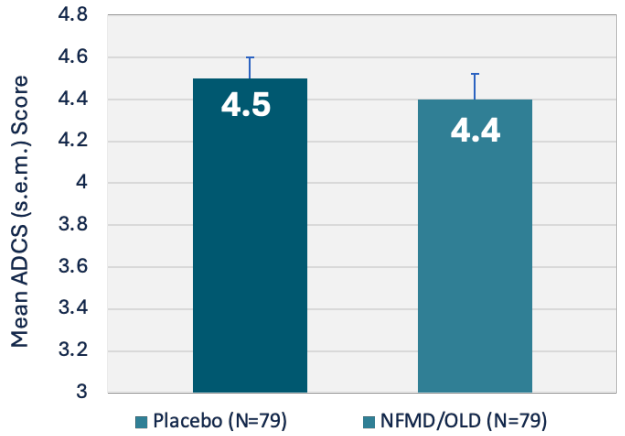
Blinded clinician's assessment of change in clinical status of patient from start of treatment

+1	+2	+3	+4	+5	+6	+7
Marked Improvement	Moderate Improvement	Mild Improvement	Neutral	Mild Worsening	Moderate Worsening	Marked Worsening

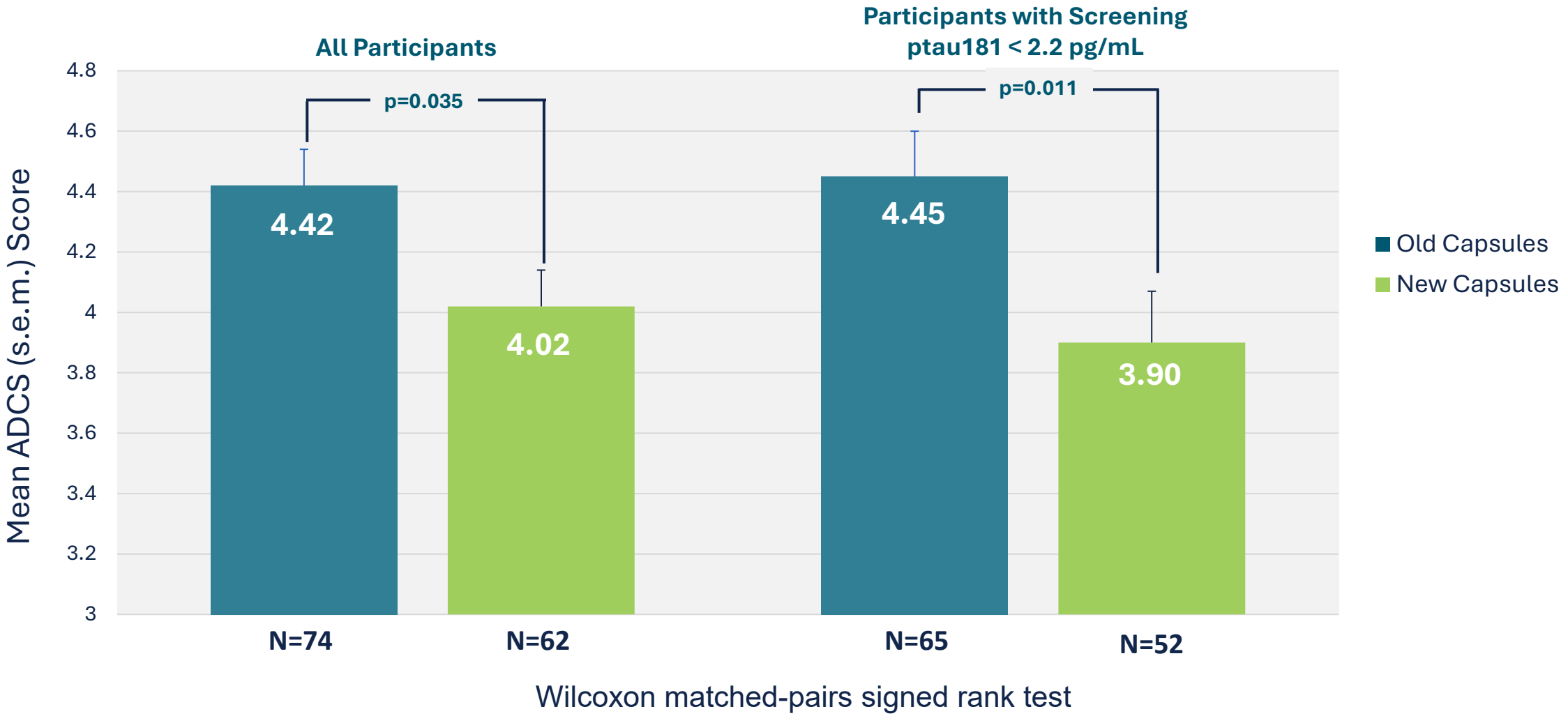
Calculate Group Means from Individual Scores

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

Results in Initial Phase of the Study



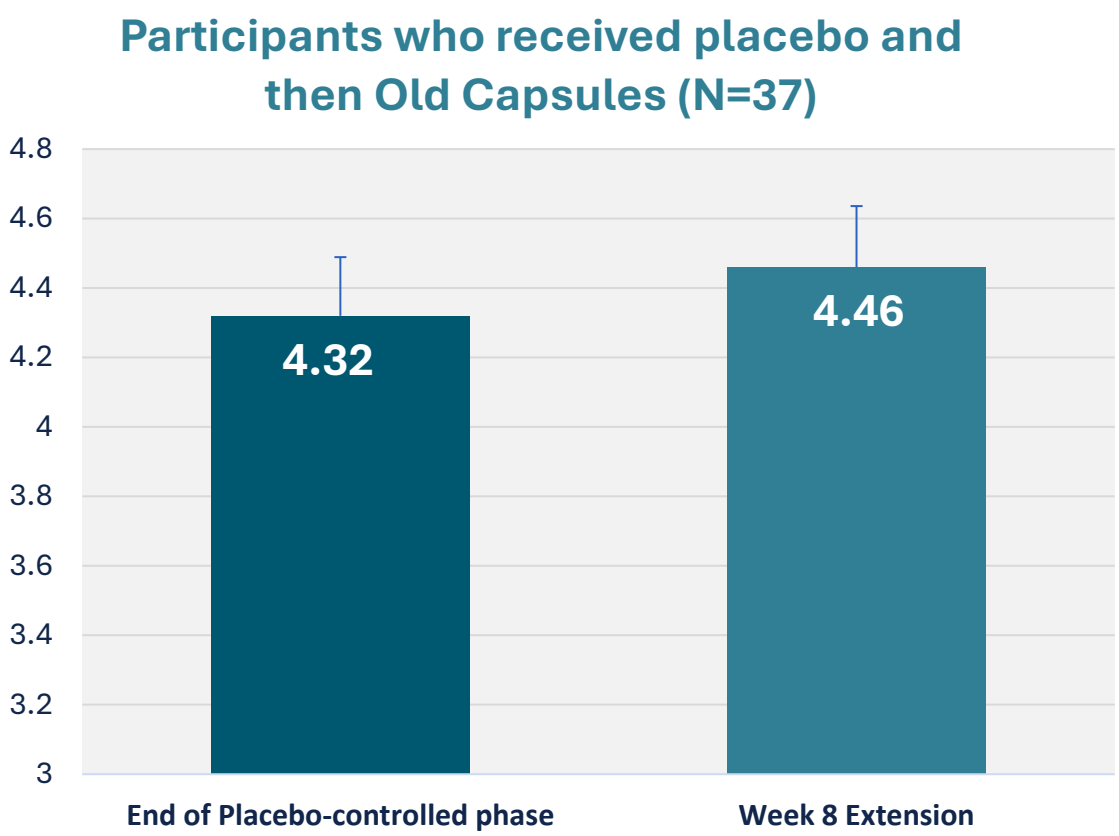
ADCS-CGIC by Capsule Form Administered during Extension Phase

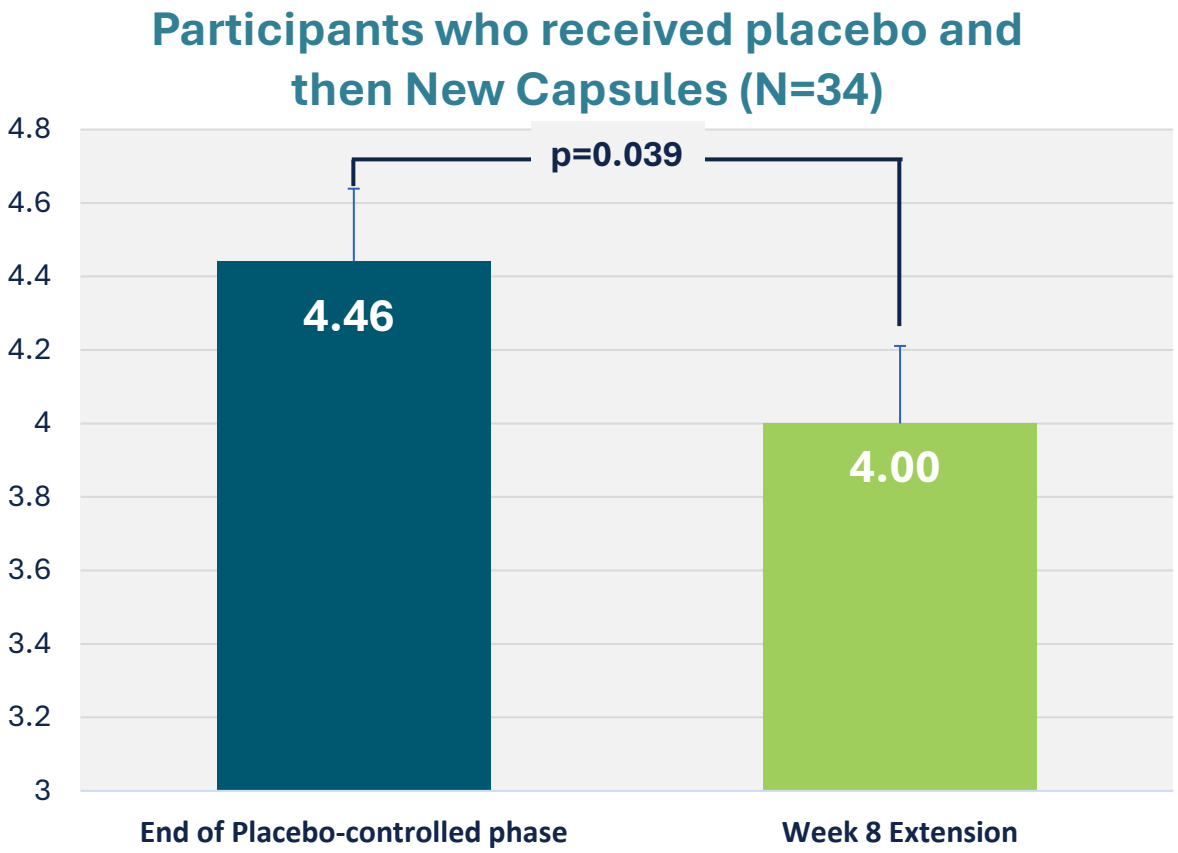


CGIC Administered at Week 8 of the Extension

Error bars represent standard error of the mean

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

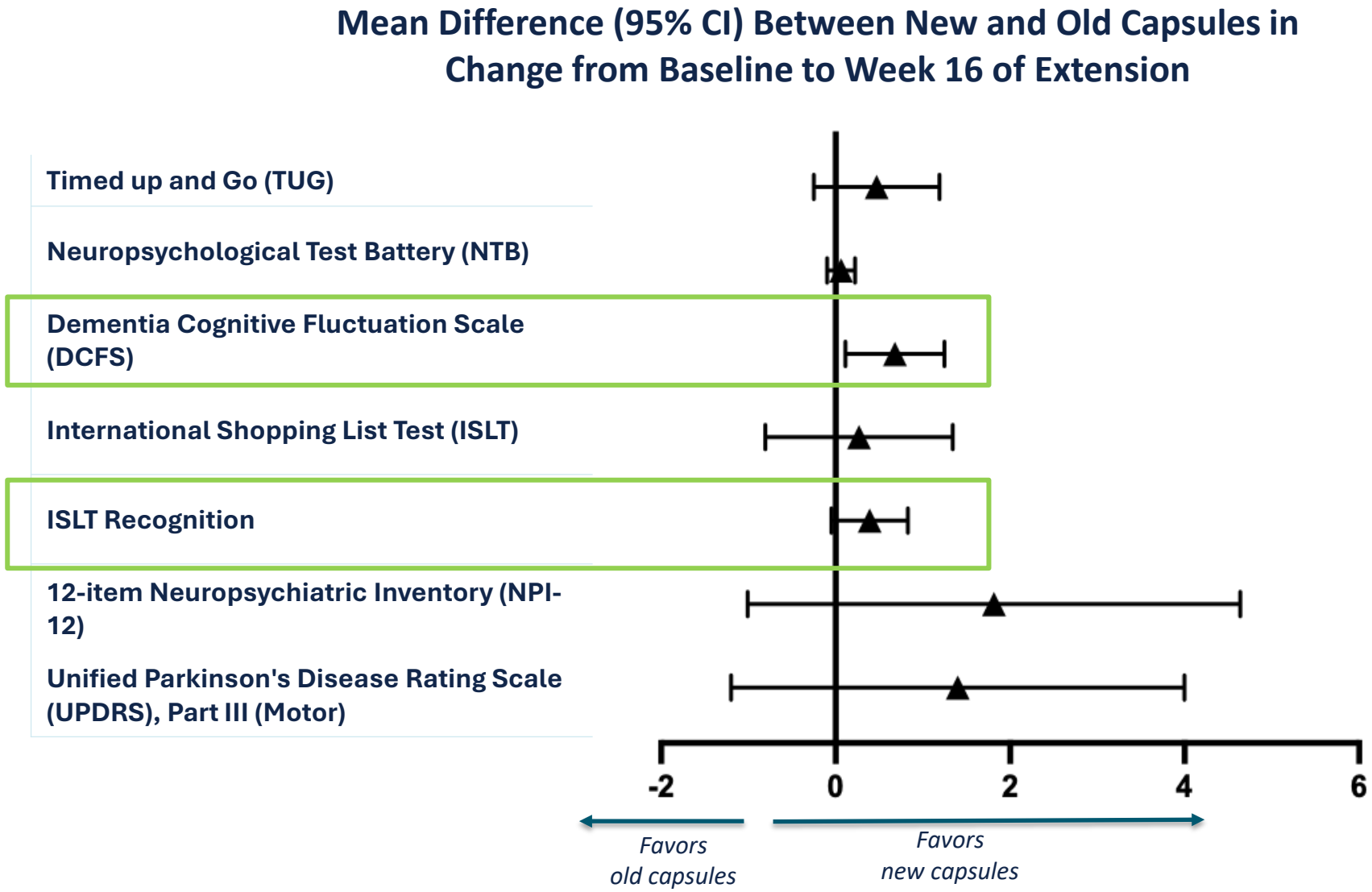




Wilcoxon matched-pairs signed rank test

Error bars represent standard error of the mean

Other Secondary and Exploratory Clinical Endpoints



Note: signs (-/+) adjusted as necessary so that (+) difference reflects better outcome

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

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%)

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

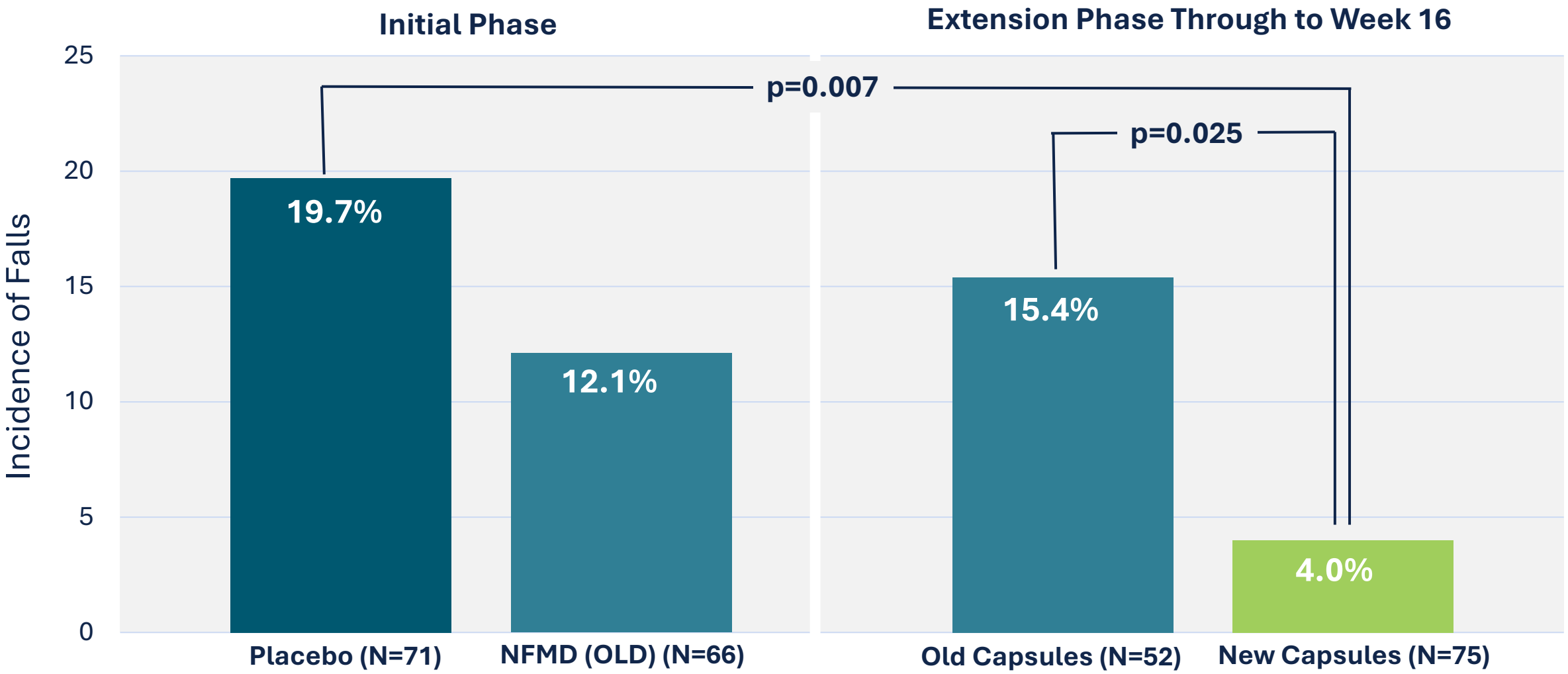
TEAE Seen At Incidence >2% During First 16 Weeks of Extension in Participants with Screening ptau181 < 2.2 pg/mL

	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%)

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



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

Positive effects with neflamapimod treatment with the New Capsules on multiple clinical endpoints:

- Improvement on primary outcome measure, 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 phase)
- Improvement on ADCS-CGIC in comparison to Old Capsules ($p=0.035$) during the Extension and in a within-participant comparison to placebo administration during the Initial phase ($p=0.039$)
- Improvement with New vs. Old capsules on DCFS (fluctuations) and ISLT-Recognition (working memory); positive trends on NPI-12, TUG and UPDRS Part III (Motor)
- 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

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

Conclusions

- The clear differences in clinical activity between New and Old Capsules is consistent with the hypothesis that the Initial phase findings in RewinD-LB were the result of not having achieved pharmacologically active plasma drug concentrations in that phase of the study
- Once target plasma drug concentrations are achieved, neflamapimod demonstrates a meaningful effect on clinical progression, as assessed by the CDR-SB and CGIC, in patients with DLB who do not have AD co-pathology
  - Findings replicate Phase 2a study results and demonstrate proof-of-concept for neflamapimod as a treatment for DLB
  - The pattern of the effects across the full set of clinical endpoints evaluated are consistent with preclinical results in which neflamapimod beneficially impacts the disease process in the basal forebrain

Acknowledgements

- Patients, caregivers, study investigators and clinical site staff involved with the RewinD-LB study
- Clinical project teams at Worldwide Clinical Trials and CervoMed Inc.
- Members of the Data Safety Monitoring Board for the RewinD-LB study: Kenneth Rockwood MD, FRCPC, FRCP, FCAHS (Chair), Jennifer Goldman MD MS, Janet Wittes, PhD
- Primary funding source for the clinical trial: US National Institutes of Aging (NIA) Grant #R01AG080536.

Backup

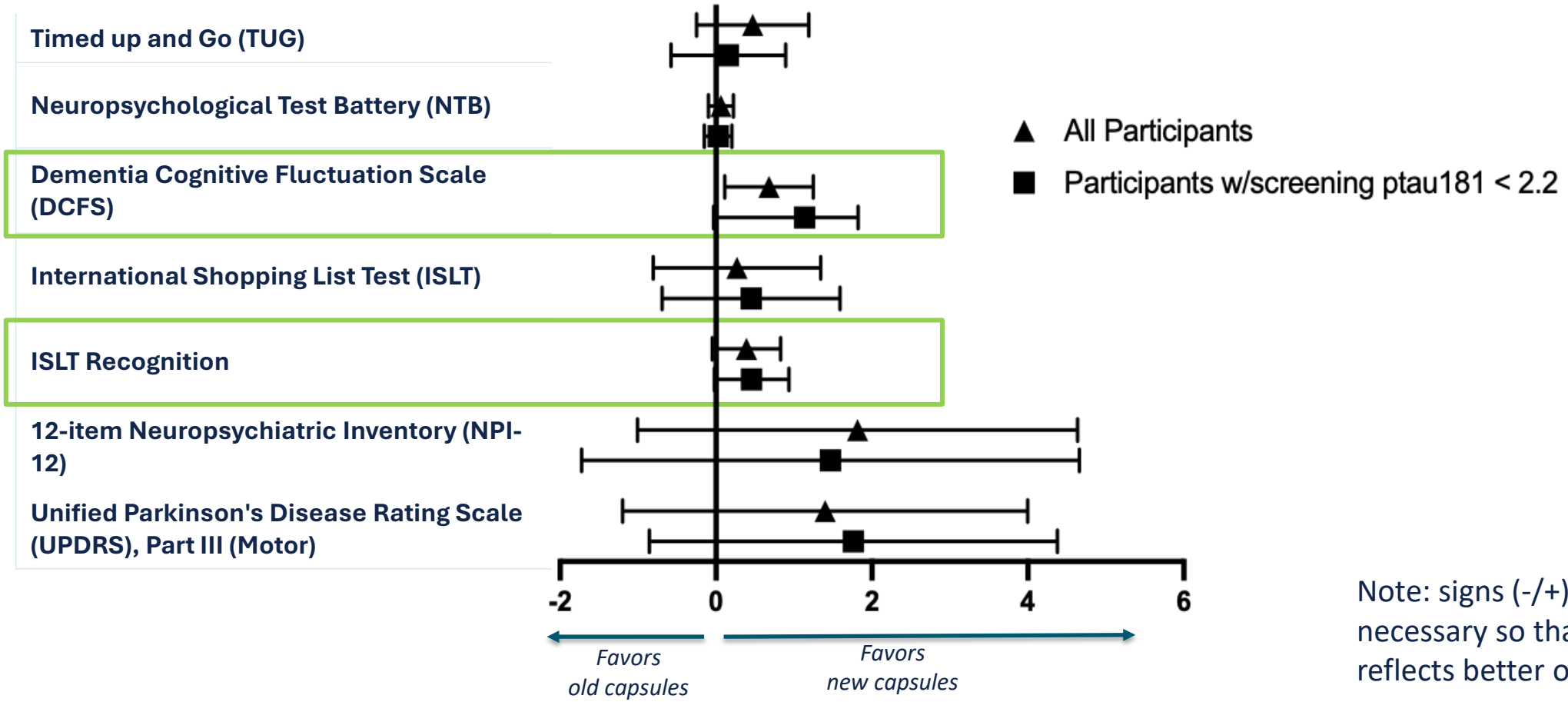
Disease Characteristics at Extension Phase Baseline (Overall Study Week 16)

	Old Capsules Only During 1st 16 Weeks of Extension (N=55)	New Capsules at Any Time During 1st 16 Weeks of Extension (N=94)
CDR-SB	**4.87** (2.41)	**4.79** (2.45)
TUG	**12.0** (4.2)	**13.9** (13.7)
DCFS	**9.6** (3.4)	**10** (3.1)
ISLT Immediate	**13.5 (**5.2)	**13.8** (5.7)
ISLT Recognition	**10.6** (1.7)	**10.2** (1.8)
NPI-12	**13.6** (16.4)	**14.3** (14.7)
UPDRS Part III	**28.9** (16.5)	**32.0** (17.8)

Mean (SD) is shown

Other Secondary and Exploratory Clinical Endpoints

Mean Difference (95% CI) Between New and Old Capsules in Change from Baseline to Week 16 of Extension



Note: signs (-/+) adjusted as necessary so that (+) difference reflects better outcome