



Zervimesine: a Once-daily Oral Therapeutic Advancing Towards Phase 3

October 2025

Forward-looking Statements

FORWARD-LOOKING STATEMENTS

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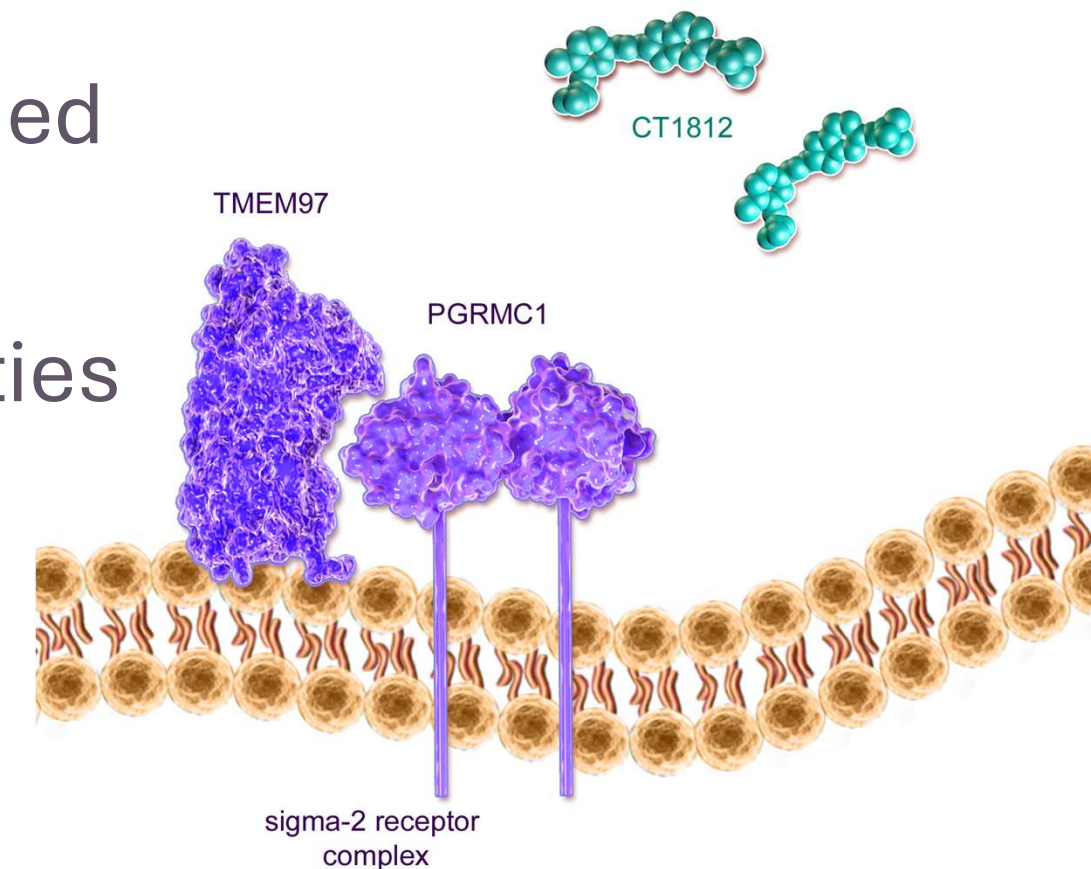
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Novel MoA Discovered Through Founder's Screening Assay

Zervimesine Interrupts Binding of Toxic Oligomers

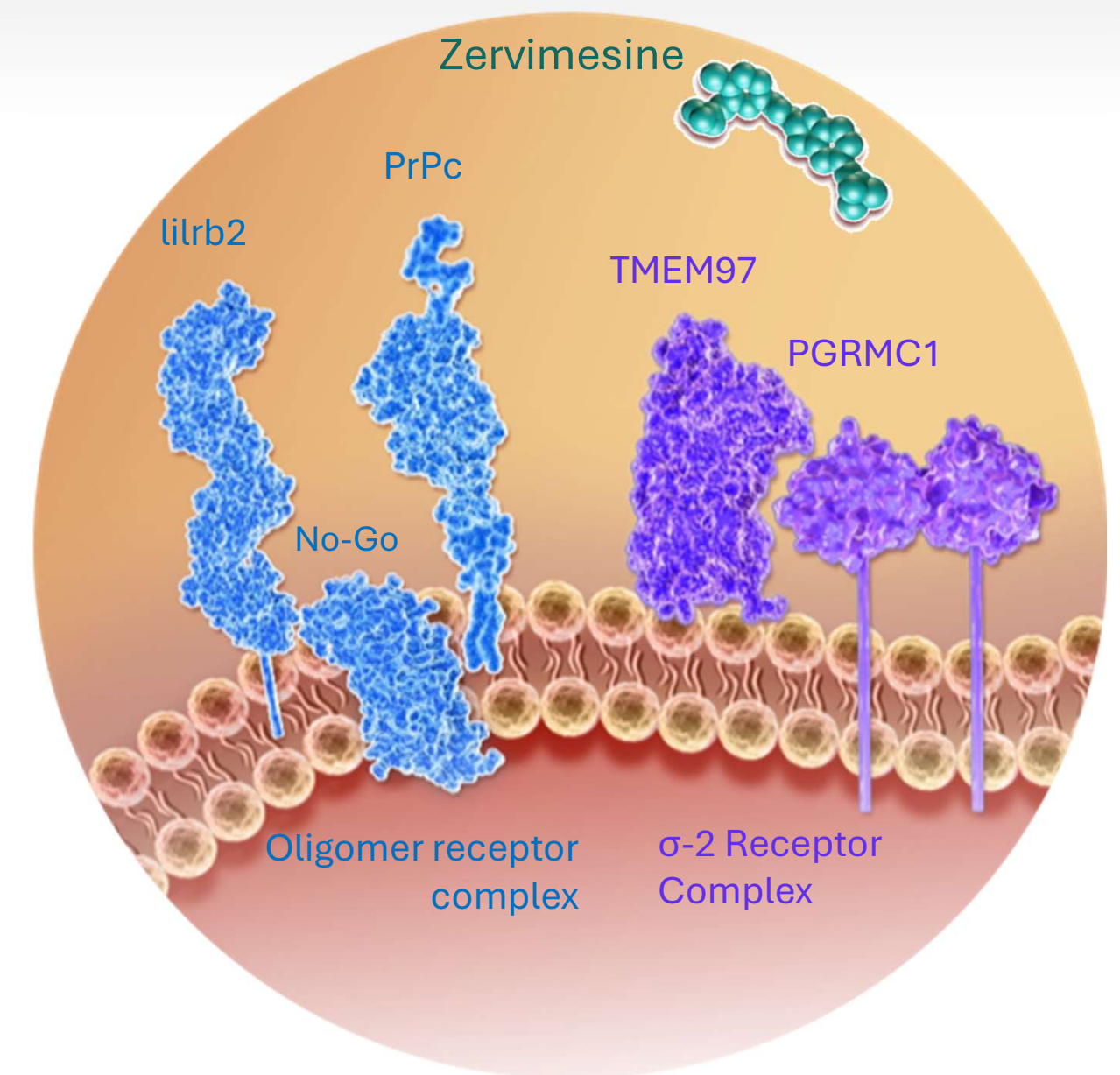
- Founders developed a method of culturing neurons to create a mature nervous system “in a dish”
- Screened 10,000 compounds through this assay and identified 5 unique chemical series
- Zervimesine readily crossed BBB with good drug-like properties
- Early work led to NIH grants, which funded through Phase 2
- Zervimesine's MoA - protecting neurons from toxic oligomers - is unique and potentially complementary



Zervimesine (CT1812) – Lead Product Candidate

Extensive comp of matter IP on zervimesine and other candidates developed from foundational platform

- BBB-penetrant small molecule oligomer antagonist
- MoA: ligand of TMEM97 (sigma-2) receptor
- Oral, once-daily dosing, favorable safety data
- Fast Track granted for Alzheimer's disease



Findings from Completed Studies Support Phase 3 Plans

Program	Preclin	Phase 1	Phase 2	Phase 3
Alzheimer's disease <i>Early-to-mild Alzheimer's disease</i>			Phase 2 COG0203 • START	
Completed Studies				
Mild-to-moderate Alzheimer's disease			Phase 2 COG0201 • SHINE	
Mild-to-moderate DLB			Phase 2 COG1201 • SHIMMER	
Dry age-related macular degeneration <i>GA secondary to dry AMD</i>			Phase 2 COG2201 • MAGNIFY	

Takeaways from completed studies

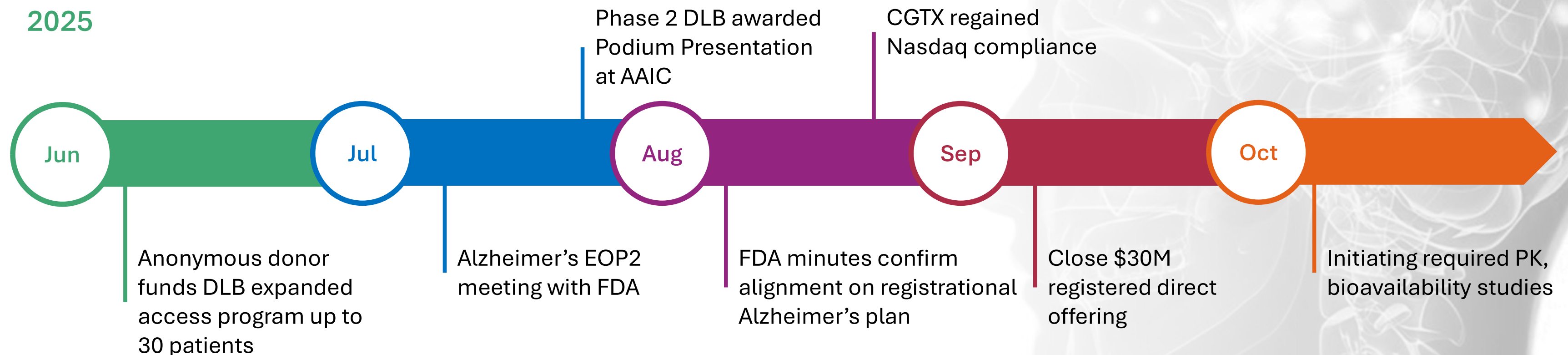
- Phase 2 SHINE Study: Efficacy across cognitive measures in mild-to-moderate Alzheimer's disease
- Phase 2 SHIMMER Study: behavioral, functional, cognitive, movement benefit in mild-to-moderate DLB
- Phase 2 MAGNIFY Study: slower lesion growth in geographic atrophy secondary to dry AMD

Executive Program Summary

Compelling data with first-in-class candidate supports registrational plan

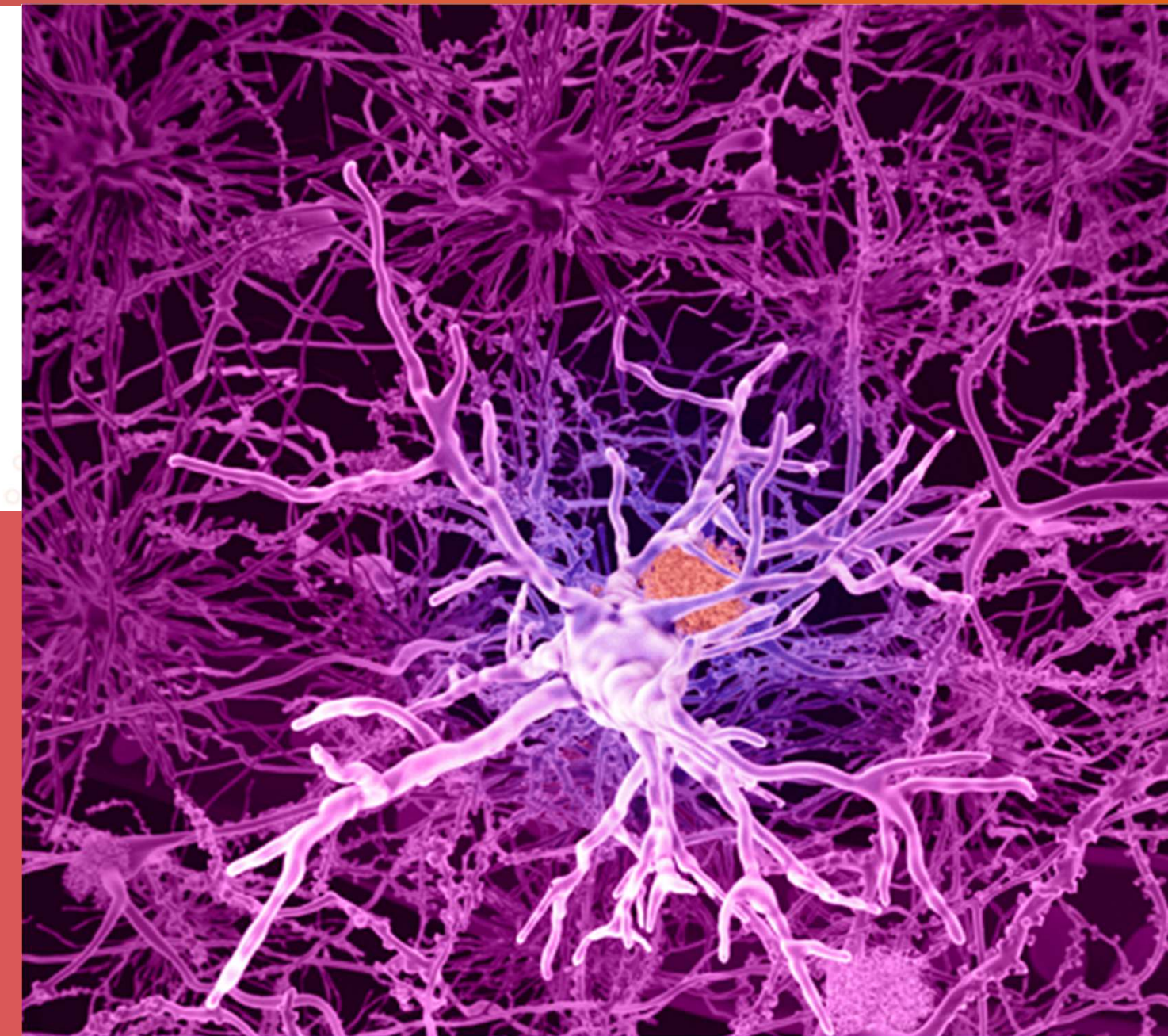
- **Consistent efficacy** signals in Alzheimer's, DLB and dry AMD
 - One of few compounds effective in *both* mild & moderate Alzheimer's disease
 - GA lesion growth reduced with zervimesine treatment
- **Well tolerated safety** profile (over 450 people treated to date)
 - **ARIA unexpected** based on MoA
 - Modest side effect profile for use in aging population
- **Oral QD** administration
 - Reduced burden compared to IV Alzheimer's therapy with required imaging surveillance; intravitreal injections for dry AMD
- **Potential first-to-market for dementia with Lewy bodies (DLB)**
 - Strong responses across **behavioral, functional, cognitive, and movement** measures in Phase 2 SHIMMER study
- **Robust intellectual property** covering platform & compounds, including zervimesine (CT1812) through 2040 with PTE

CGTX Company Summary: With Recent Raise, Advancing Towards Late-stage Studies Following EOP2 FDA Meeting



Alzheimer's Disease

95% slowing of cognitive decline in lower-p-tau217 'SHINE' participants



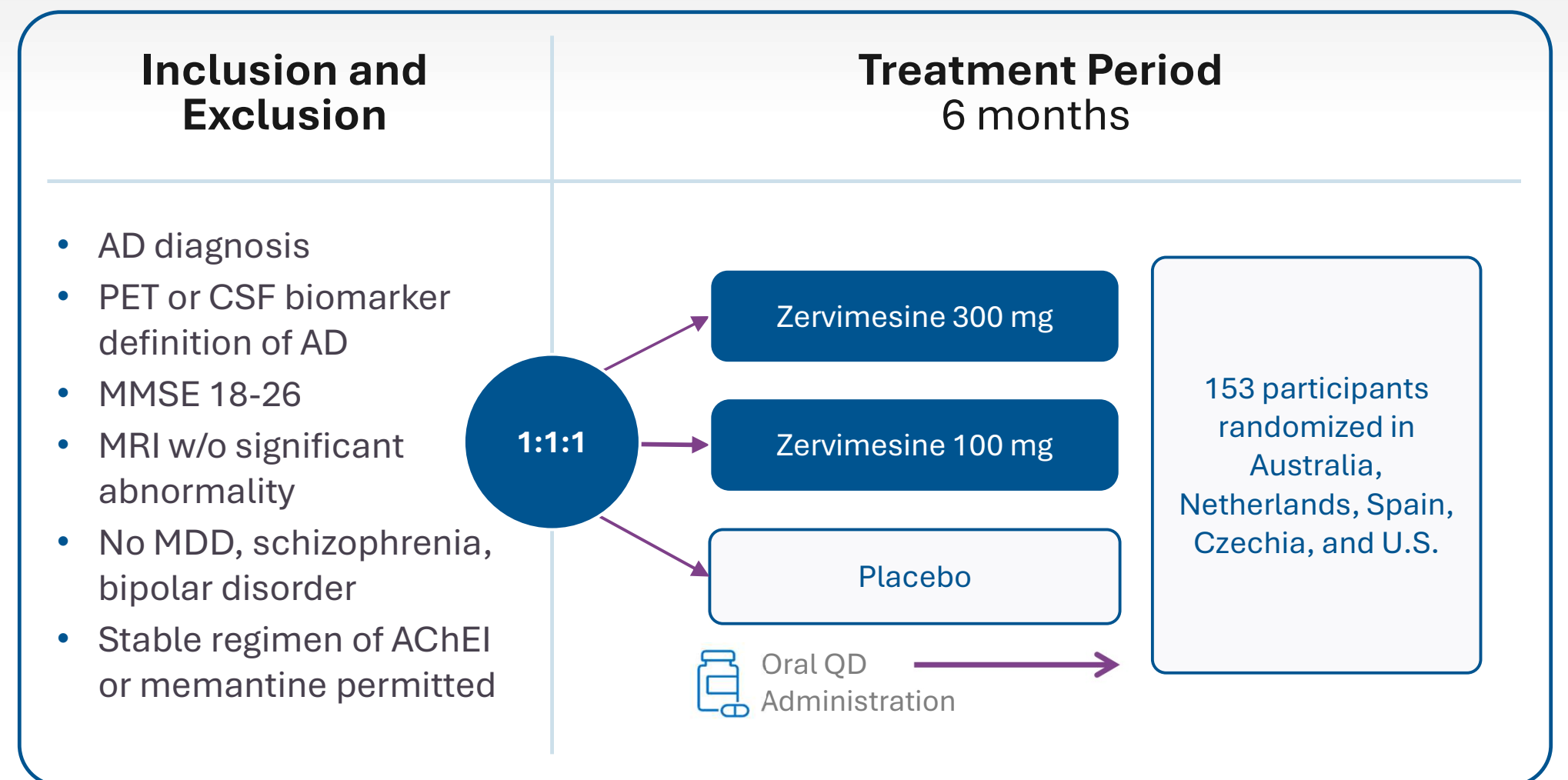
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SHINE: Phase 2 PoC in Mild-to-Moderate Alzheimer's Disease

Well-executed, over-enrolled study, supports advancing clinical development

Enrolled Population:

- PET- or biomarker-confirmed AD
- Majority of participants were female (60%), Caucasian (96%), ~ 72 yo
- Mean MMSE score upon entry: 21.37
- ~60% of patients carry the ApoE4 gene
- Characteristics well-balanced between all 3 arms



SHINE COG0201 study (NCT03507790) partially funded by \$31M NIA grant R01AG058660

SHINE
COG0201

Up to 108% Percent Slowing on Assessments

Strong, consistent efficacy signals across measures

Zervimesine
Pooled
(100/300mg)

↓ median
p-tau217

 Cognition			 Function	
ADAS-Cog 11	ADAS-Cog 13	MMSE	ADCS-ADL	ADCS-CGIC
▼	▼	▼	▼	▼
95%	103%	108%	68%	61%

Tau Burden in Amyloid-related AD Clinical Trials

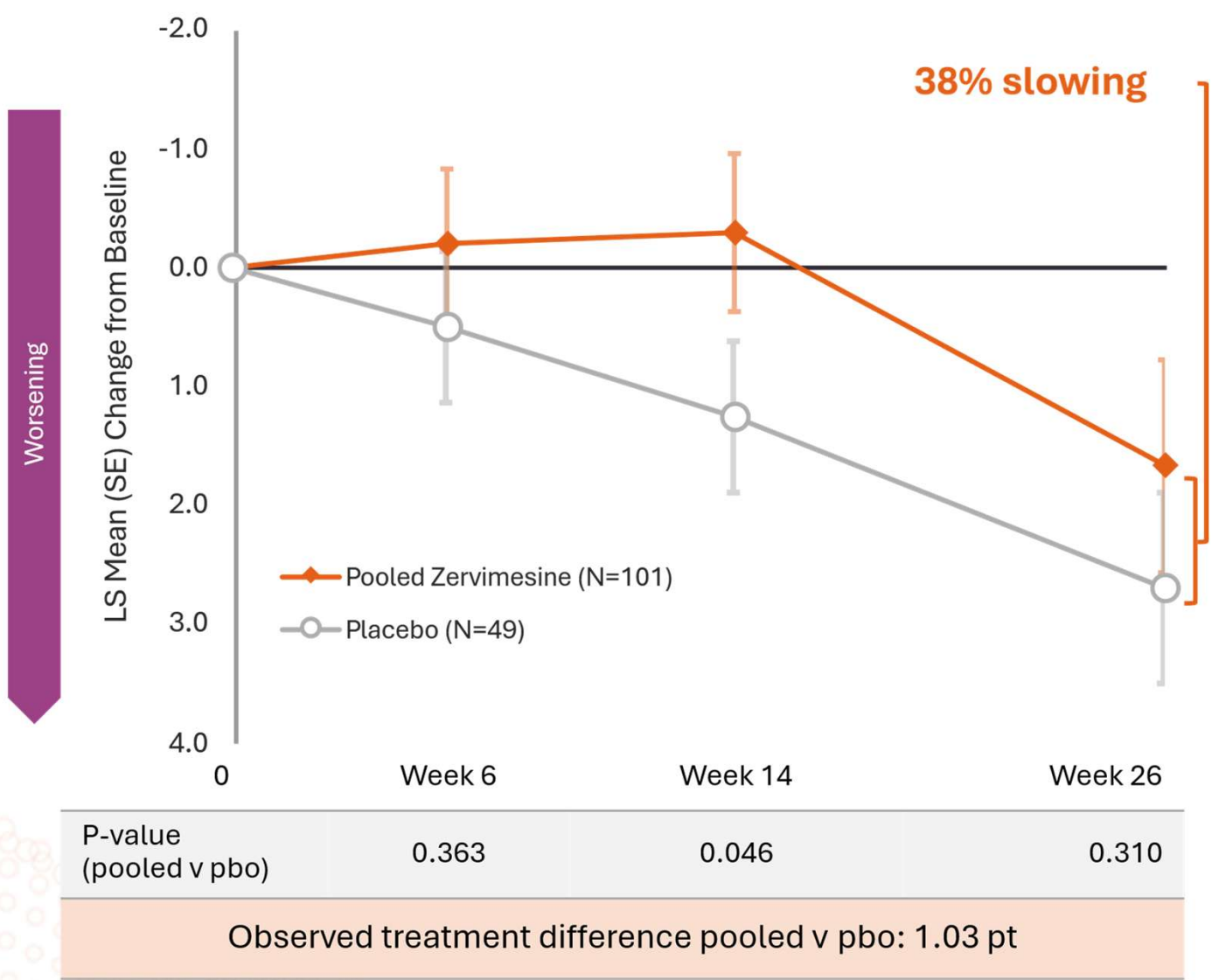
Baseline plasma p-tau217: a predictive biomarker of response to therapy

- Plasma p-tau217 reflects brain amyloid and tau burden
- Prior data indicate that individuals with lower AD pathology at baseline, as reflected by lower levels of plasma p-tau217, have greater response to amyloid-based therapies, eg:
 - Donanemab TRAILBLAZER 2*
 - iADRS: 36% slowing in low tau tercile
 - iADRS: 21% slowing in high tau tercile
- Given zervimesine's MoA of displacing A β oligomers, we hypothesized that larger treatment effect may be observed in participants with lower plasma p-tau217
- Prespecified subgroup analysis defined by median baseline plasma p-tau217 within study population

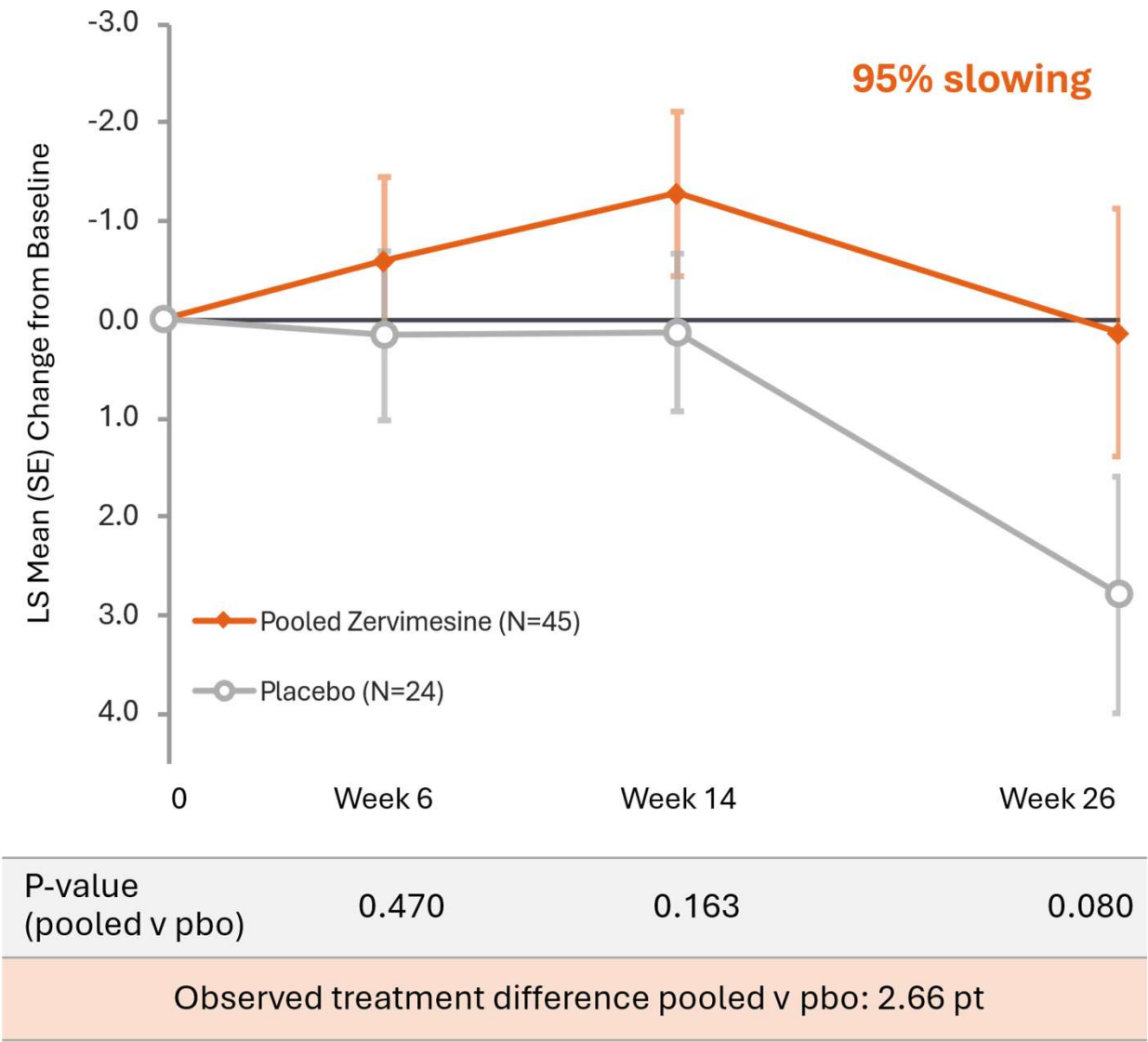
Participants with Below Median p-tau217 Experienced Profound Treatment Effect

Preservation of ADAS-Cog 11 in participants below median plasma p-tau217†

ADAS-Cog 11* mITT population (n=150)



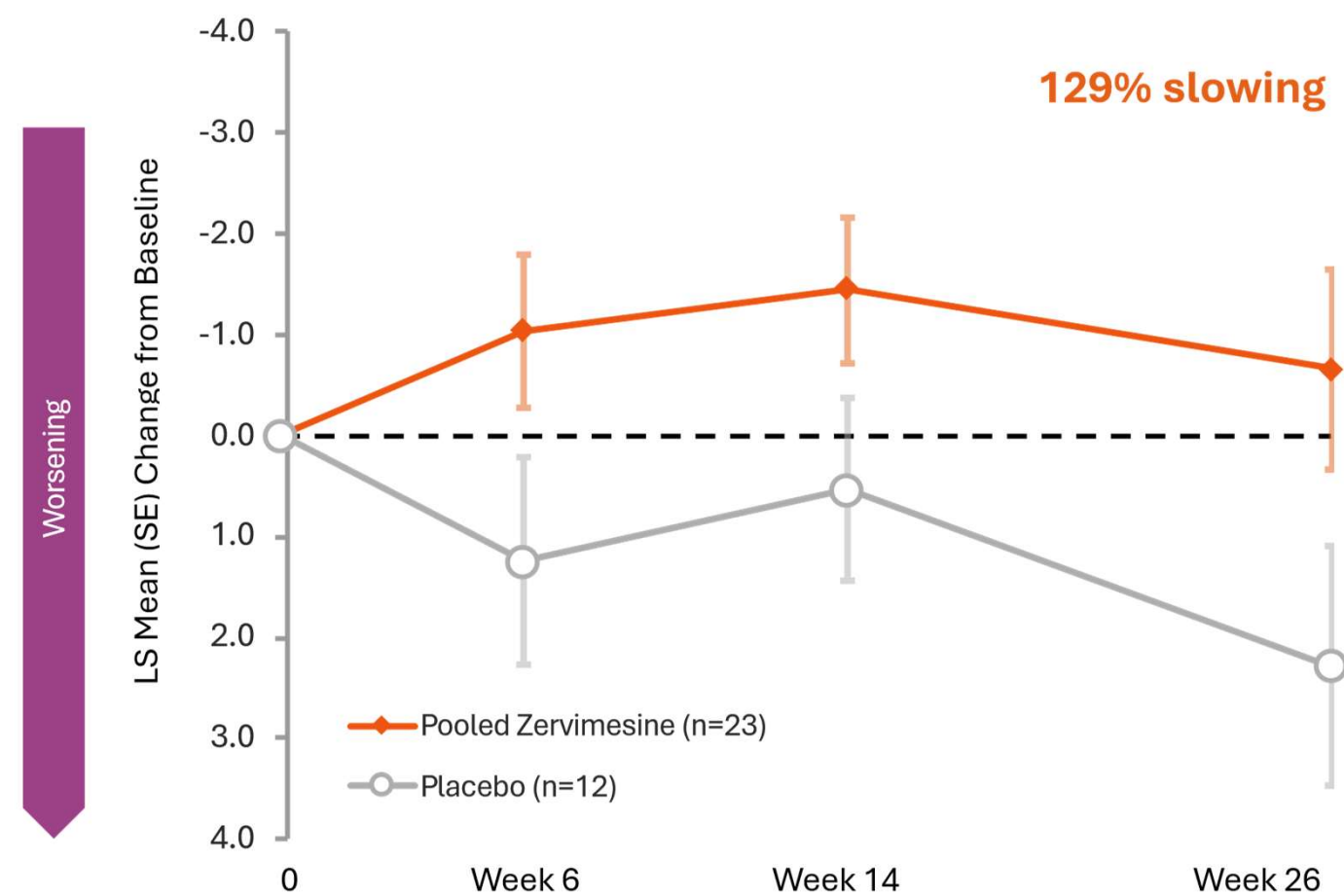
Below median p-tau217 (n=69)



Consistent Treatment Impact in Participants with Lower p-tau217 Across Baseline MMSE scores

Cognitive preservation (ADAS-Cog 11) observed across MMSE range

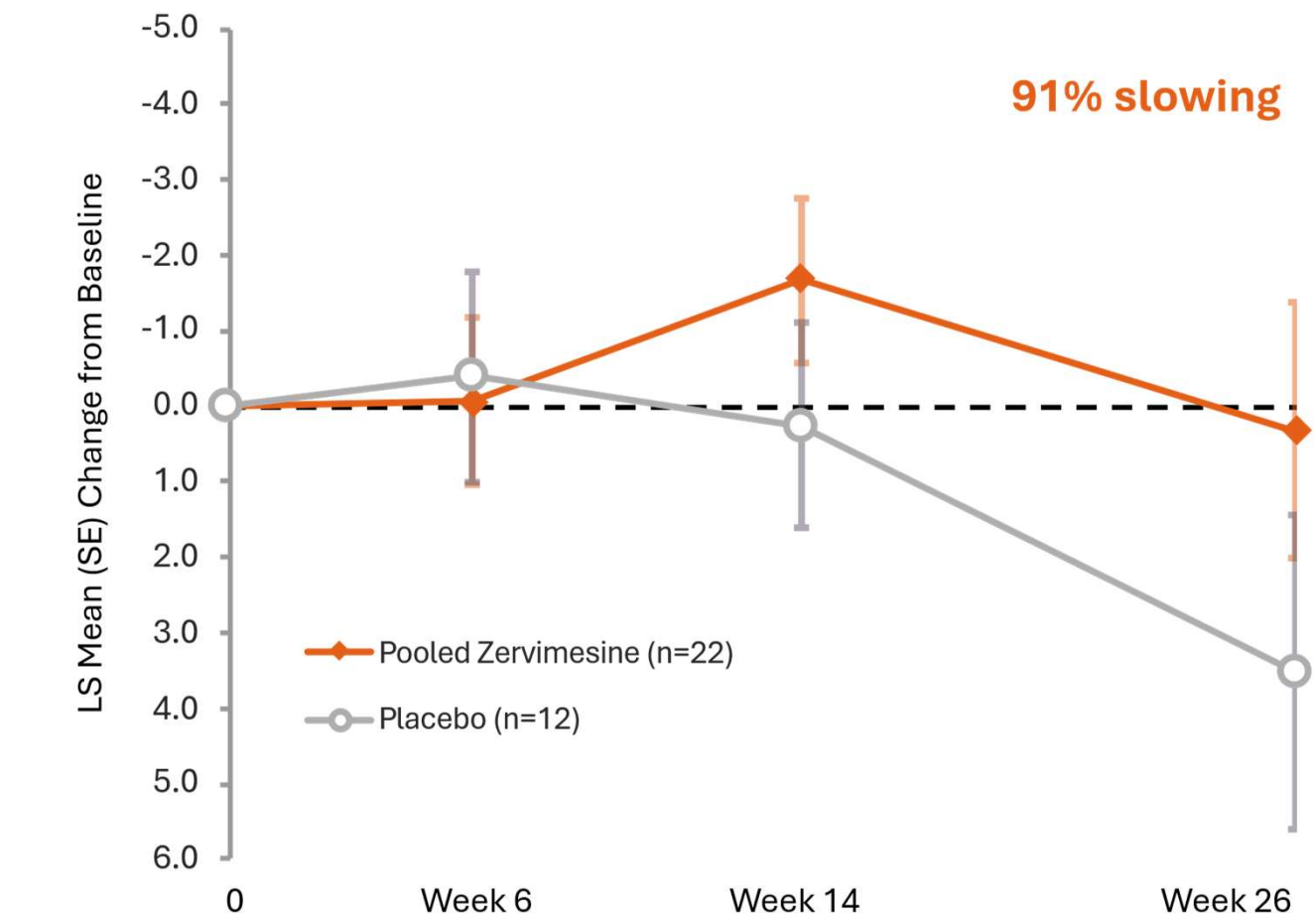
Zervimesine-Treated **Mild** (MMSE 22-26)



P-value (pooled v pbo)	0.087	0.100	0.069
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Observed treatment difference pooled v pbo: 2.9 pt

Zervimesine-Treated **Moderate** (MMSE 18-21) Participants

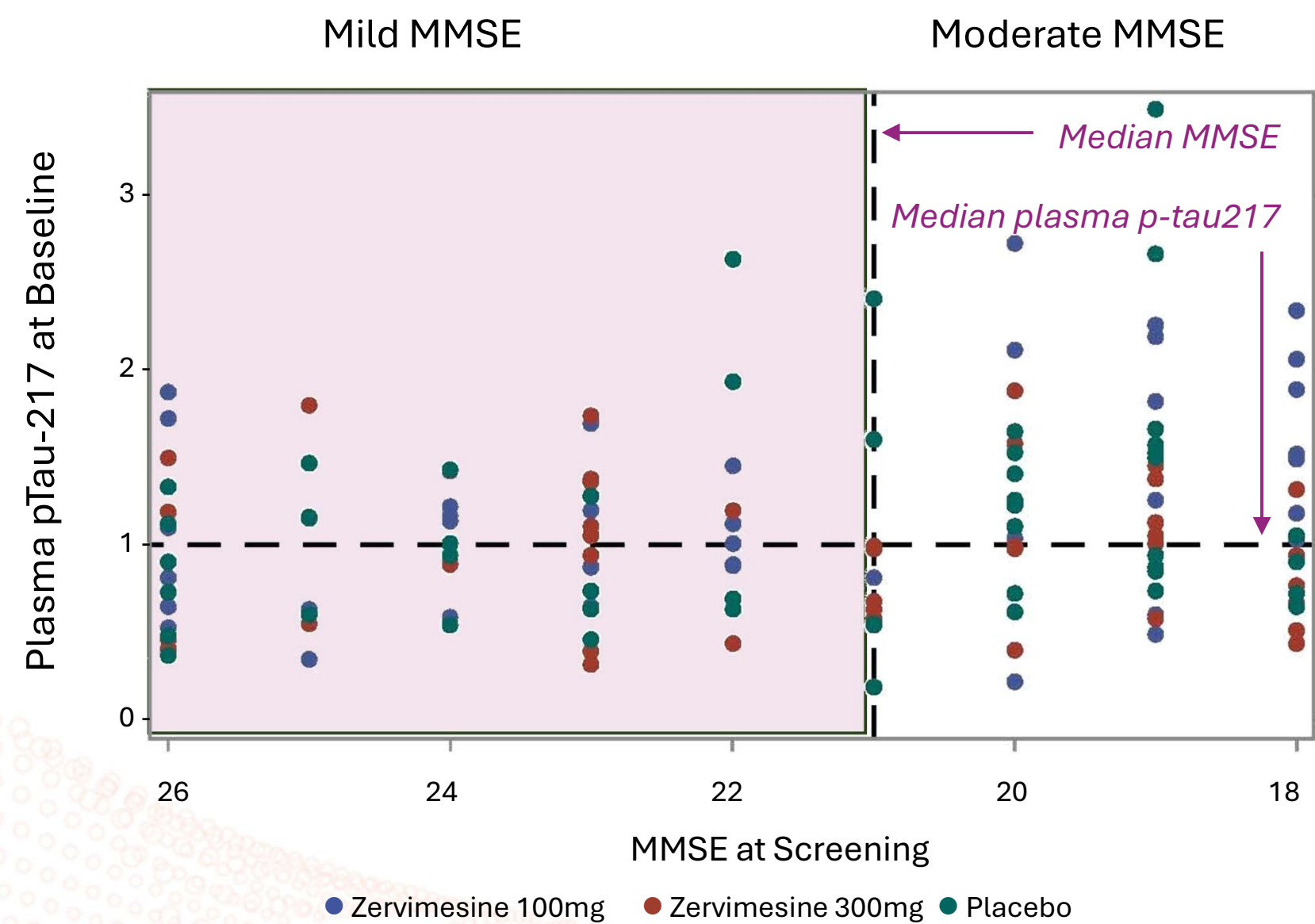


P-value (pooled v pbo)	0.847	0.260	0.237
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Observed treatment difference pooled v pbo: 3.2 pt

Participants Evenly Distributed by Median p-tau217 and MMSE Severity

MMSE at Screening vs p-tau217 at Baseline in SHINE



Baseline Plasma p-tau217			
MMSE at Screening	Below Median	Above Median	Total
Mild (22-26)	35	32	67
Moderate (18-21)	34	37	71
Total	69	69	138

FDA Confirms Phase 3 Plan in Alzheimer's Disease

Alignment reached with FDA during end-of-Phase 2 meeting

- End-of-Phase 2 meeting conducted July 9, 2025
- FDA minutes received August 12, 2025
 - Aligned on following design:
 - Disease stage: Adults with mild-to-moderate Alzheimer's disease
 - Biomarker: P-tau217 at screening $\leq 1.0\text{pg/mL}$
 - Treatment period: 6 months
 - Randomization: 1:1 zervimesine (100mg) vs placebo
 - Endpoints: composite cognitive and functional measure
 - Open-label extension to follow

START – Phase 2 Early AD Study Reaches 75% Enrollment

First study to allow *lecanemab* as background therapy in combination with zervimesine

Enrollment Criteria	Treatment Period 18 months	Assessments	Program Objectives
- Ages 50-85 - Diagnosis of MCI due to AD or mild AD dementia - Brain amyloid via PET - MRI - MMSE: 20-30	Randomized 1:1:1 Zervimesine 200 mg Zervimesine 100 mg Placebo  Oral QD Administration Recruiting 540 adults with early AD at 30+ sites, including ACTC centers of excellence	- Safety - Cognitive and functional testing: - CDR-SB - ADAS-Cog 13, - ADCS-ADL-MCI - Biomarkers - Fluid - imaging	✓ Identify efficacy signal(s) ✓ Confirm safety and tolerability after longer exposure ✓ Identify dose(s) for Phase 3

START COG0203 study (NCT05531656) partially funded by \$81M NIA grant R01AG065248

Dementia Programs:

Strong clinical signals in the two primary causes of dementia:

- Dementia with Lewy Bodies (DLB)
- Mild-to-Moderate Alzheimer's Disease

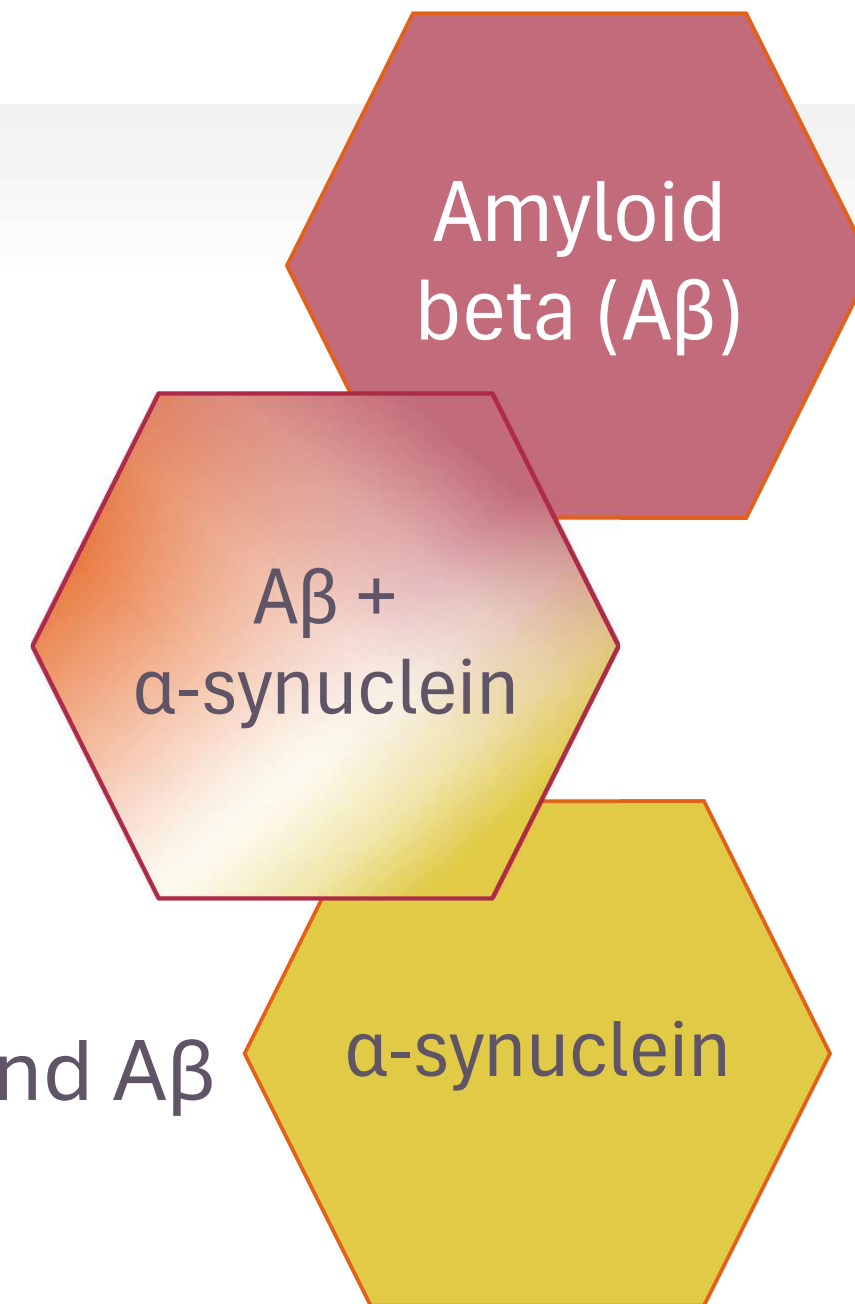


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AD and DLB: 2 Diseases with Overlapping Pathology

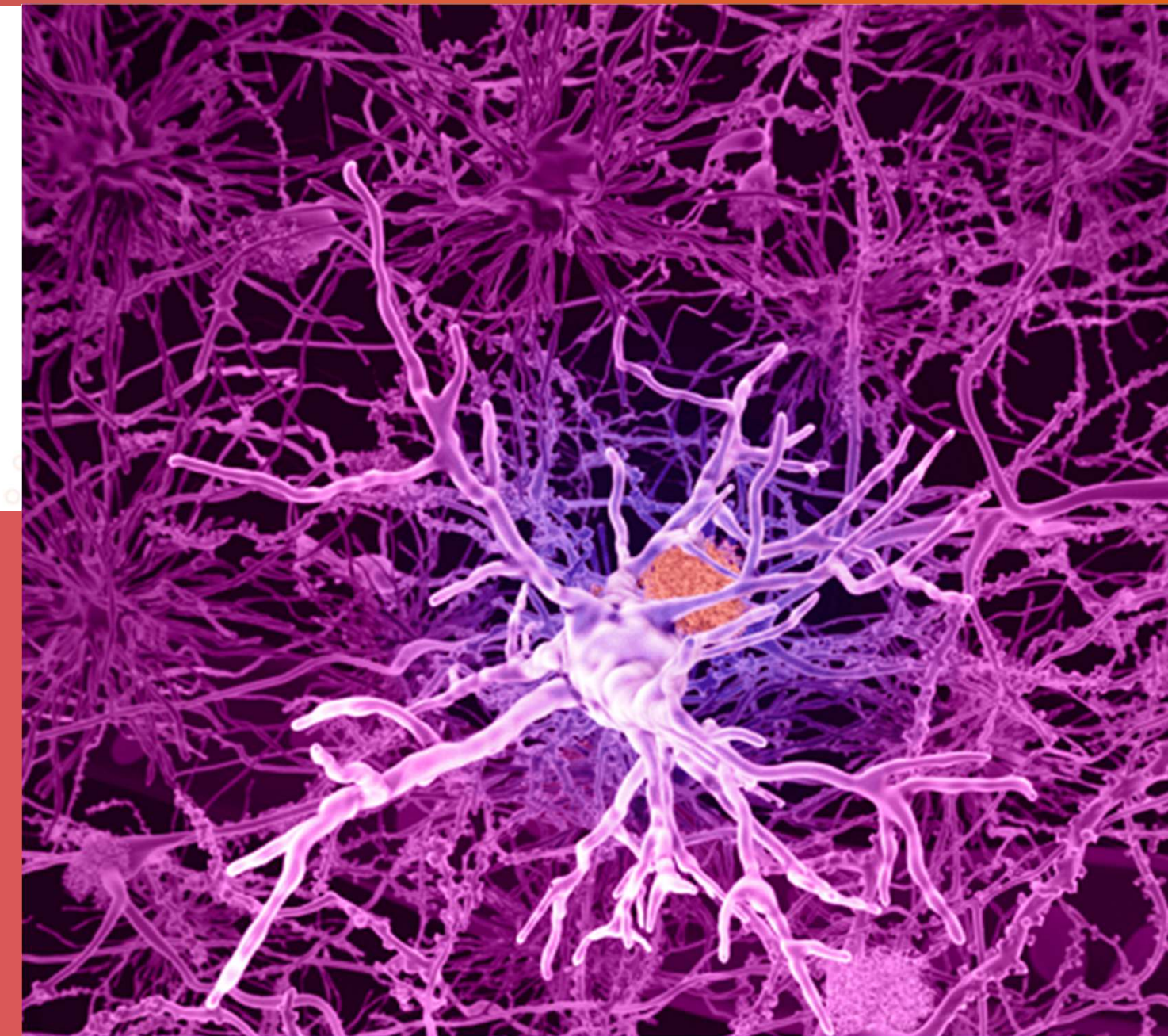
Primary treatment goal – slow the progression of cognitive decline

- A β : closely associated with Alzheimer's pathogenesis
- α -synuclein: closely associated with Lewy body dementias
- Co-pathology is common
 - Up to 80% of DLB patients have BOTH α -synuclein and Amyloid beta (A β)¹
 - Appx 50% of Alzheimer's patients have BOTH A β and α -synuclein²
- Zervimesine has shown protective function against α -synuclein and A β



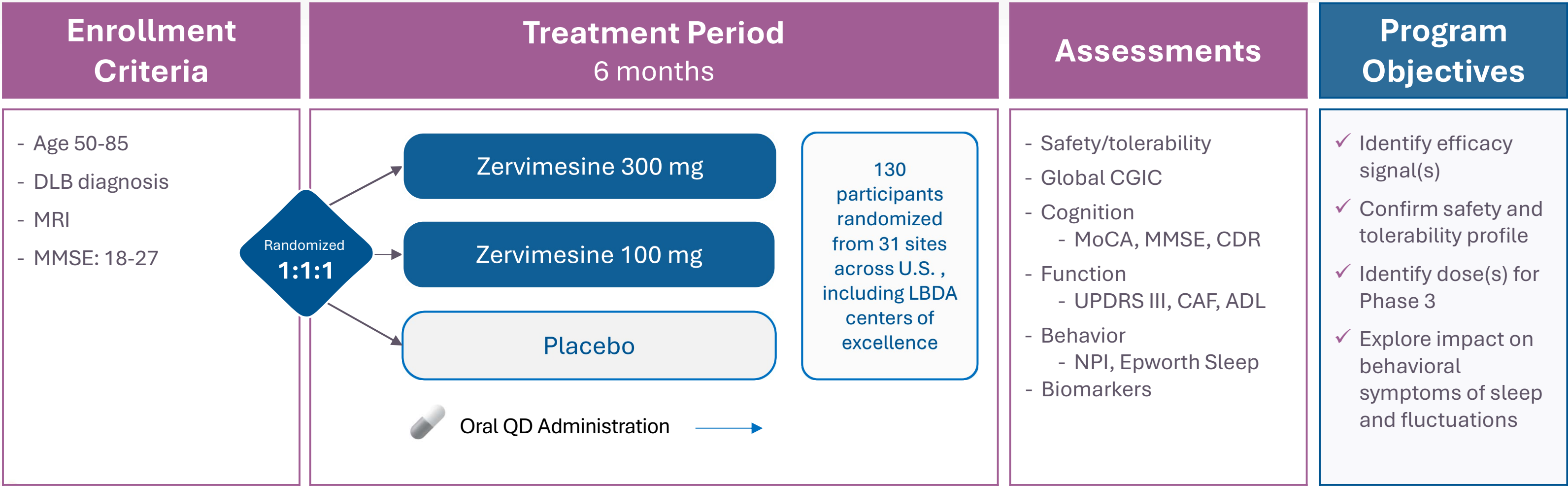
Dementia with Lewy Bodies (DLB)

Strong clinical signals across four major symptom domains in Phase 2 SHIMMER Study



SHIMMER Study in Dementia with Lewy Bodies

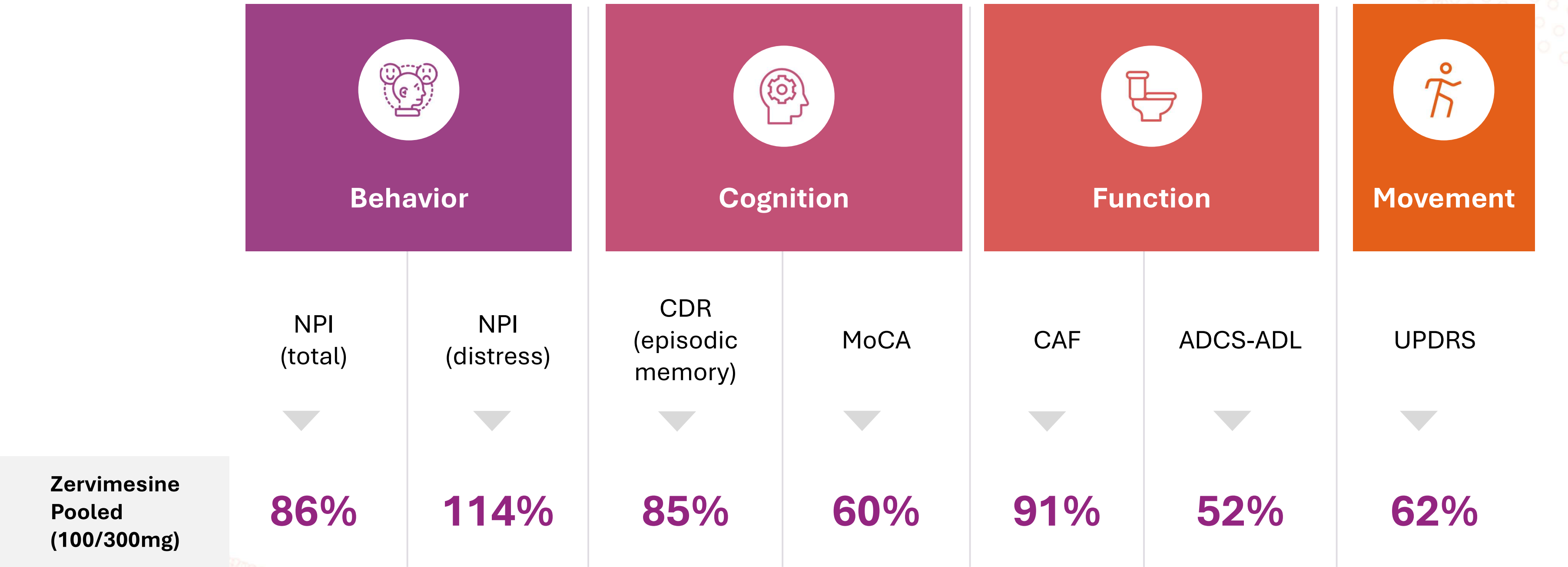
Conducted in collaboration with experts at LBDA and University of Miami



SHIMMER COG1201 study (NCT05225415) partially funded by \$30M NIA grant R01AG071643

Up to 91% Percent Slowing on Assessments

Strong clinical signals across major DLB symptoms relative to placebo



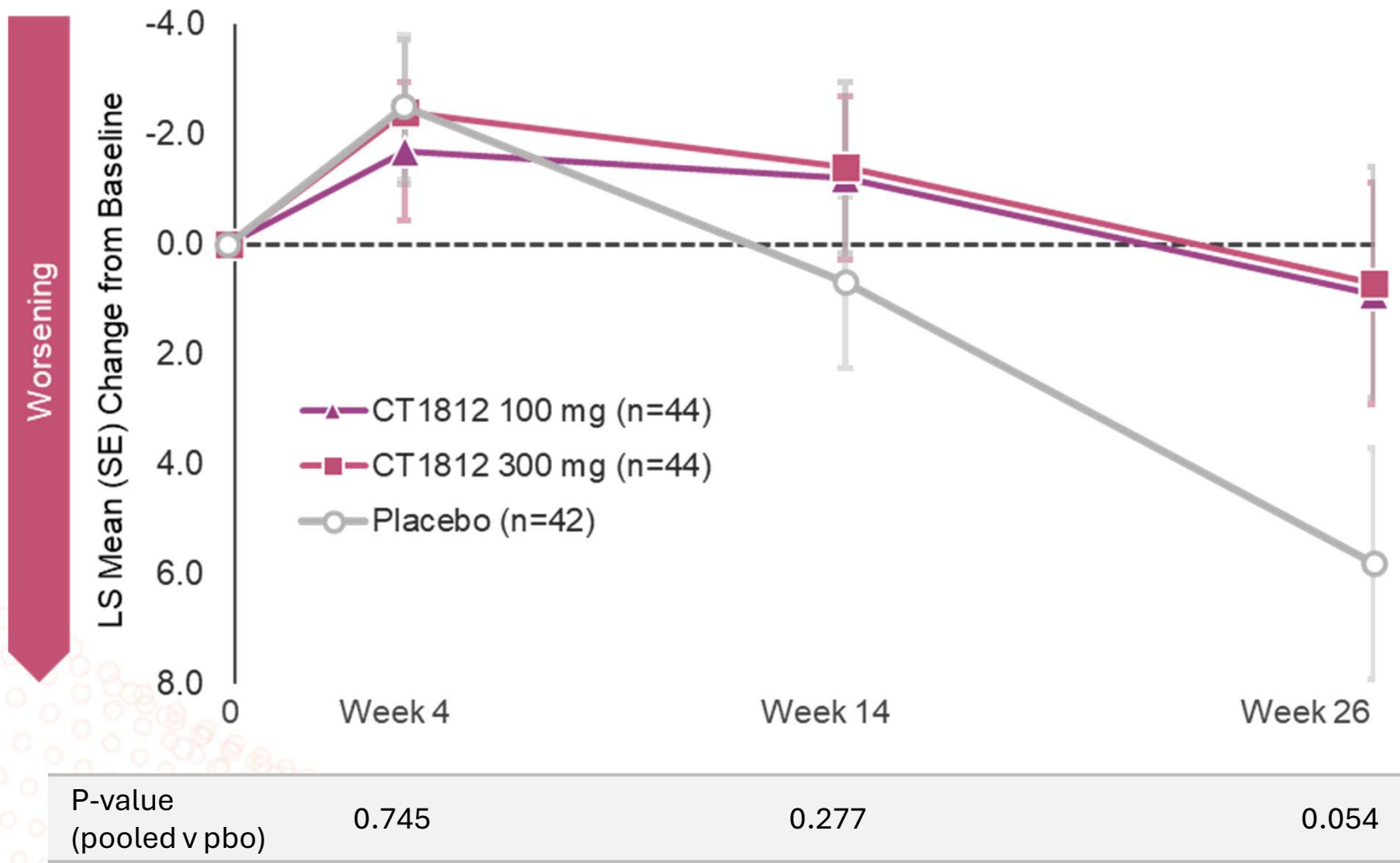
Zervimesine Showed Dramatic 86% Impact on Neuropsychiatric Measures

NPI captures a variety of patient disturbances, including hallucinations, anxiety, and delusions

NPI

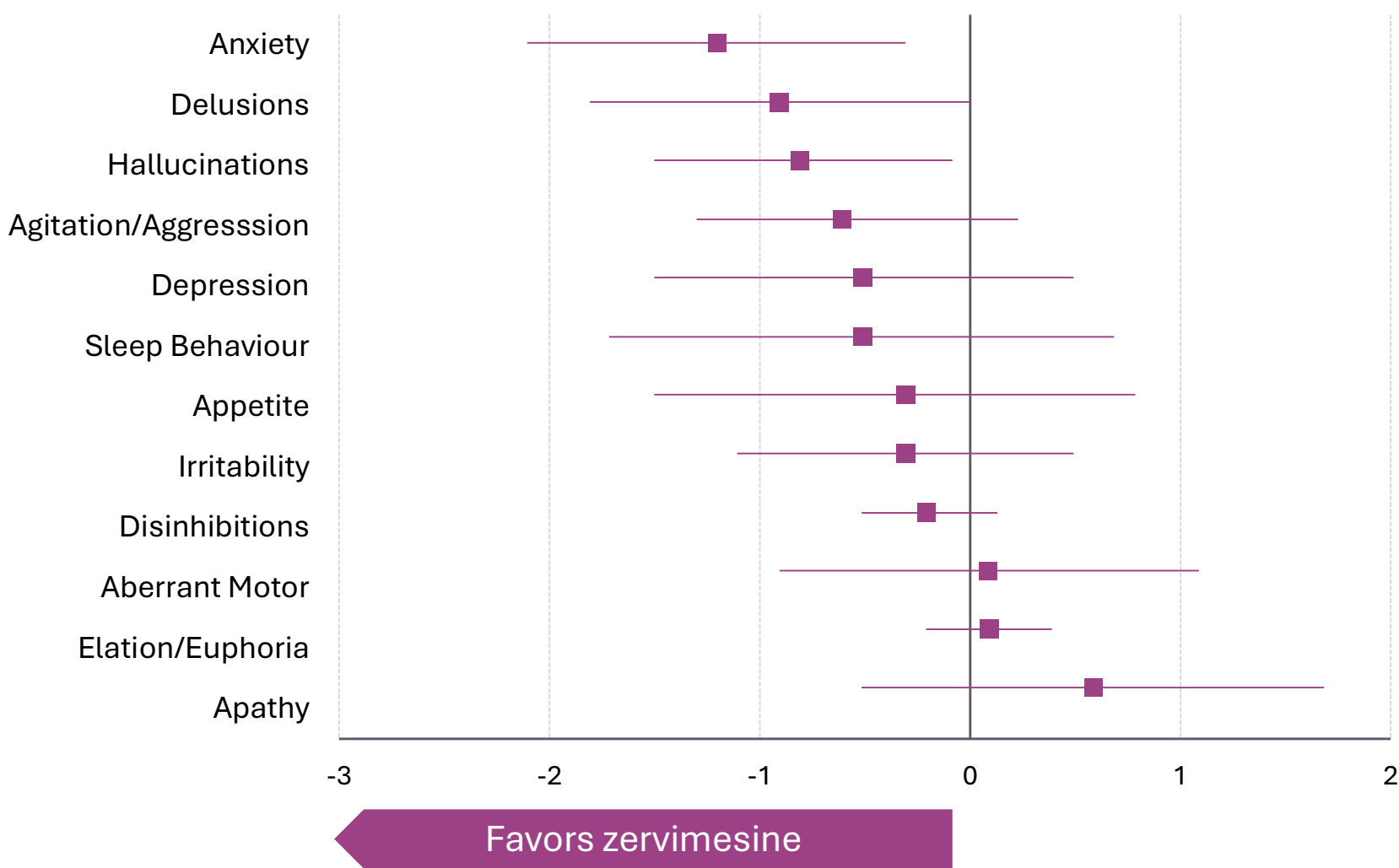
NPI Total Score (A-L)

86% Slowing



NPI favor Treatment with Zervimesine

LS Mean Difference from Placebo 95% CI

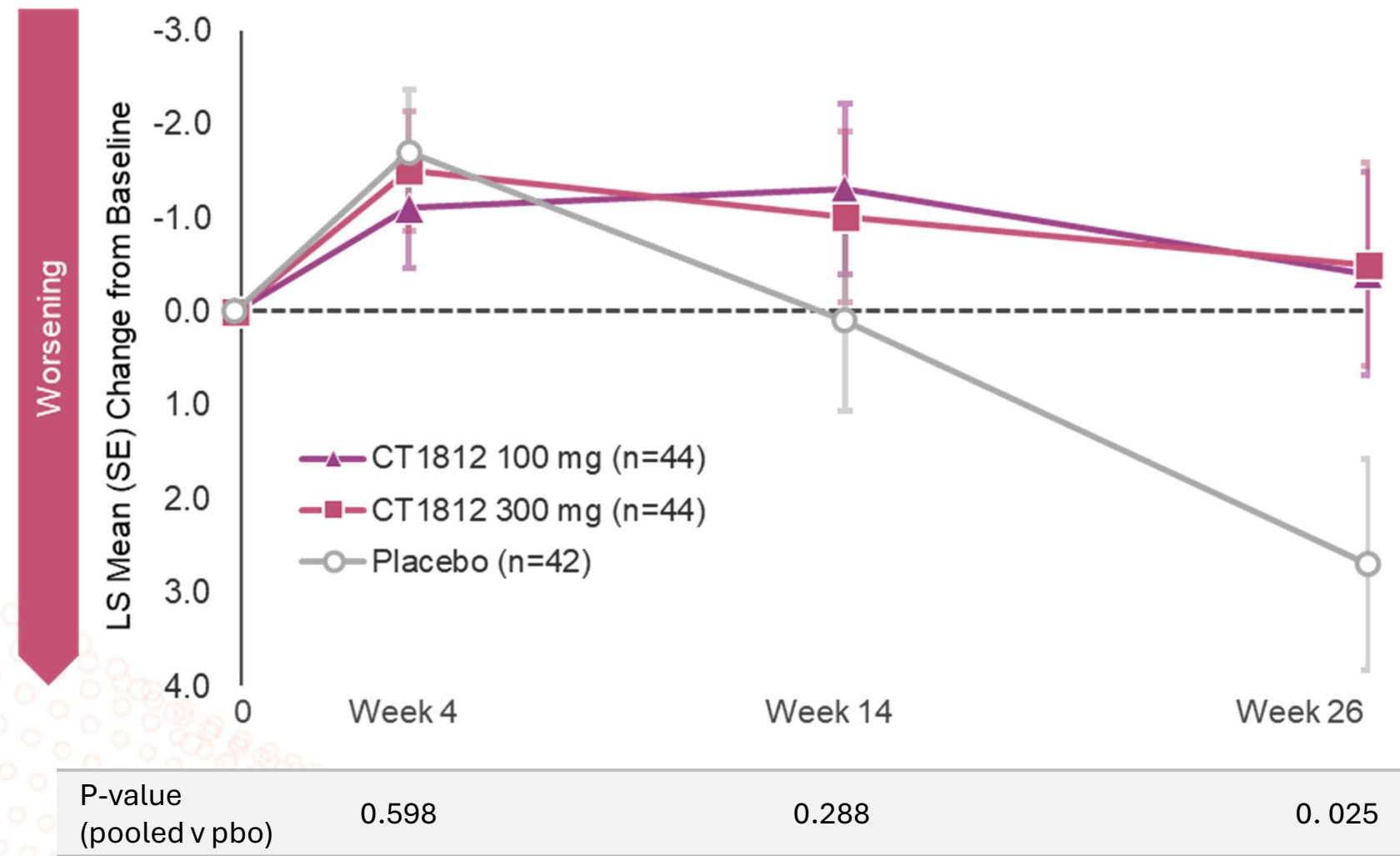


Because Participants Improved in Hallucinations, Delusions & Anxiety, Caregivers were Notably Better

New tool created to measure caregiver burden in DLB

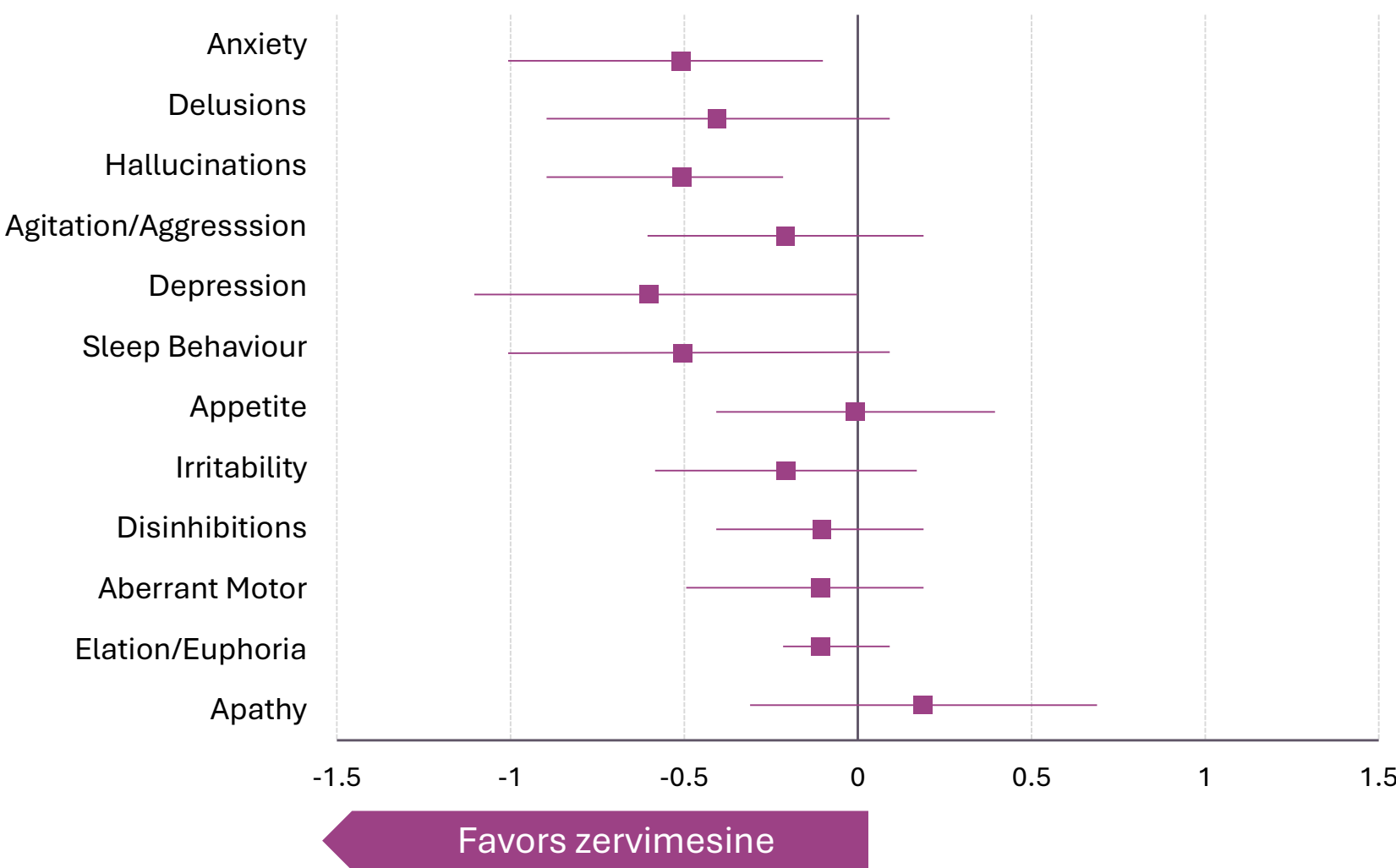
NPI Distress

NPI Total Score (A-L) Caregiver Distress



NPI Distress favors Treatment with Zervimesine

LS Mean Difference from Placebo 95% CI

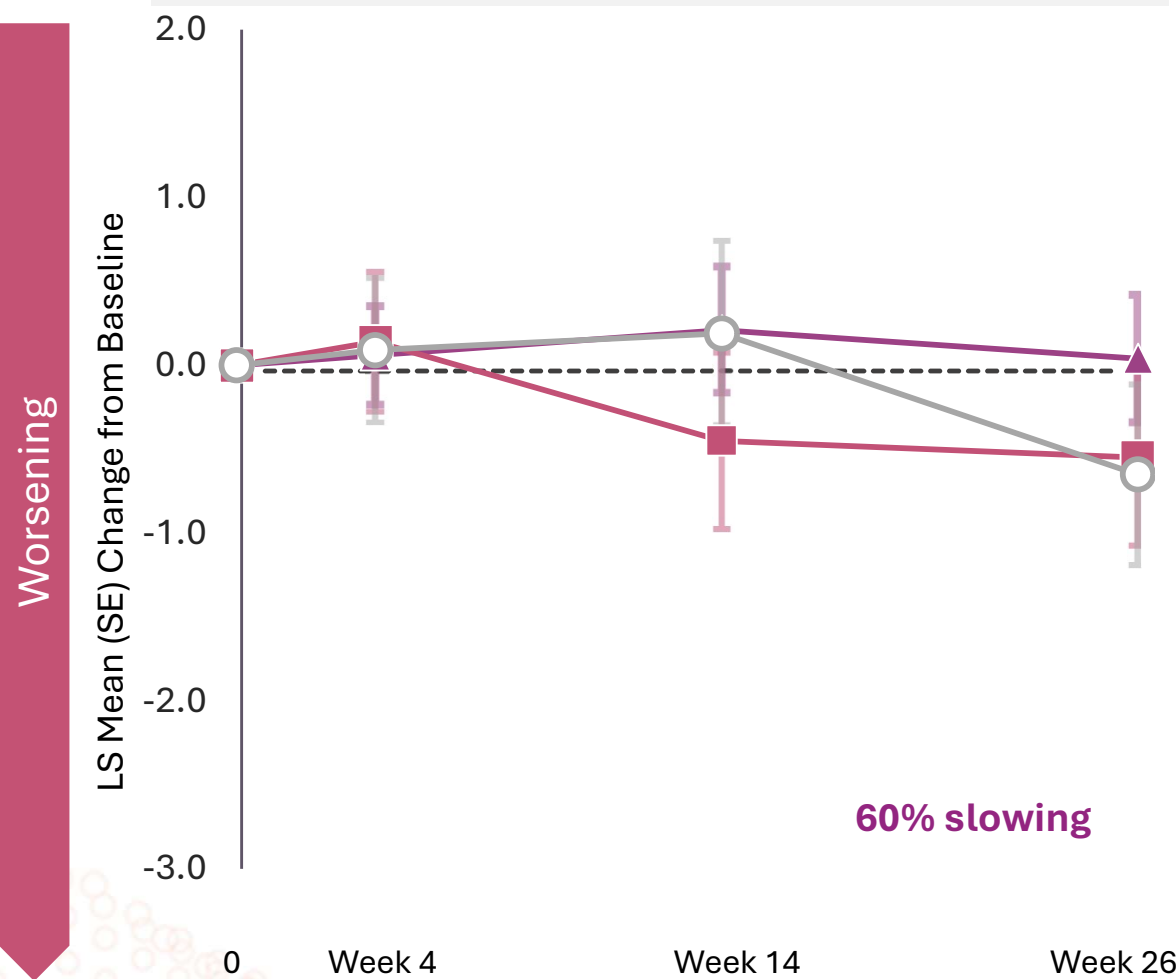


Up to 91% Slowing of Cognitive Decline Across Assessments

Zervimesine improved patients' attentiveness and problem solving

- CT1812 100mg (n=44)
- CT1812 300mg (n=44)
- Placebo (n=42)

MoCA (ITT)



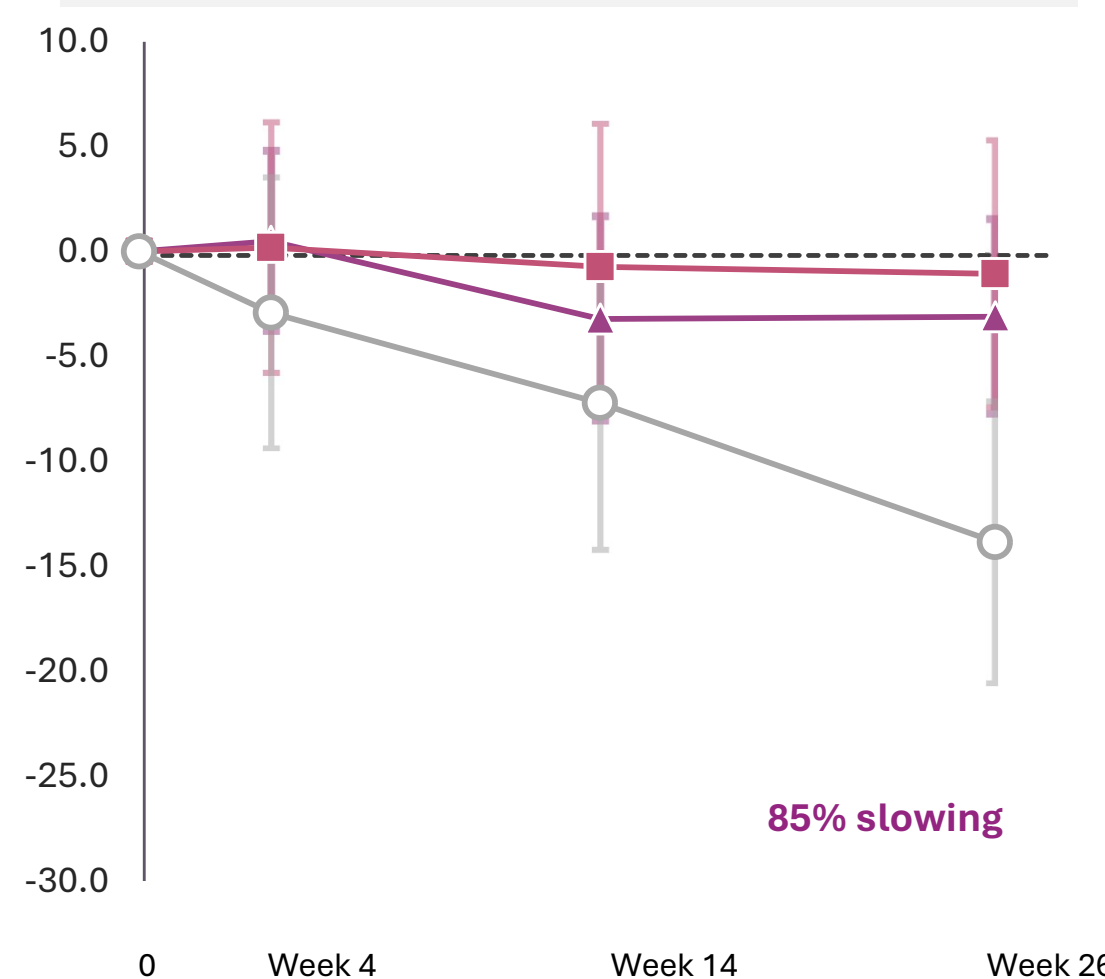
P-value
(pooled v pbo)

0.979

0.643

0.550

CDR - Episodic Memory (ITT)

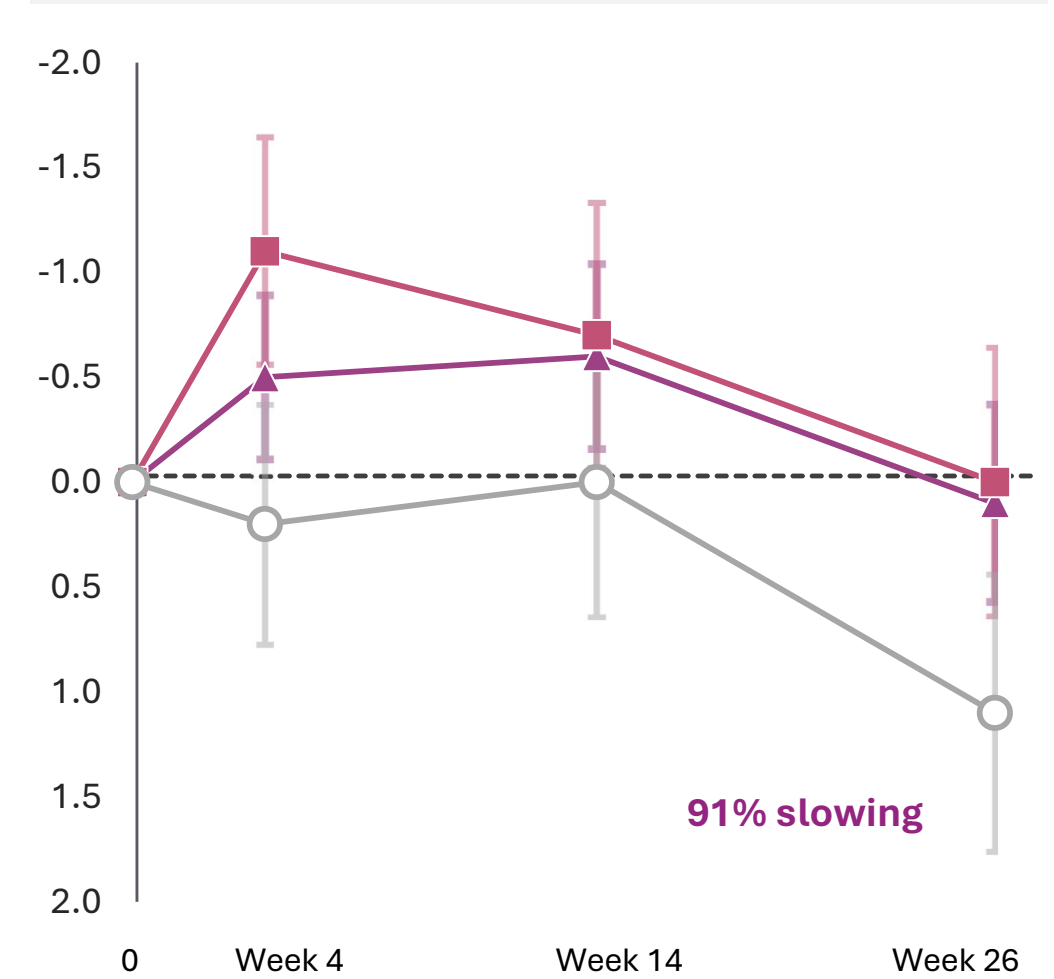


0.674

0.539

0.152

CAF (Fluctuations) (ITT)



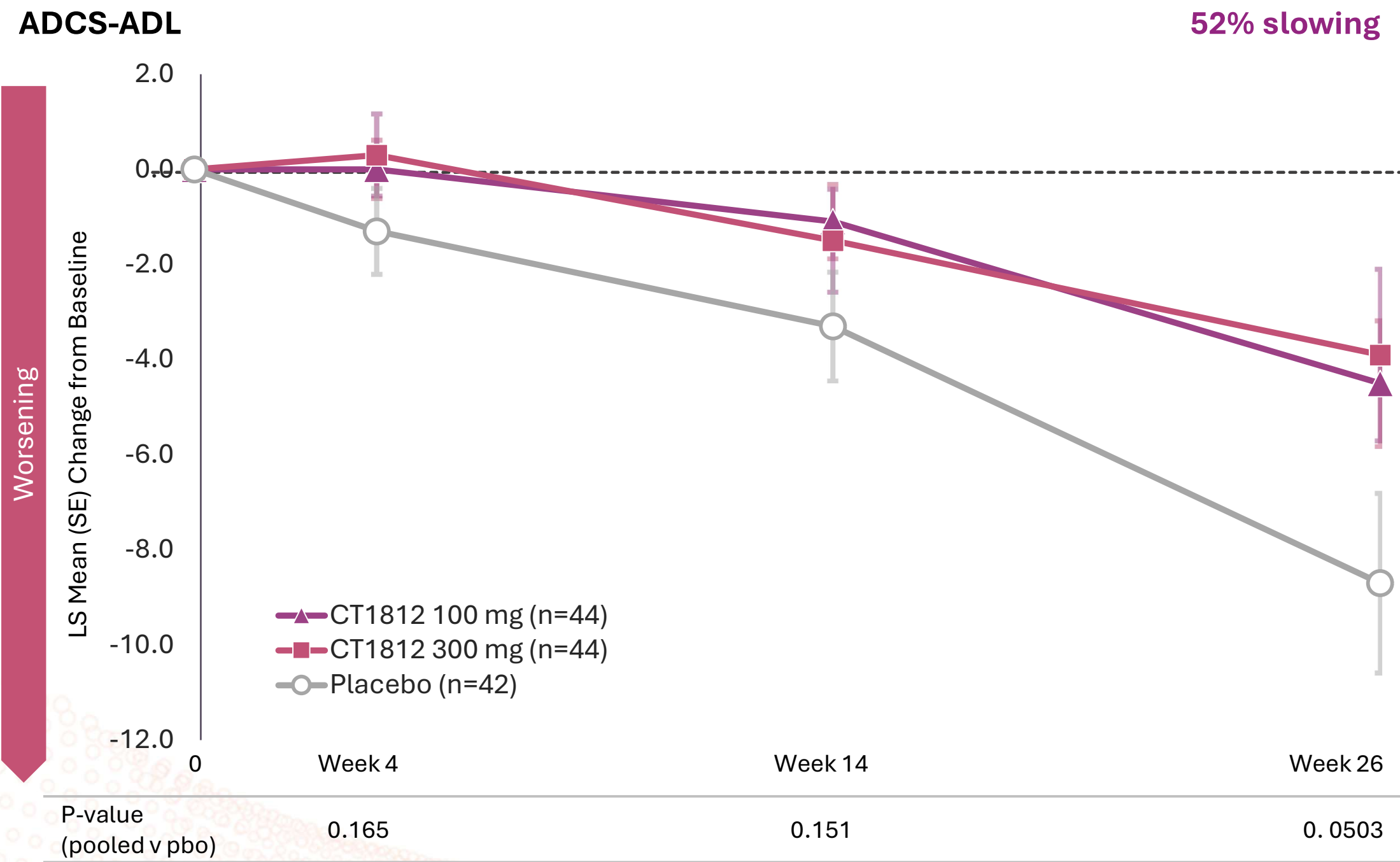
0.137

0.429

0.2097

People on Zervimesine Maintained Self-care

52% preservation in activities of daily living (ADL) measures



Components of ADL Score



Bathing



Toileting



Dressing



Conversing



Grooming



Shopping



Feeding

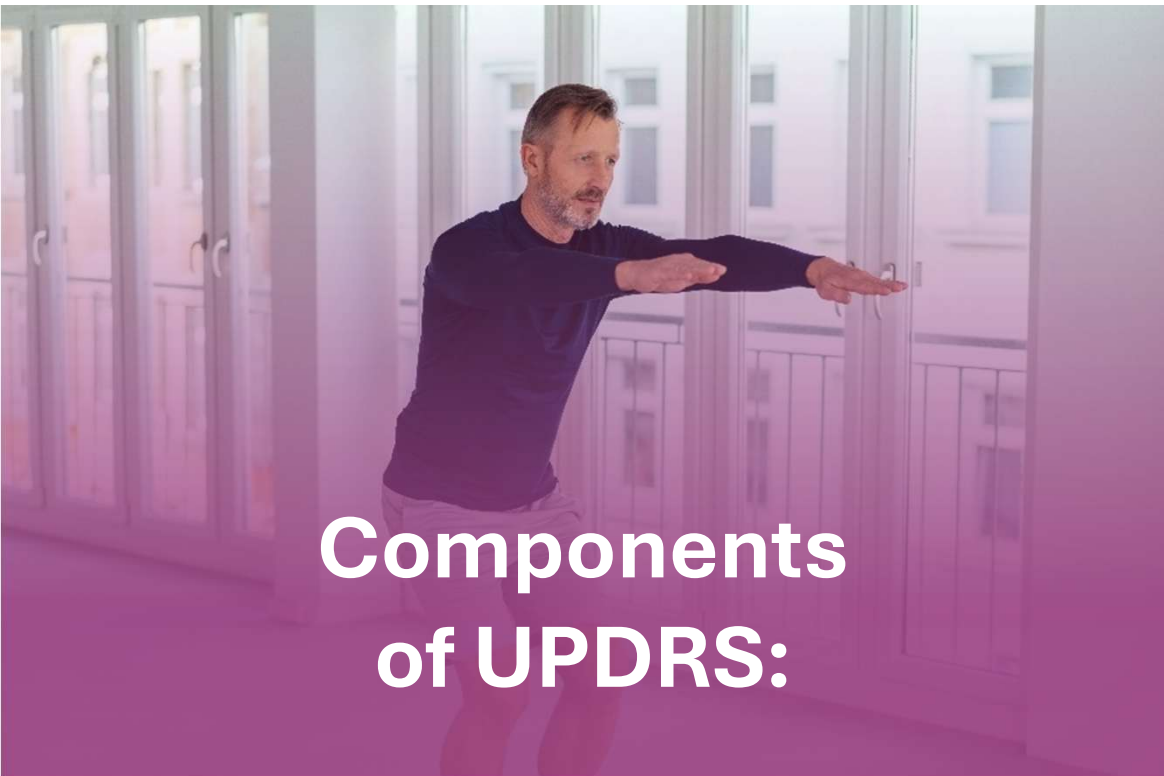
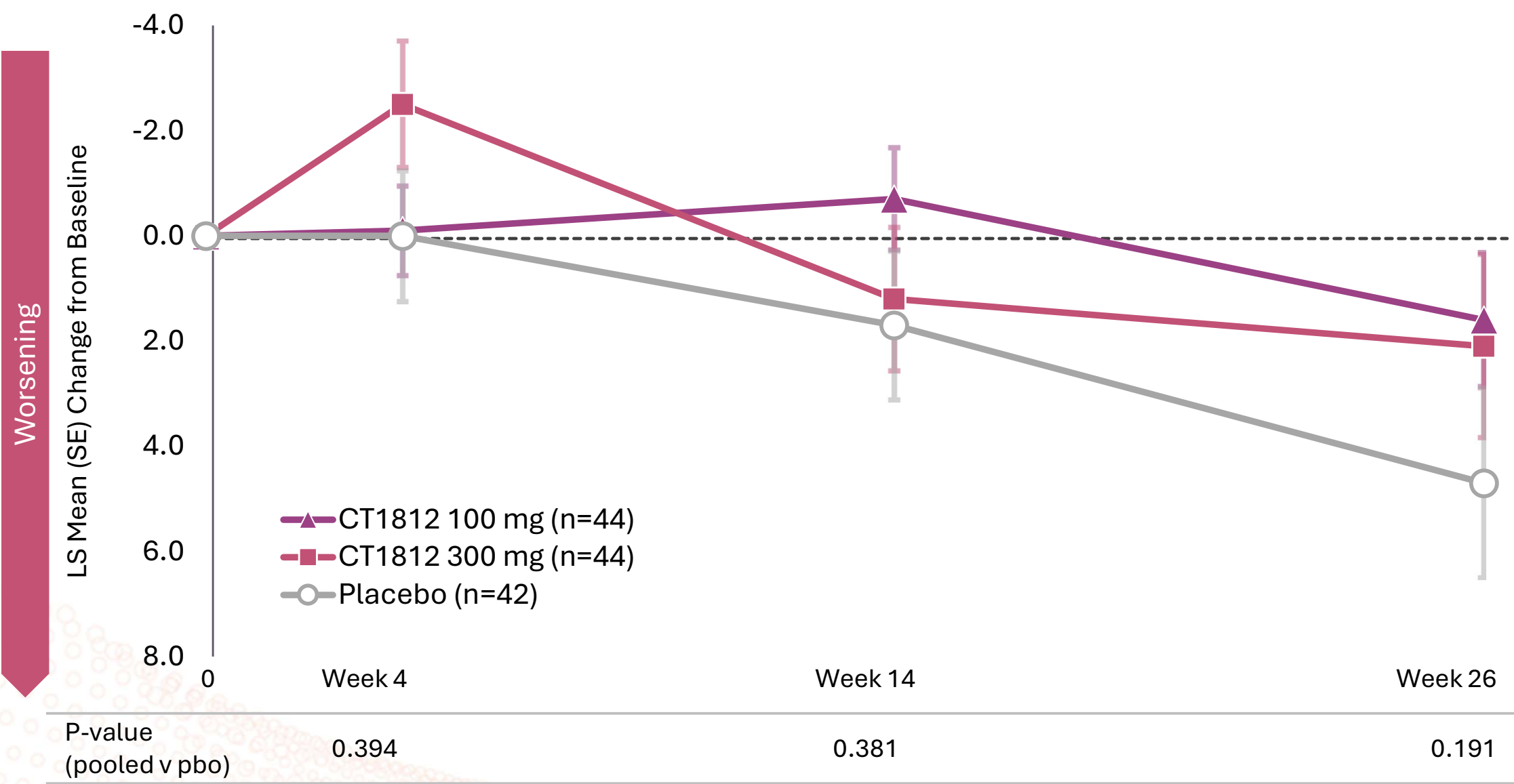


Writing

People Treated with Zervimesine Maintained Motor Function

62% preservation in measures of movement

MDS-UPDRS3



Components of UPDRS:



Balance



Gait



Speech



Facial expression



Rigidity



Tremor

Summary of SHIMMER Safety and Tolerability findings

Favorable safety profile, AEs balanced between arms – Consistent with SHINE Results

- ➡ Total AE frequency was similar in CT1812 and placebo

➡ Most AEs were mild or moderate

➡ Fewer Serious AE occurred in the CT1812 treated group compared to placebo treated
- ➡ There were no deaths related to study drug

➡ Study Discontinuations due to AEs not related to LFTs:

 - Placebo – 4.8%
 - 100mg CT1812 – 4.5%
 - 300 mg CT1812 – 9.3%
- ➡ Participants with LFT elevations $\geq 3\times$ ULN

 - 100mg CT1812 – 3
 - 300mg CT1812 – 6
 - Placebo – 0

➡ Most common AEs* (other than increased LFTs) in the CT1812 group were diarrhea and abdominal discomfort

	Adverse Events	Serious AEs	Deaths [†]
CT1812	94.3%	10.3%	2 (2.2)%
Placebo	88.1%	19.0%	1 (2.4)%

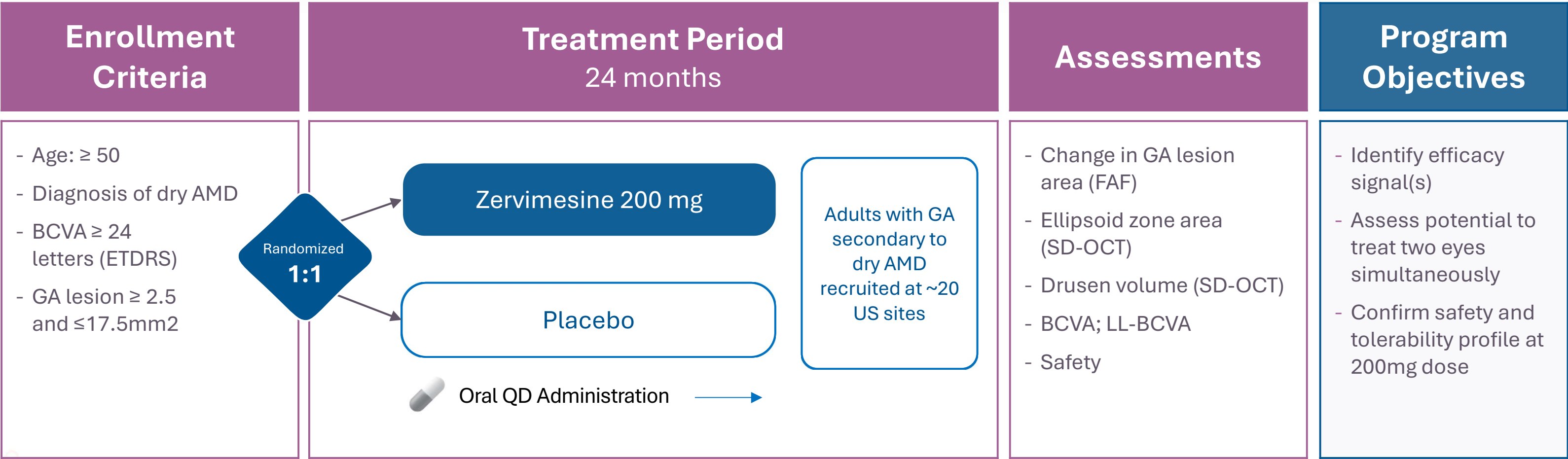
MAGNIFY Topline Results

GA lesion growth slower with
zervimesine treatment



MAGNIFY Trial in Dry AMD/GA

Zervimesine: oral drug development candidate for geographic atrophy



BCVA, best corrected visual acuity; FAF, fundus autofluorescence; SD-OCT, spectral domain optical coherence tomography

Zervimesine Treatment Slowed GA Lesion Growth



Effect size increases with exposure

- 29% mean rate of change (slope) in GA lesion area vs placebo (p=0.0538)
- Change in GA progression rate favored zervimesine vs placebo at each timepoint
 - 6-months: -11.79%
 - 12-months: -15.83%
 - 18-months: -28.19% (p=0.0074)
- Effect size increases with longer study duration
- Safety profile consistent with AD/DLB studies

Zervimesine Slowed GA Lesion Growth Rate (slope) and Area (observed)



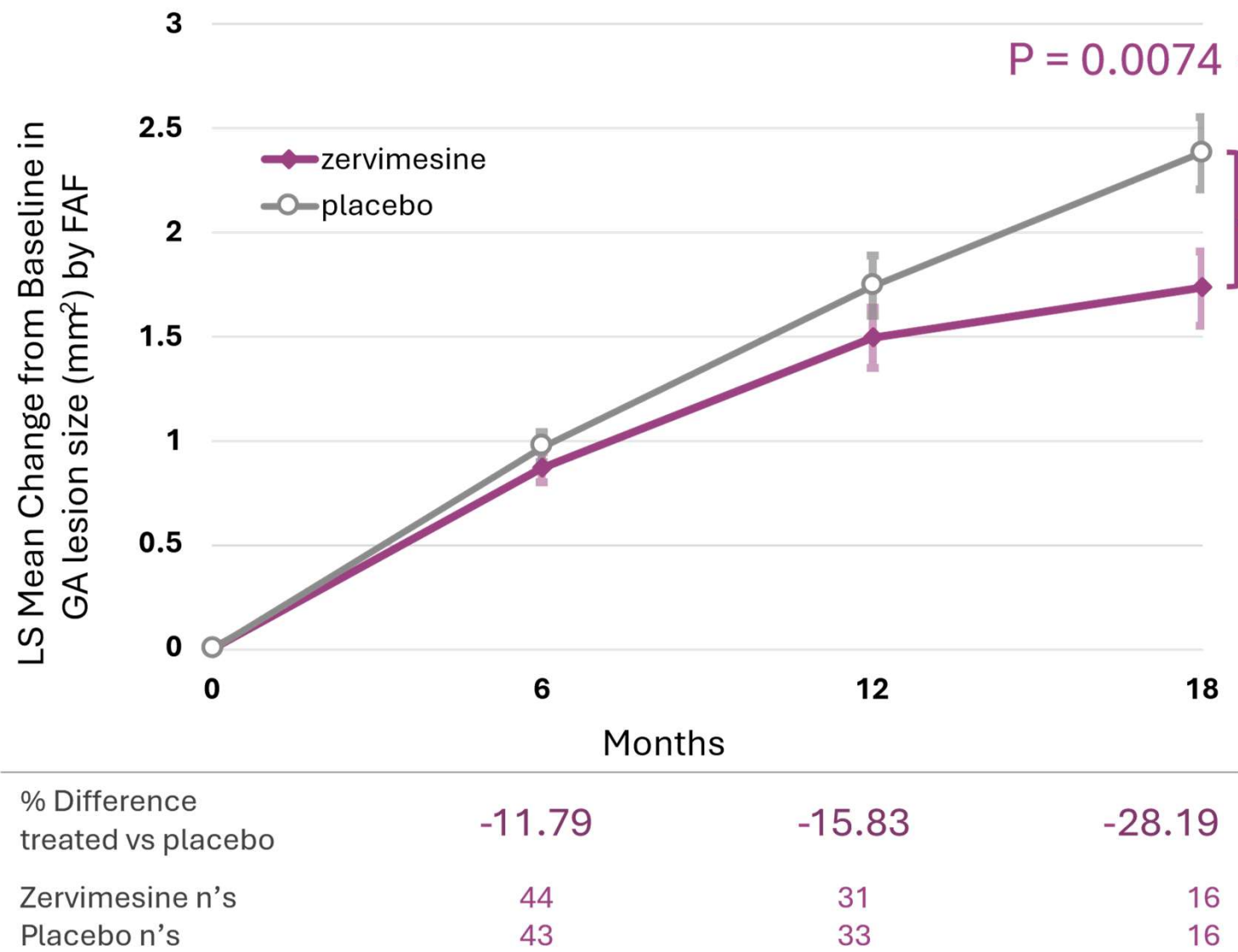
Slope Analysis¹

	Zervimesine	Placebo	Diff
Growth rate (mm ² / month)	0.10 ± 0.015	0.14 ± 0.014	- 0.04
Annualized Growth rate (mm ² / year)	1.23	1.73	- 0.50

Percent Difference from Placebo

29%
(P=0.054)

Mean Area by Time¹



Zervimesine Effect Size Comparable to SoC IVT with Oral Once-Daily Dosing



Compared to Published Results^{1,2}:

IZERVAY Avacincaptad pegol (2mg)¹

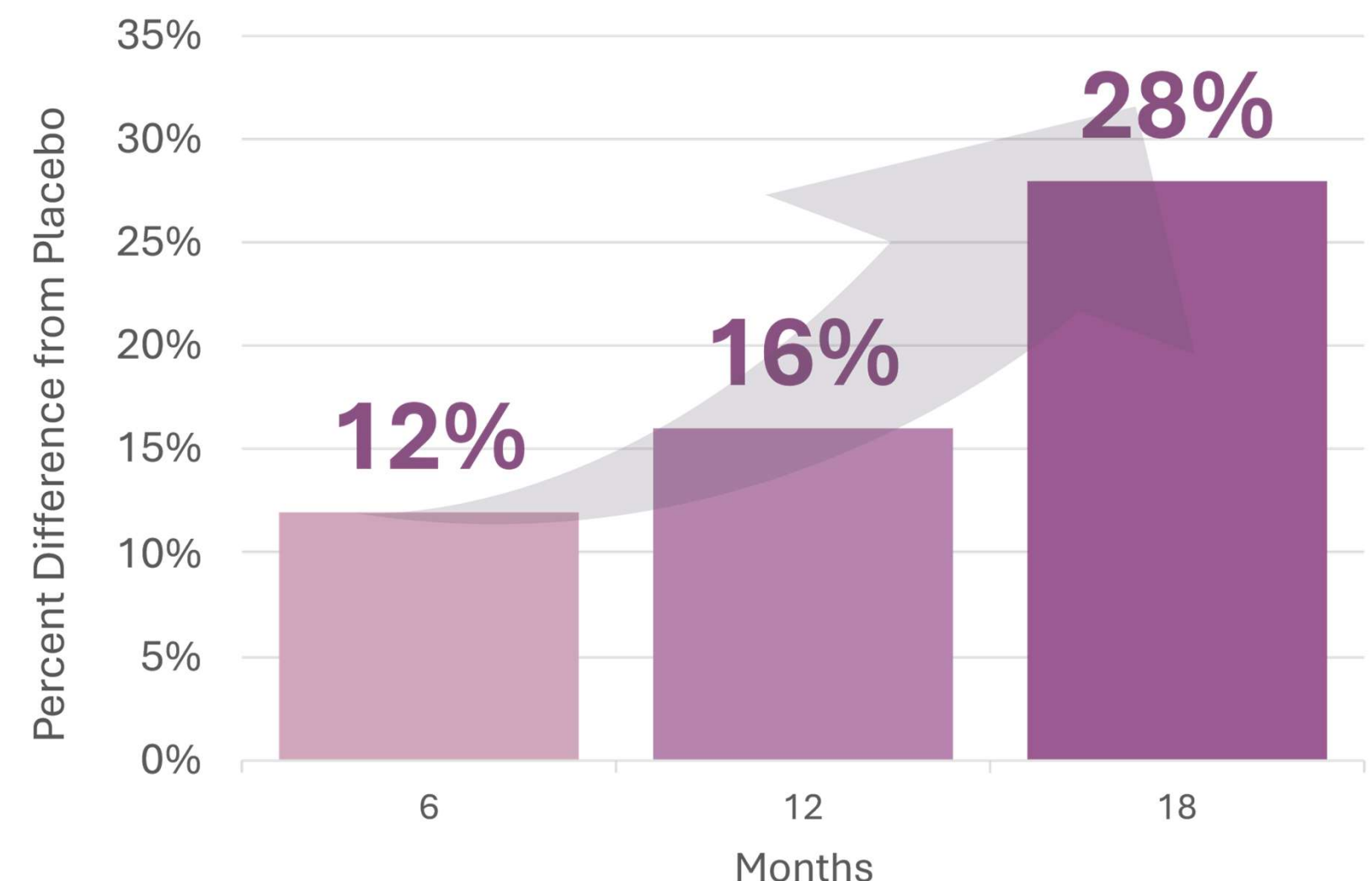
- Gather1 at 18 months – 35%
- Gather2 at 12 months – 18%
- Gather2 at 24 months – 14%

SYFOVRE Pegcetacoplan (15mg)²

- Derby at 18 months – 13%
- Oaks at 18 months – 22%

Topline MAGNIFY Results³

Percent Reduction in GA Lesion Growth Over Time



3 Major Diseases Addressed with Once-Daily Oral Pill

Collective Phase 2 Results Supports Advancing Zervimesine (CT1812) to Registrational Studies



Dementia with Lewy Bodies

Marked slowing of progression
across multiple domains



Alzheimer's Disease

Slowing of progression; robust
response in lower tau cohort



Geographic Atrophy

Slowing of GA growth
rate and area



\$30 Million Equity Raise Closed August 2025

Current Financial Position

As of quarter ended June 30, 2025

Cash and cash equivalents

Proforma including August Raise \$ 39.6 M

Grant funding for zervimesine studies

Preclinical through Phase 2 ~\$171 M

Approximate funding used (\$129 M)

Remaining grant funding \$42 M





Thank You

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