



Targeting Pathogenic Oligomers:

A Disruptive Approach to the
Treatment of Neurodegenerative Diseases

August 2025

Forward-looking Statements

FORWARD-LOOKING STATEMENTS

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Executive Summary

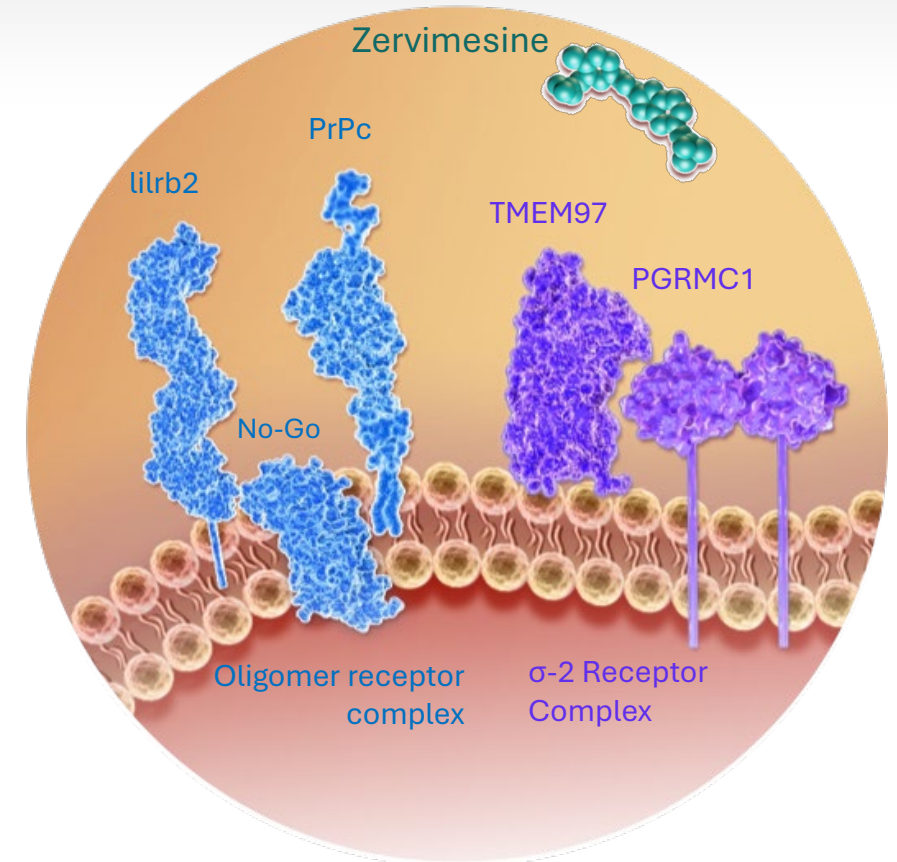
Compelling data with first-in-class candidate supports registrational plan

- **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
- **Generally 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

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
- Distinct MoA: ligand of TMEM97 (sigma-2) receptor
- Oral, once-daily dosing, favorable safety data
- Fast Track granted for Alzheimer's disease
- Phase 2 PoC in three indications



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				
Dry age-related macular degeneration <i>GA secondary to dry AMD</i>	Phase 2 COG2201 • MAGNIFY			*
Mild-to-moderate DLB	Phase 2 COG1201 • SHIMMER			
Mild-to-moderate Alzheimer's disease	Phase 2 COG0201 • SHINE			

Takeaways from completed studies

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

* We made the strategic decision to voluntarily discontinue the MAGNIFY study to prioritize our resources on our ongoing programs in Alzheimer's and dementia with Lewy bodies. The discontinuation was not the result of any safety concerns.

MAGNIFY Topline Results

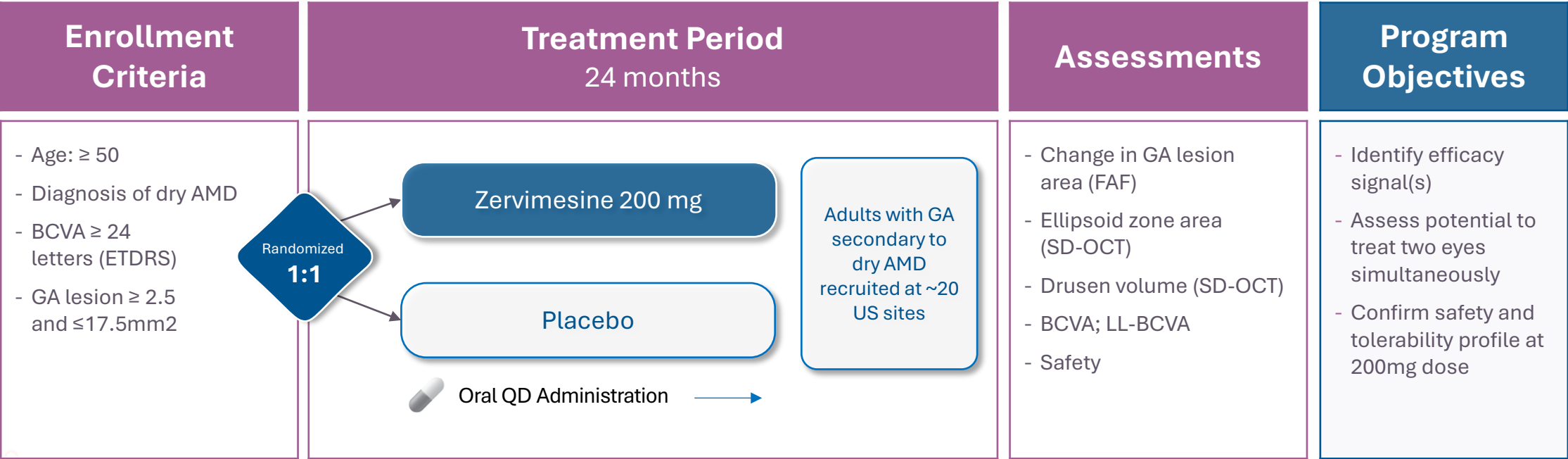
GA lesion growth slower with
zervimesine treatment

Topline results reported May 8, 2025



MAGNIFY Trial in Dry AMD/GA

Zervimesine: oral drug development candidate for geographic atrophy



BVCA, 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

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



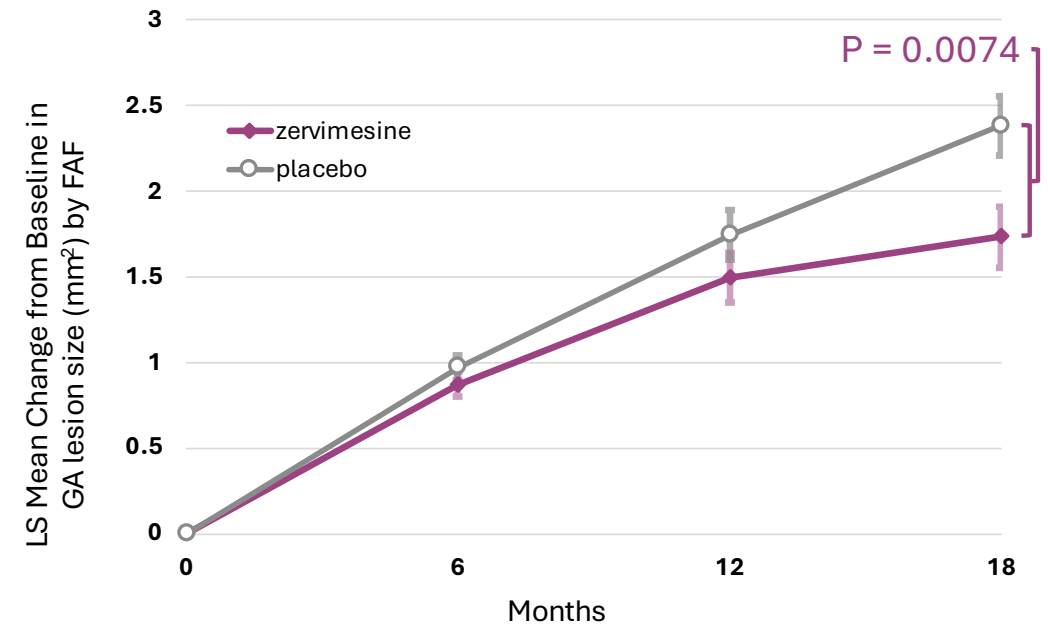
Slope Analysis¹

	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



% Difference treated vs placebo	-11.79	-15.83	-28.19
Zervimesine n's	44	31	16
Placebo n's	43	33	16

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



Compared to Published Results^{1,2}:

IZERVAY Avacincaptad pegol (2mg)¹

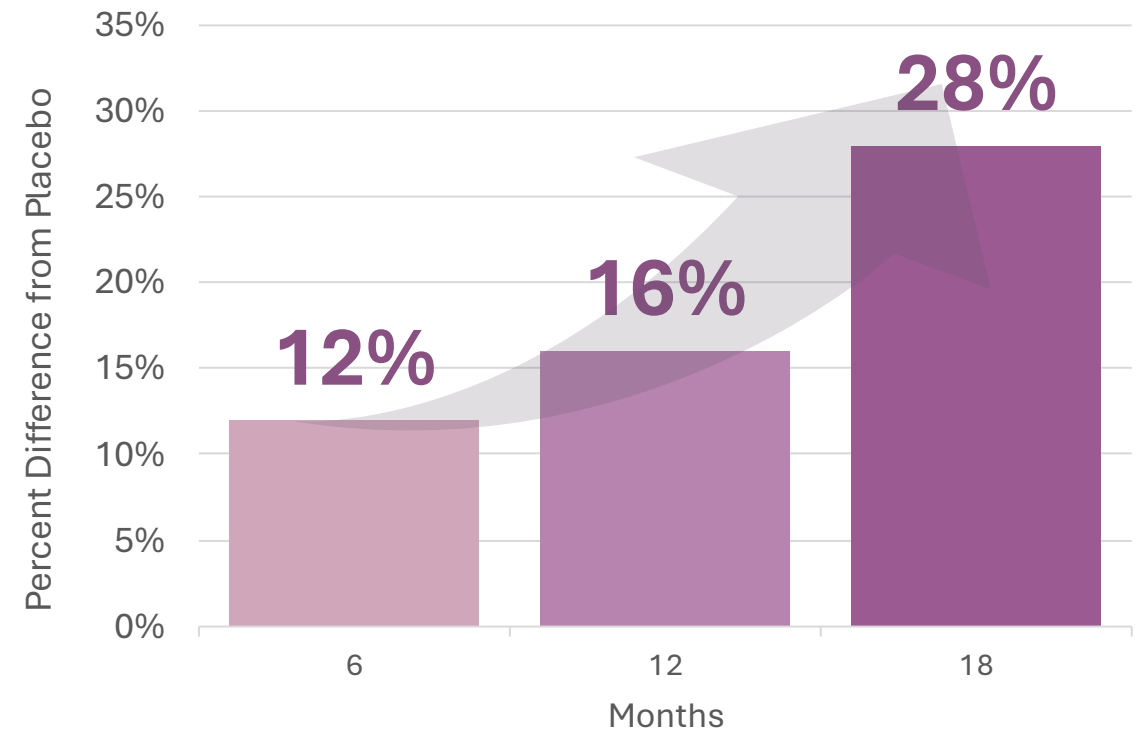
- Gather1 at 18 months – 35%
- Gather2 at 12 months – 18%
- Gather2 at 24 months – 14%

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





COG2201 (MAGNIFY): Safety Summary

Favorable safety and
tolerability profile

Subjects with:	Zervimesine (n=49)	Placebo (N=51)	Total (N=100)
At least one TEAE, n (%)	38 (77.6%)	36 (70.6%)	74 (74.0%)
At least one TEAE possibly/probably related to treatment	12 (24.4%)	5 (9.8%)	17 (17.0%)
At least one TEAE leading to treatment discontinuation	4 (8.2%)	3 (5.9%)	7 (7.0%)
At least one <i>ocular</i> TEAE leading to treatment discontinuation	1 (2.0%) *	0	1 (1.0%)
At least one serious AE leading to treatment discontinuation	0	1 (2.0%)	1 (1.0%)
Serious TEAEs	6 (12.2%)	6 (11.8%)	12 (12.0%)
Serious <i>ocular</i> TEAEs	0	0	0
AE of special Interest: LFTs \geq 3x ULN (AST or ALT)	4 (8.2%)	0	4 (4.0%)
AE severity- subjects with:			
Mild	18 (36.7%)	15 (29.4%)	33 (33.0%)
Moderate	17 (34.7%)	17 (33.3%)	34 (34.0%)
Severe	3 (6.1%)	4 (7.8%)	7 (7.0%)

Dementia Programs:

Strong clinical signals in the two primary causes of dementia:

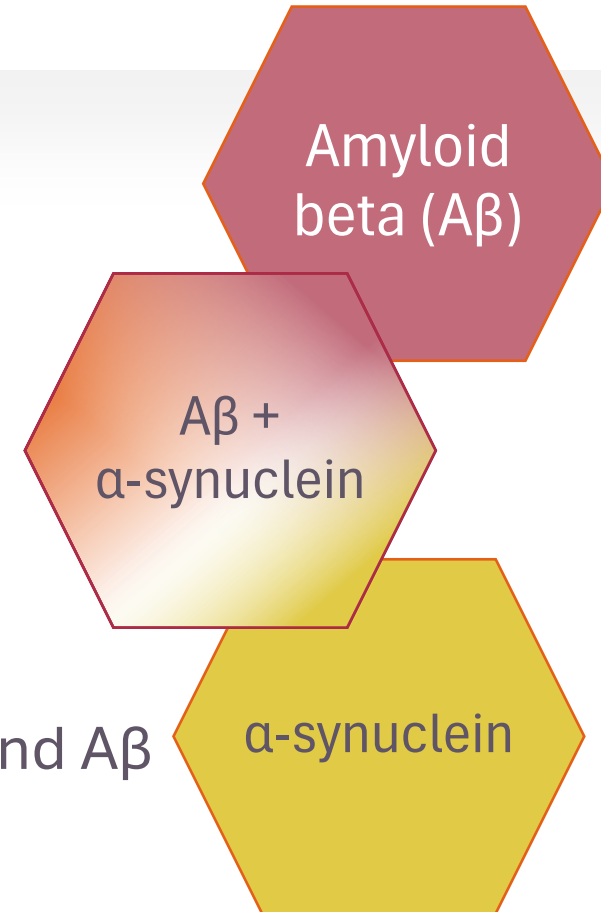
- Dementia with Lewy Bodies (DLB)
- Mild-to-Moderate Alzheimer's Disease



AD and DLB: 2 Diseases with Overlapping Pathology

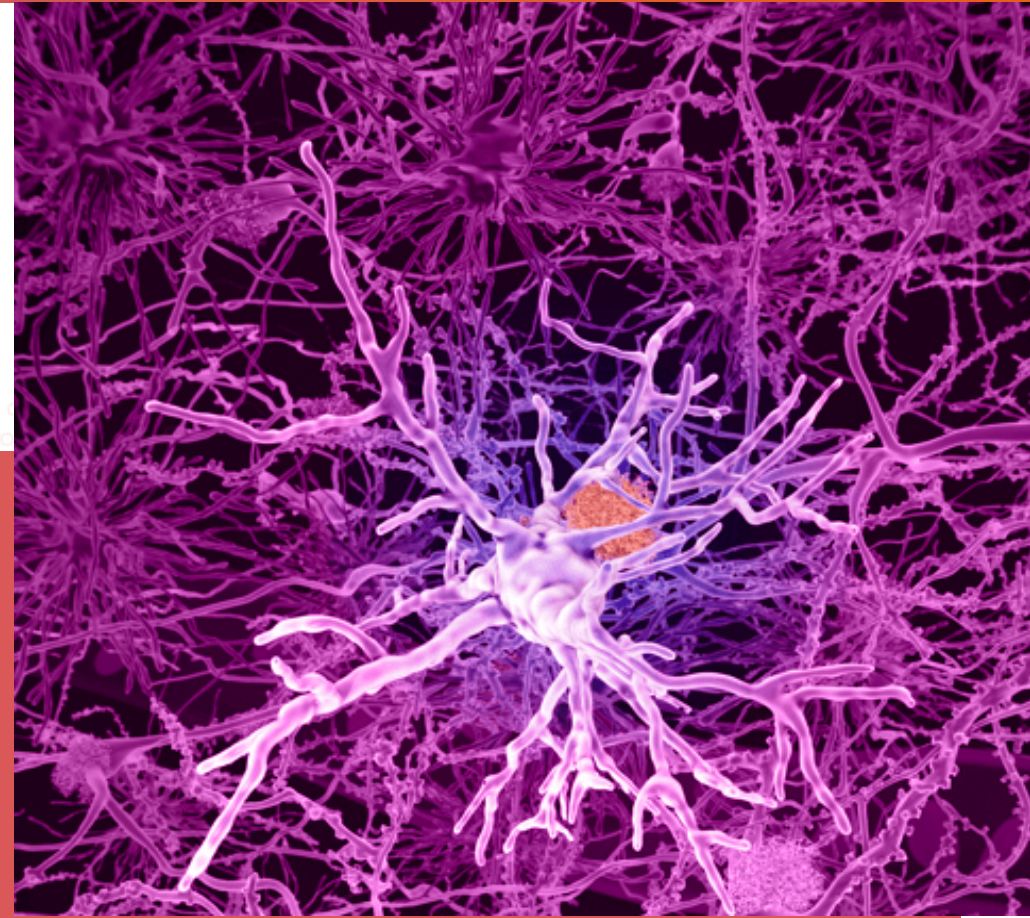
Primary treatment goal – slow the progression of cognitive decline

- 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



Dementia with Lewy Bodies (DLB)



2nd most common cause of dementia after Alzheimer's disease



Patients may have faster decline than Alzheimer's



Characterized by cognitive impairment that precedes development of motor symptoms



Patients often require several physician visits over 18 months before being correctly diagnosed



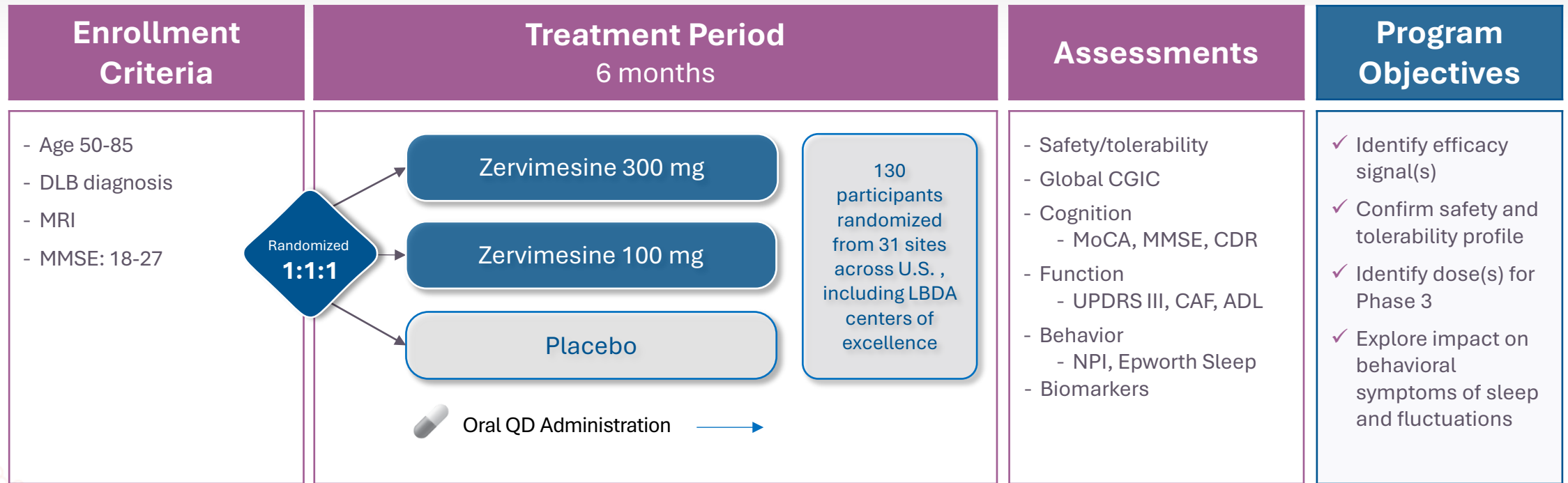
More common in men

Core Symptoms of DLB

- Fluctuating cognition and alertness
- Neuropsychiatric symptoms such as visual hallucinations, anxiety, depression and delusions
- Decline in cognition, attention, executive function
- Spontaneous parkinsonism
- REM sleep behavior disorder

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

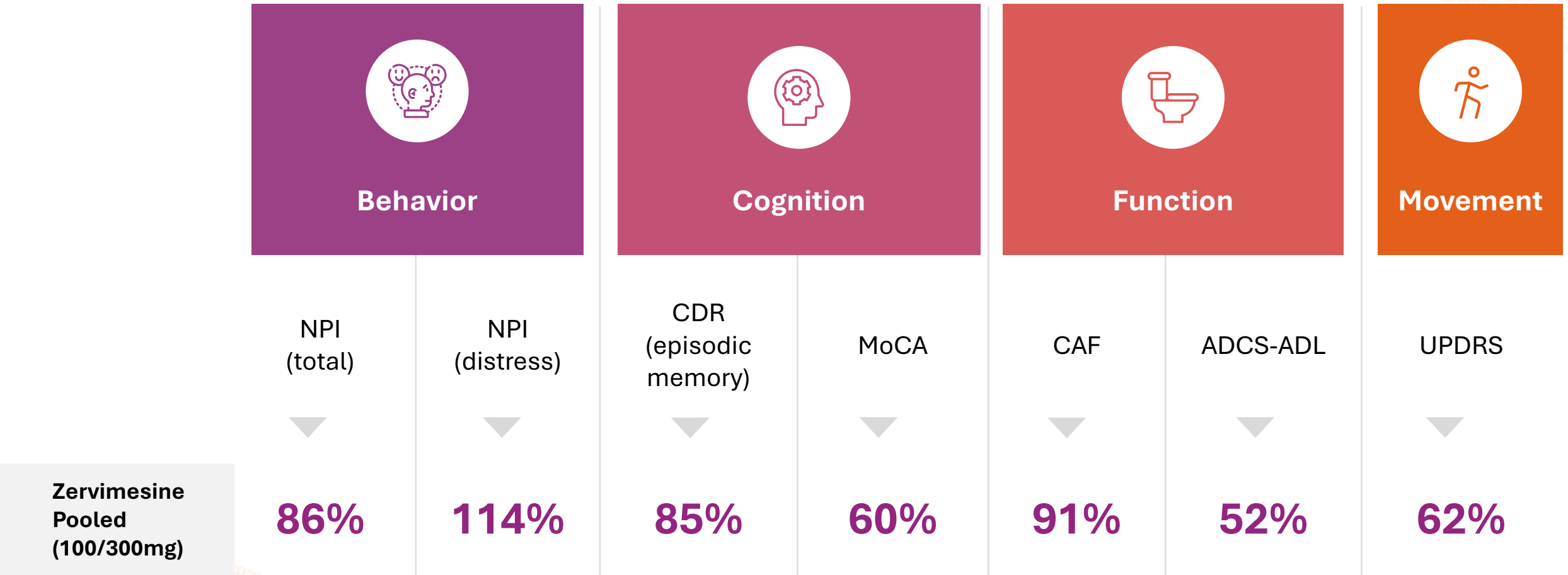
Four Symptom Domains Drive Lewy Body Disease Burden

“A multifactorial disease with a buffet of symptoms”

	 Behavior	 Cognition	 Function	 Movement
Patient symptom	Hallucinations, anxiety, delusions	Memory and problem solving	Bathing, toileting, shopping, meal preparation	Standing, maintaining balance
Assessment tool	<ul style="list-style-type: none">➔ Neuropsychiatric Inventory (NPI)➔ Care Partner's NPI of "Distress"	<ul style="list-style-type: none">➔ Cognitive Drug Research (CDR) System➔ Montreal Cognitive Assessment (MoCA)	<ul style="list-style-type: none">➔ ADCS-Activities of Daily Living (ADL)➔ Clinician Assessment of Fluctuation (CAF)	<ul style="list-style-type: none">➔ MDS-Unified Parkinson's Disease Rating Scale (UPDRS)

Up to 91% Percent Slowing on Assessments

Strong clinical signals across major DLB symptoms relative to placebo

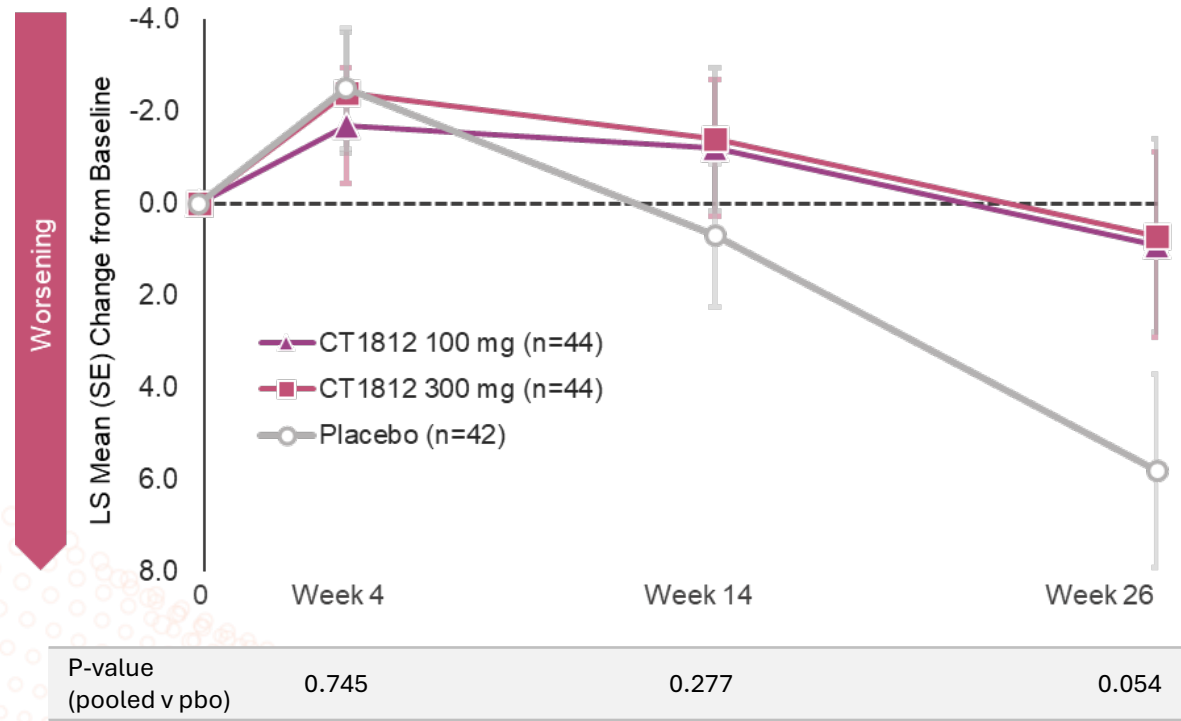


Zervimesine Showed Dramatic 86% Impact on Neuropsychiatric Measures

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

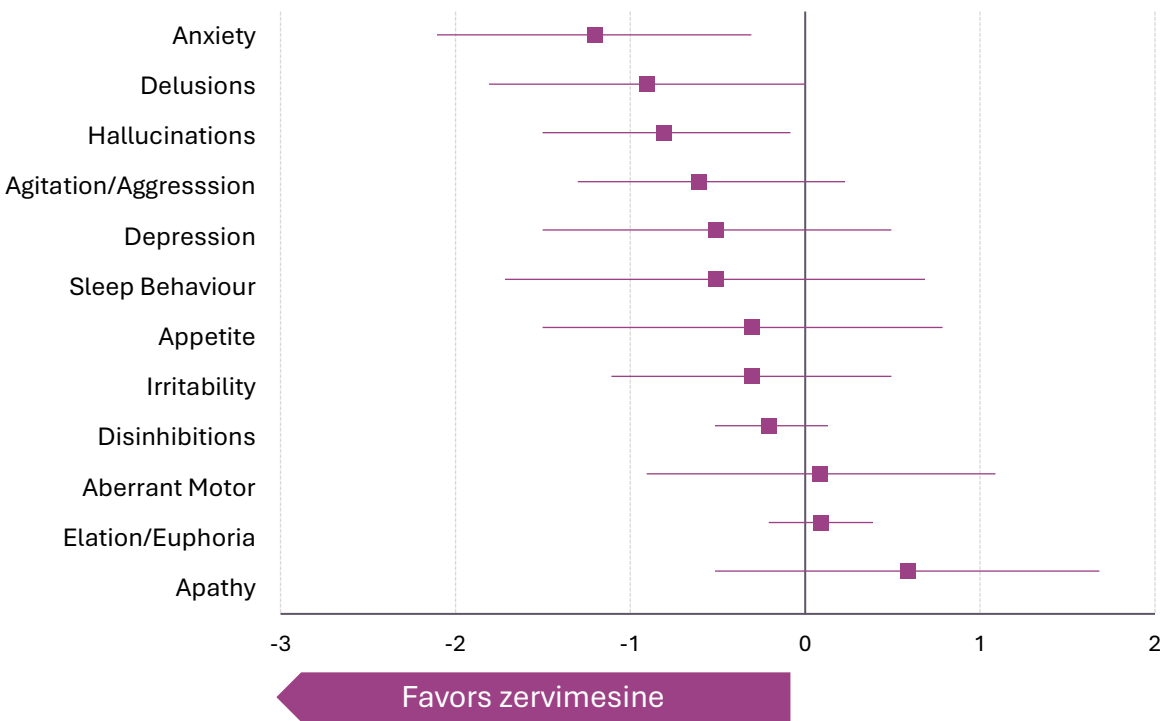
NPI

NPI Total Score (A-L)



NPI favor Treatment with Zervimesine

LS Mean Difference from Placebo 95% CI



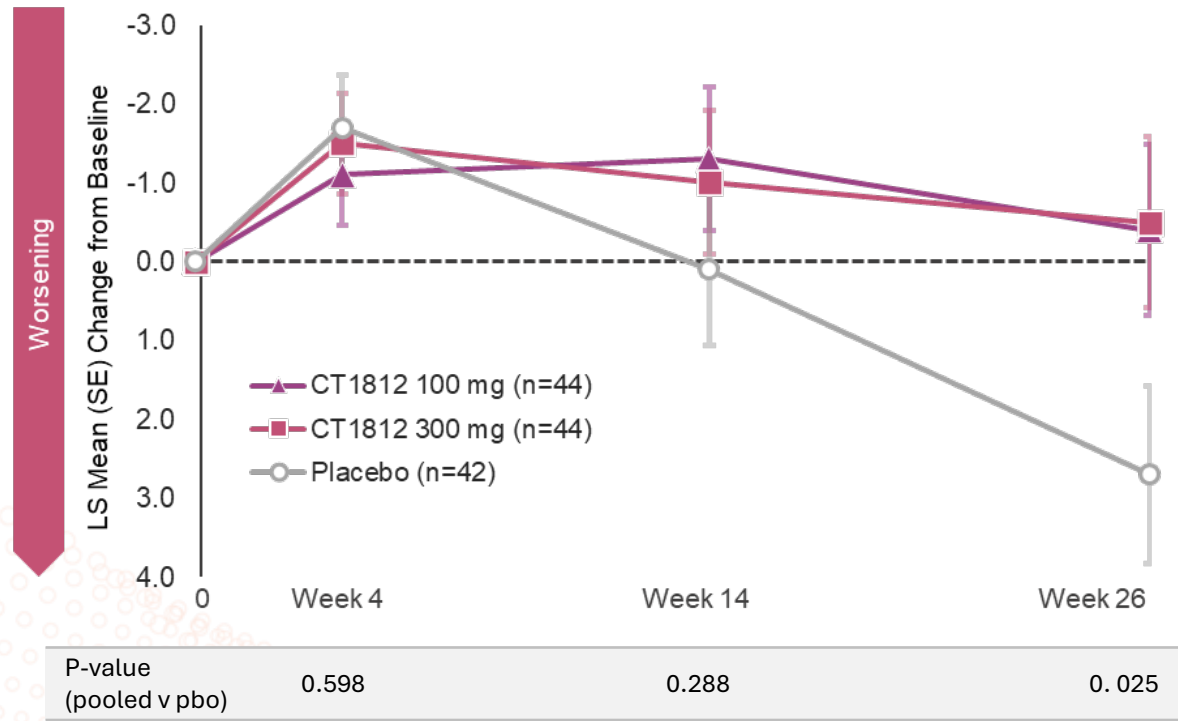
Because Participants Improved in Hallucinations, Delusions & Anxiety, Caregivers were Notably Better

New tool created to measure caregiver burden in DLB

NPI Distress

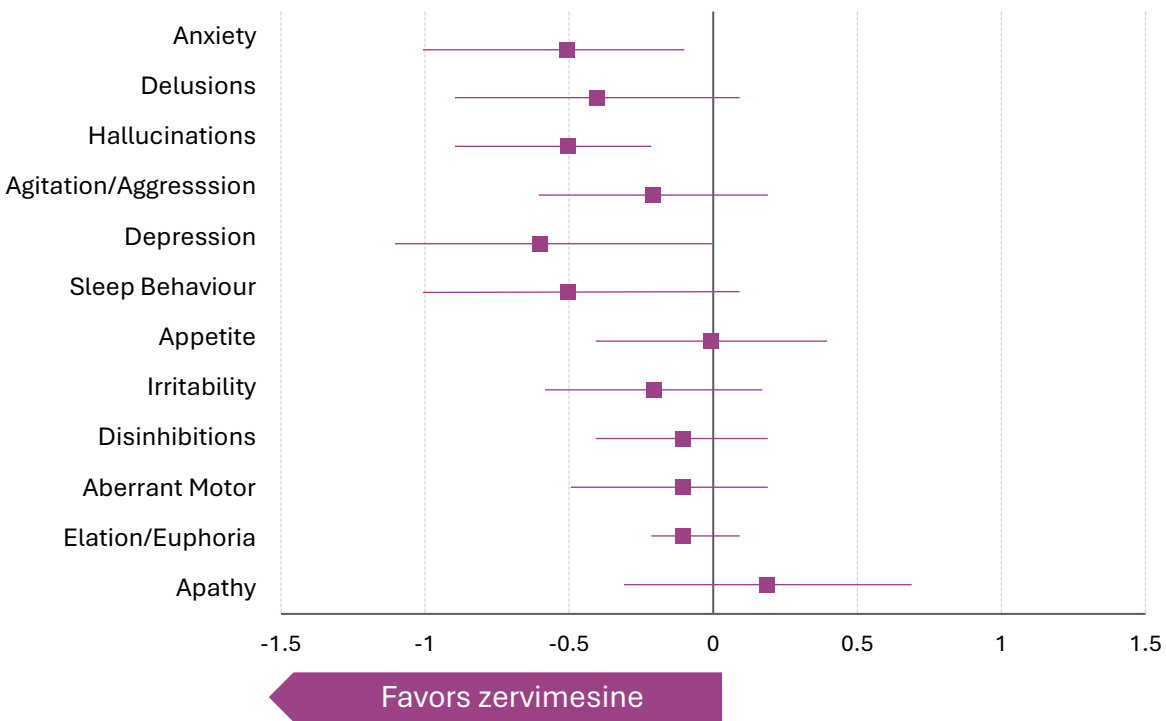
NPI Total Score (A-L) Caregiver Distress

114% Slowing



NPI Distress favors Treatment with Zervimesine

LS Mean Difference from Placebo 95% CI

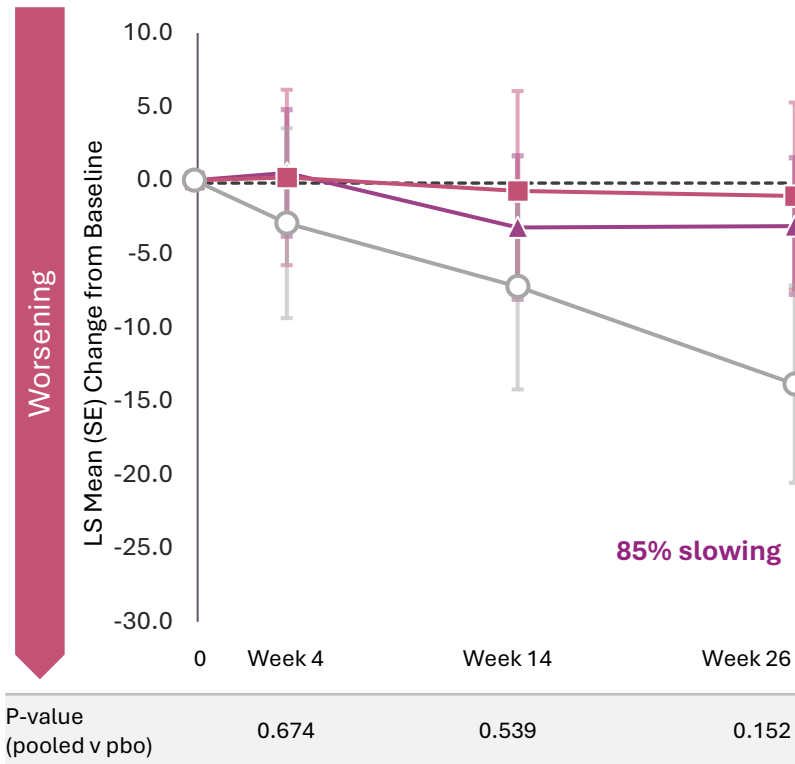


Up to 91% Slowing of Cognitive Decline Across Assessments

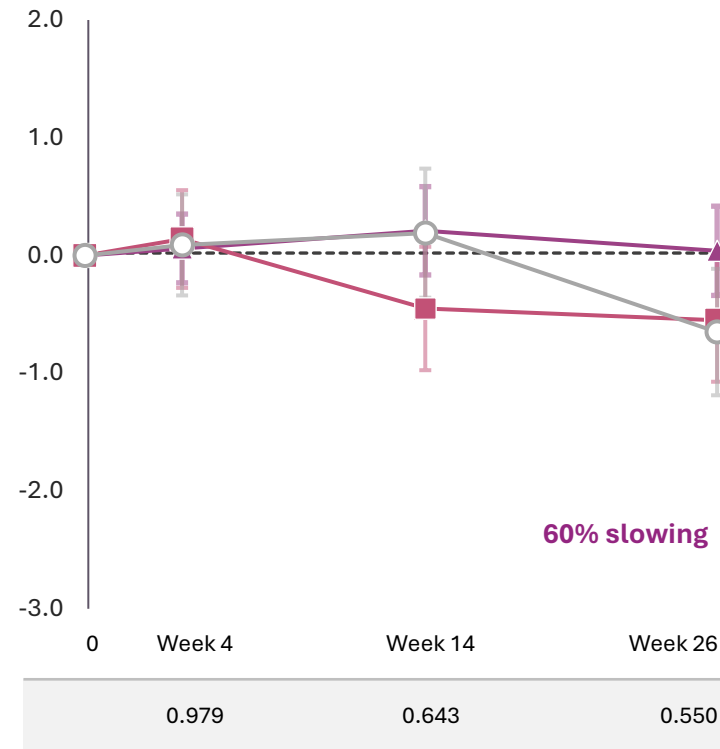
Zervimesine improved patients' attentiveness and problem solving

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

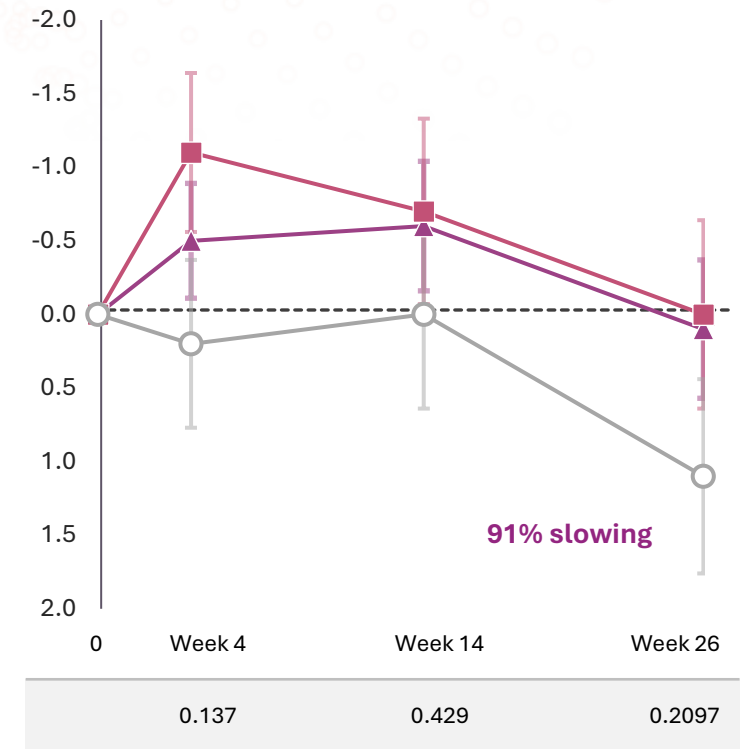
CDR - Episodic Memory (ITT)



MoCA (ITT)

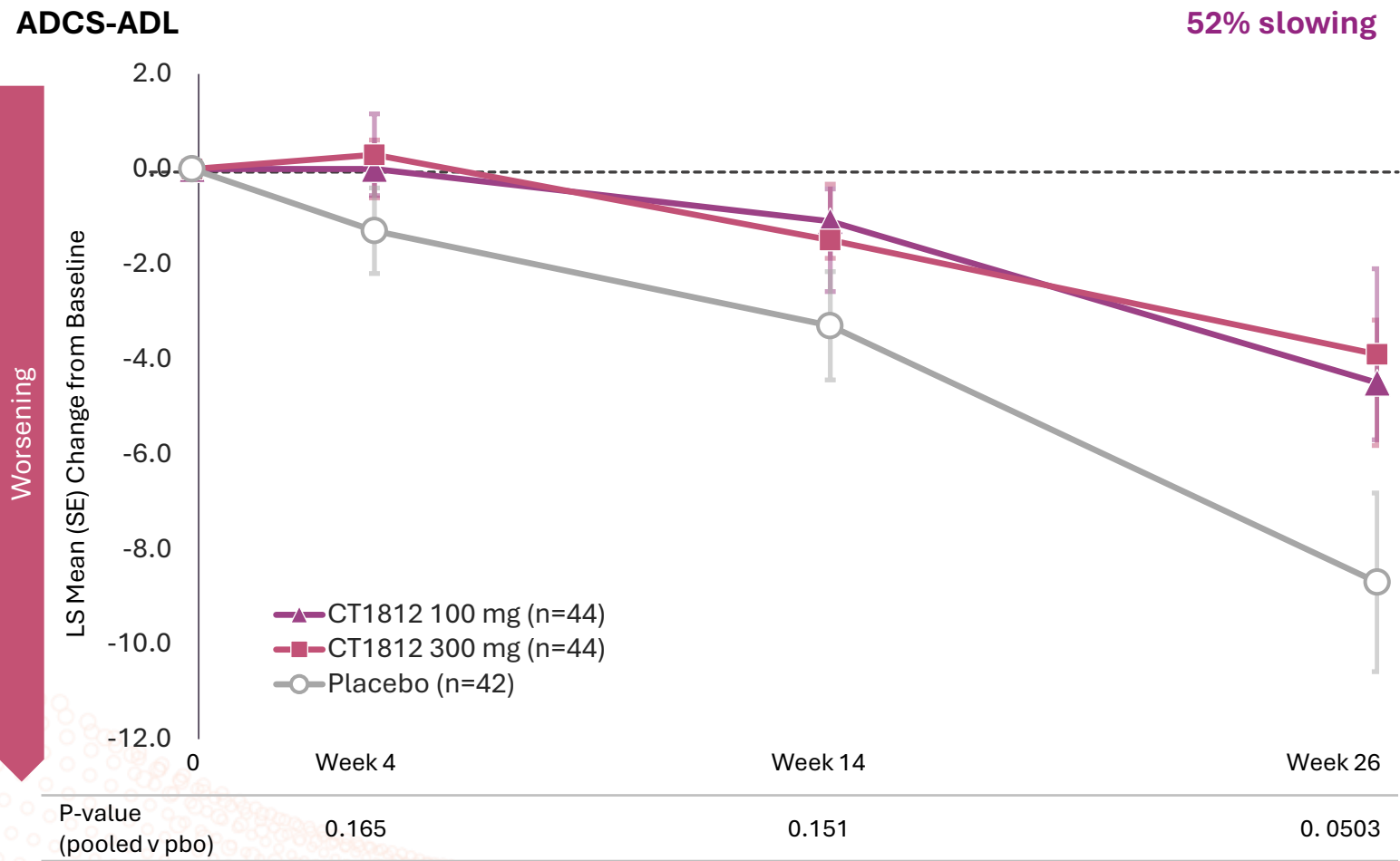


CAF (Fluctuations) (ITT)



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



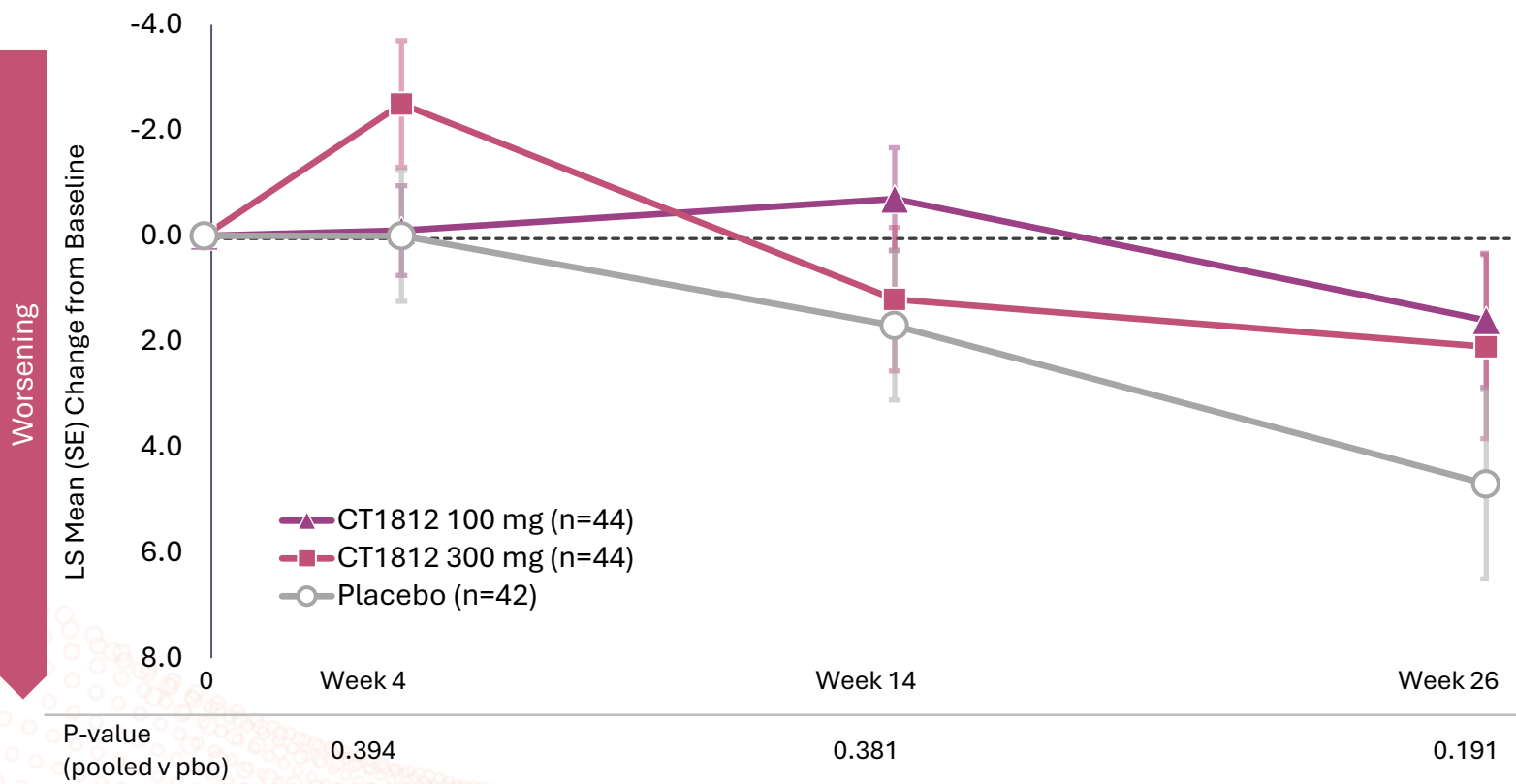
Writing

People Treated with Zervimesine Maintained Motor Function

62% preservation in measures of movement

MDS-UPDRS3

62% slowing



Components of UPDRS:



Balance



Gait



Speech



Facial expression



Rigidity



Tremor

SHIMMER Met and Exceeded Objectives and Expectations

Identified consistent signals of efficacy with a favorable tolerability profile

COG1201 SHIMMER was a phase 2a safety and tolerability study seeking signals of efficacy in people with dementia with Lewy bodies

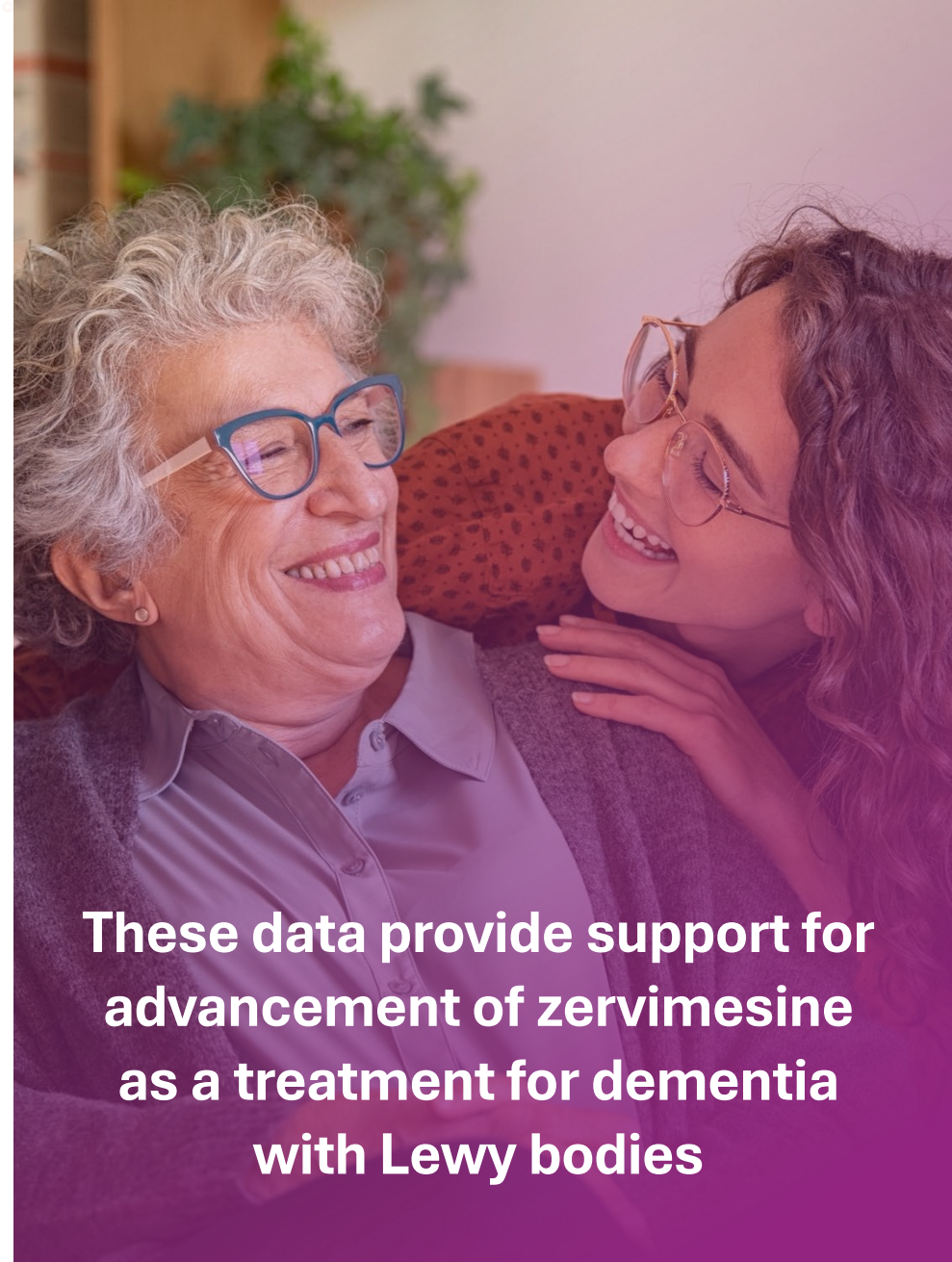


The safety and tolerability profile was similar to past experience with CT182



Clear signals of efficacy were observed

- Across Behavioral, Cognitive, Functional and Motor domains
- Treatment differences increased over 6 months



These data provide support for advancement of zervimesine as a treatment for dementia with Lewy bodies

Summary of SHIMMER Safety and Tolerability findings

Favorable safety profile vs placebo, AEs well balanced between arms

➡ 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

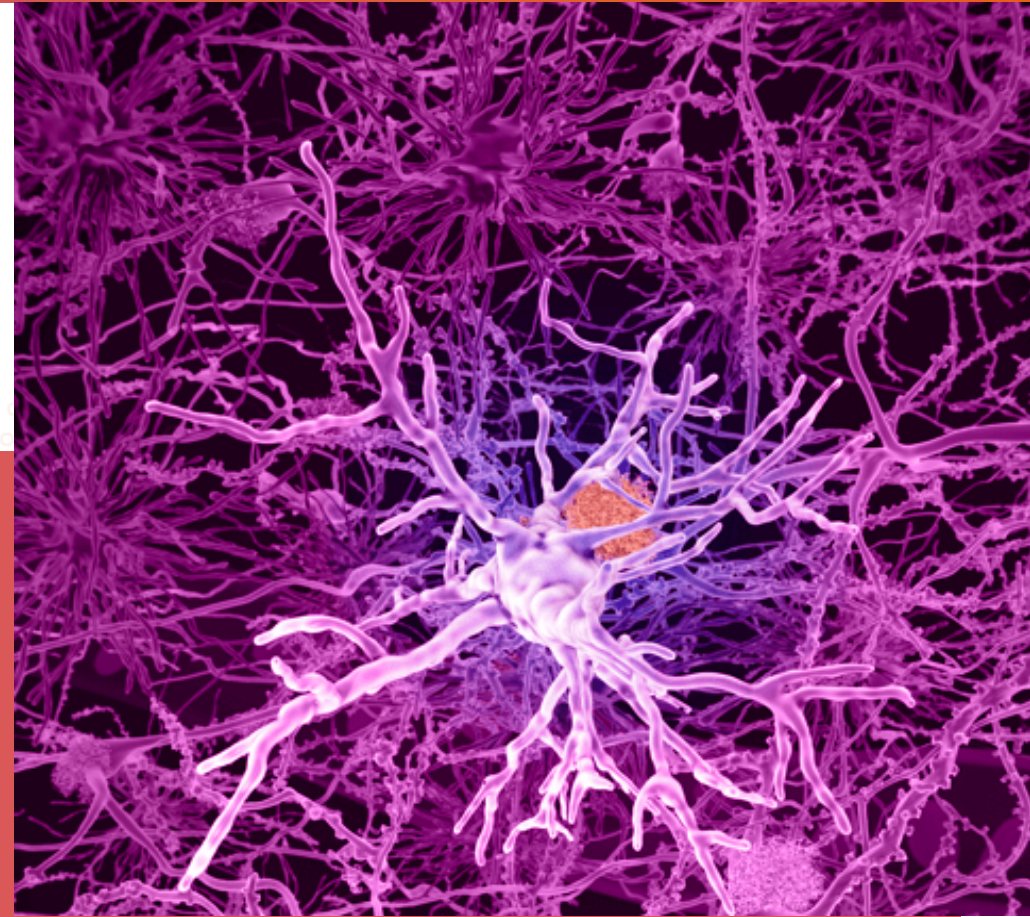
➡ Most common AEs* (other than increased LFTs) in the CT1812 group were diarrhea and abdominal discomfort

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

Alzheimer's Disease

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

Amyloid positivity confirmed for all participants by CSF or PET

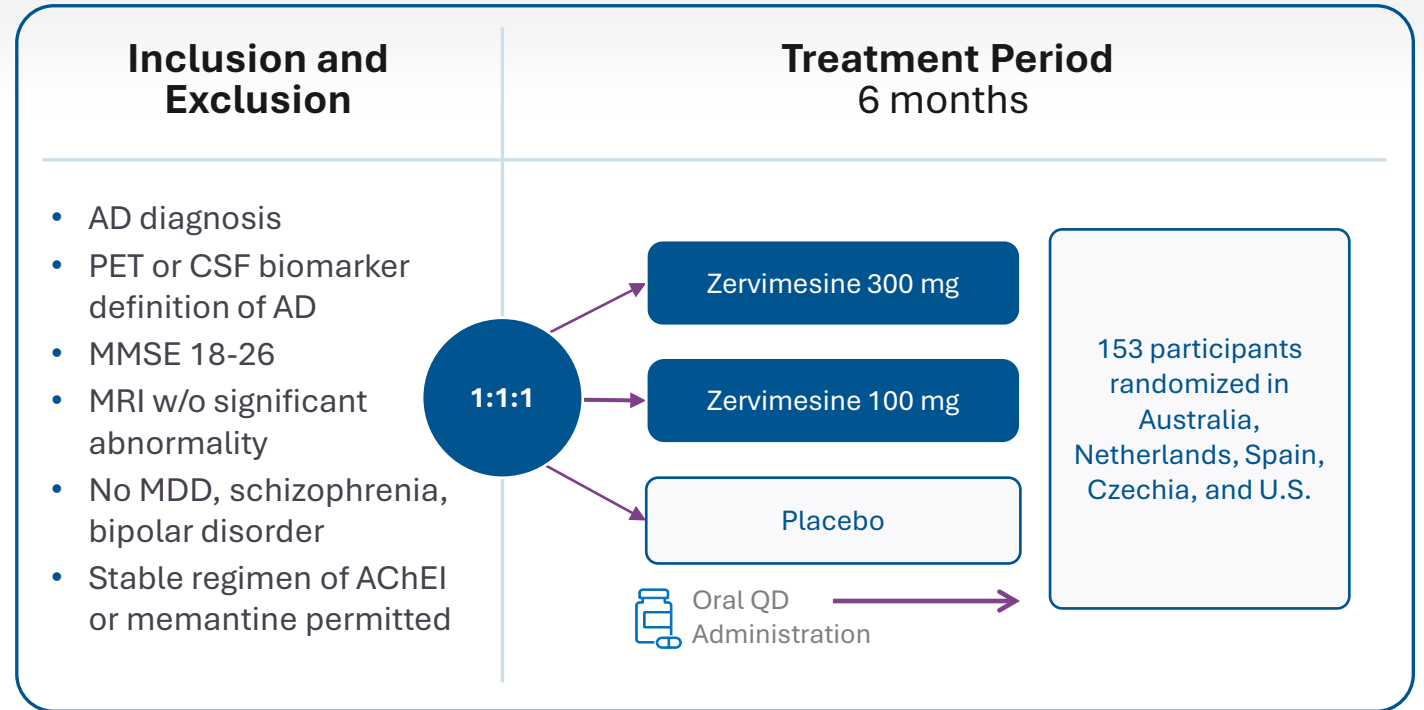


SHINE: Phase 2 PoC in Mild-to-Moderate Alzheimer's Disease

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

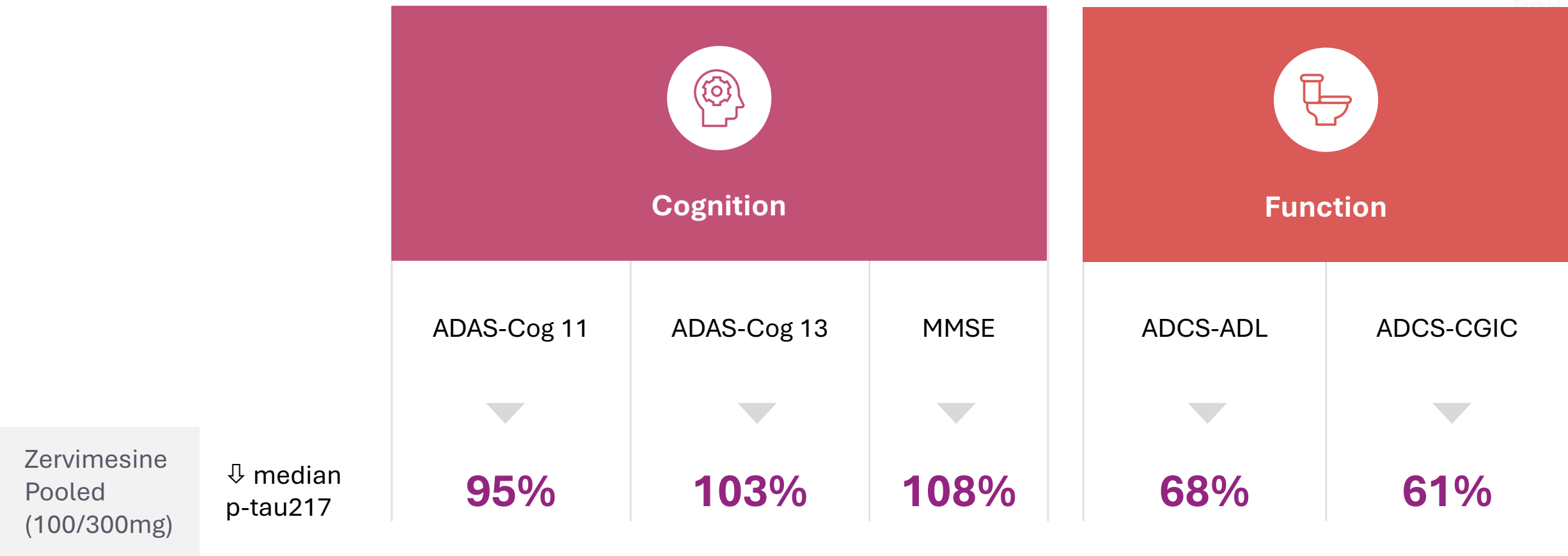


SHINE COG0201 study (NCT03507790) partially funded by \$31M NIA grant R01AG058660

SHINE
COG0201

Up to 108% Percent Slowing on Assessments

Strong, consistent efficacy signals across measures



Tau Burden in Amyloid-related AD Clinical Trials

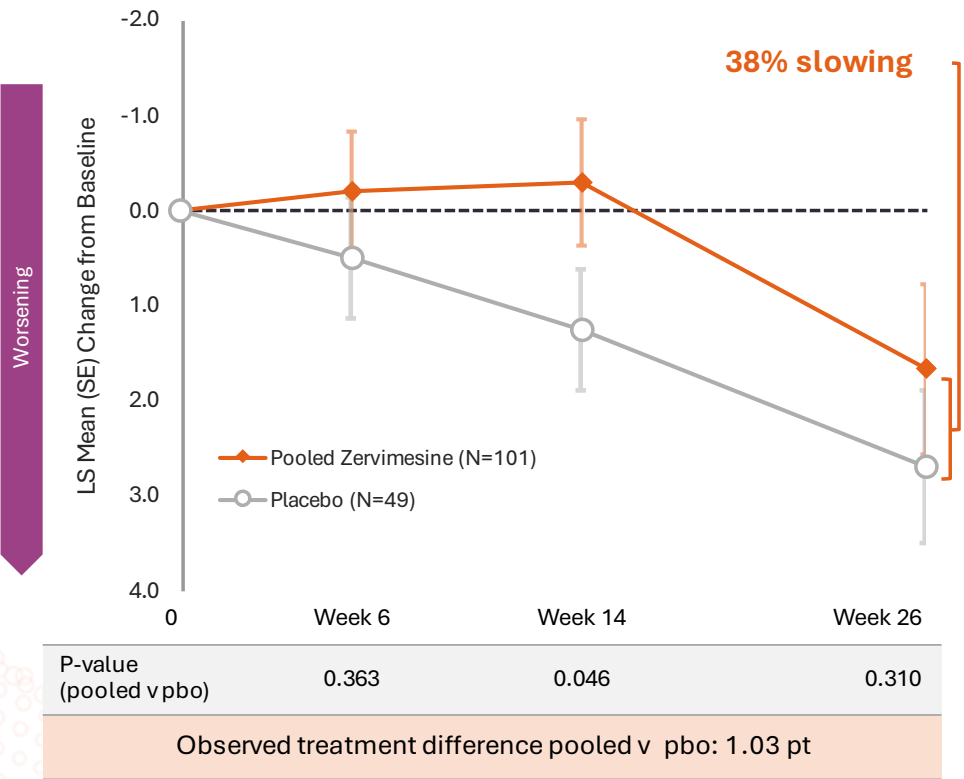
Baseline plasma p-tau217: a predictive biomarker of response to therapy

- 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

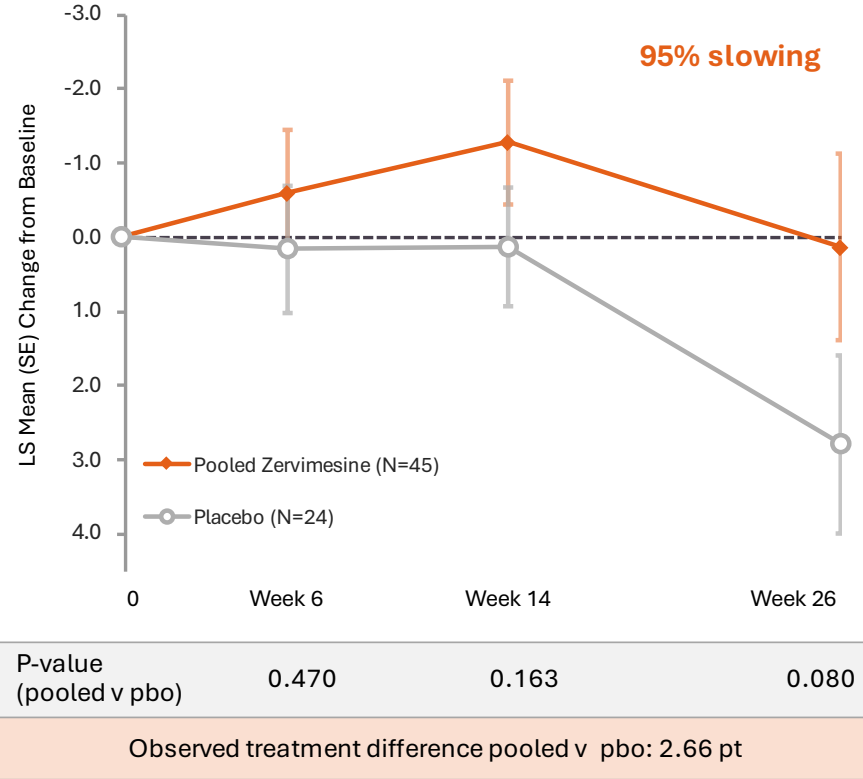
Below Median p-tau217, Treated Participants Experienced Profound Cognitive Effect

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

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



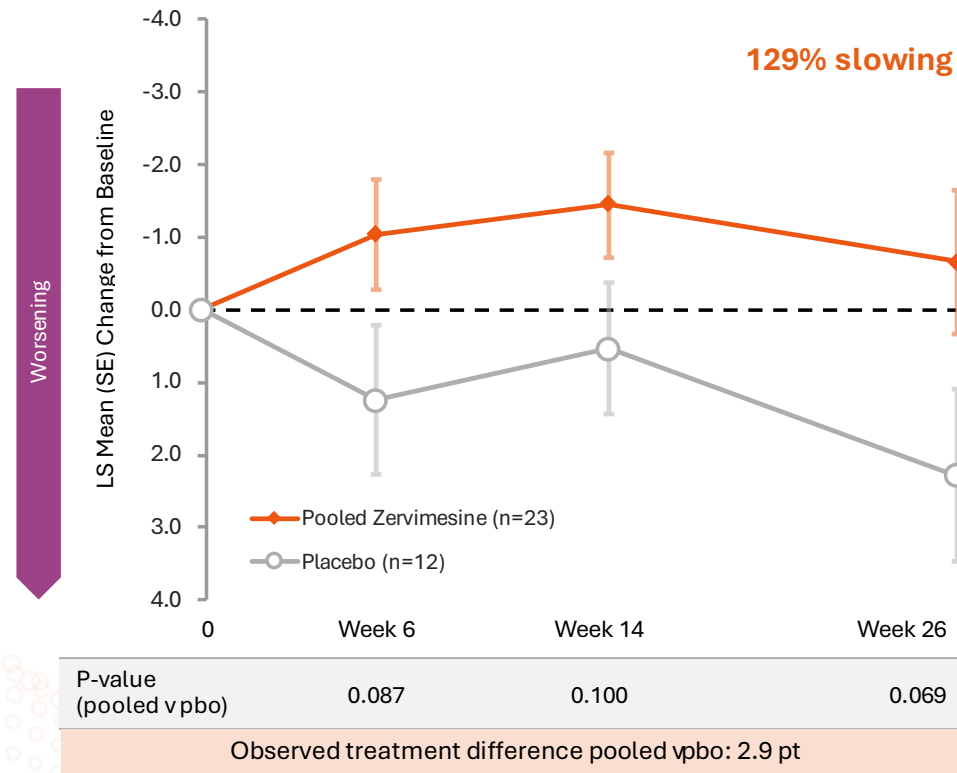
Below median p-tau217 (n=69)



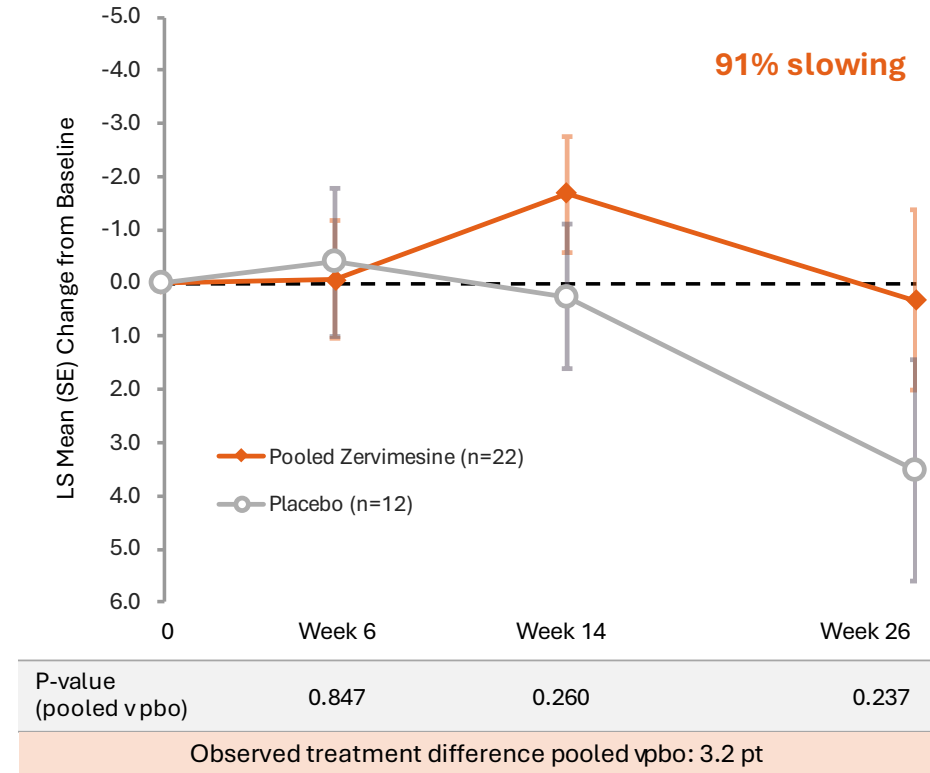
Treatment Impact in Below Median p-tau217 Consistent Across Baseline MMSE scores

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

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

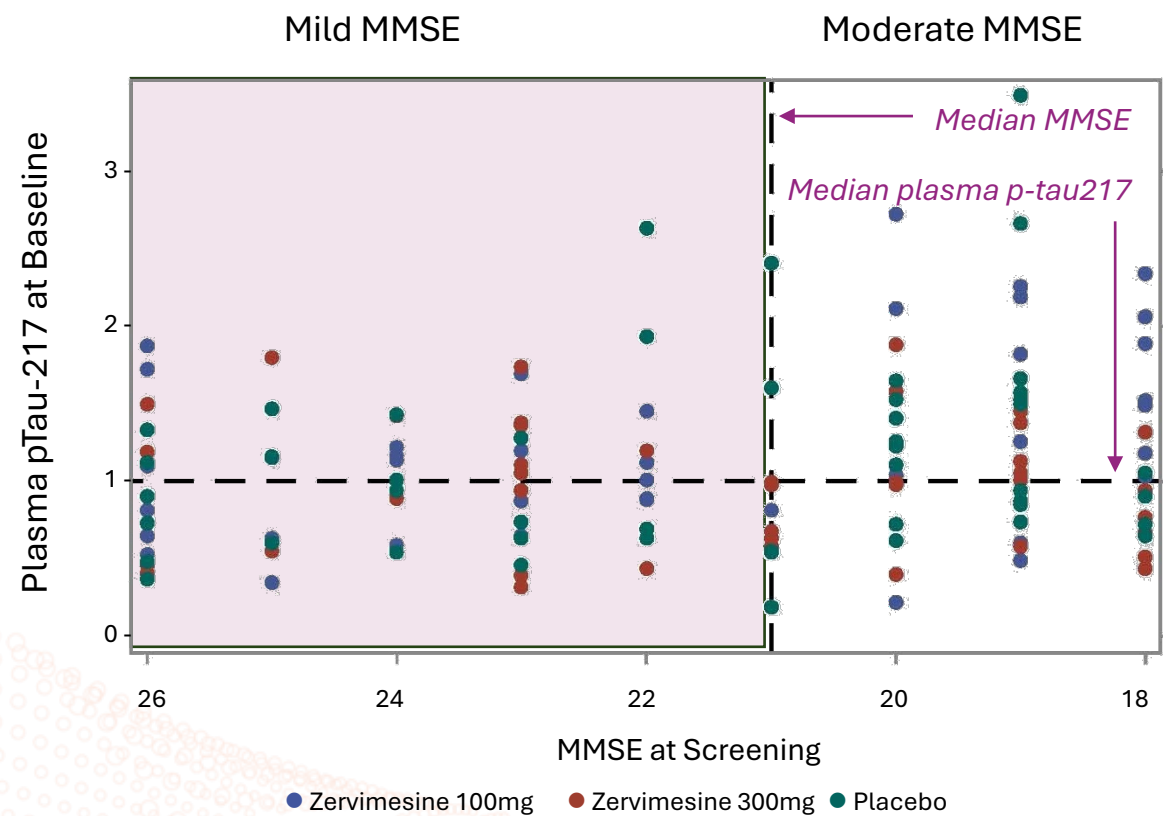


Zervimesine-Treated **Moderate** (MMSE 18-21) Participants



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

Summary of SHINE Safety and Tolerability findings

Favorable safety profile vs placebo,
AEs well balanced between arms, no ARIA

- Zervimesine demonstrated a favorable safety and tolerability profile
- Most TEAEs were mild or moderate in severity
- Similar percentages of adverse events in treated (76.5%) and placebo (78%) groups
- No discontinuations due to AEs in the 100mg dose group
- Most discontinuations were in 300mg group and all the reportable liver enzyme elevations were in 300mg group

Adverse Events

Zervimesine	76.5%
Placebo	78.0%

Serious AEs

Zervimesine	4.9%
Placebo	10.0%

Deaths[†]

Zervimesine	0
Placebo	1 (cancer)

Zervimesine SHINE Study: Summary and Conclusions

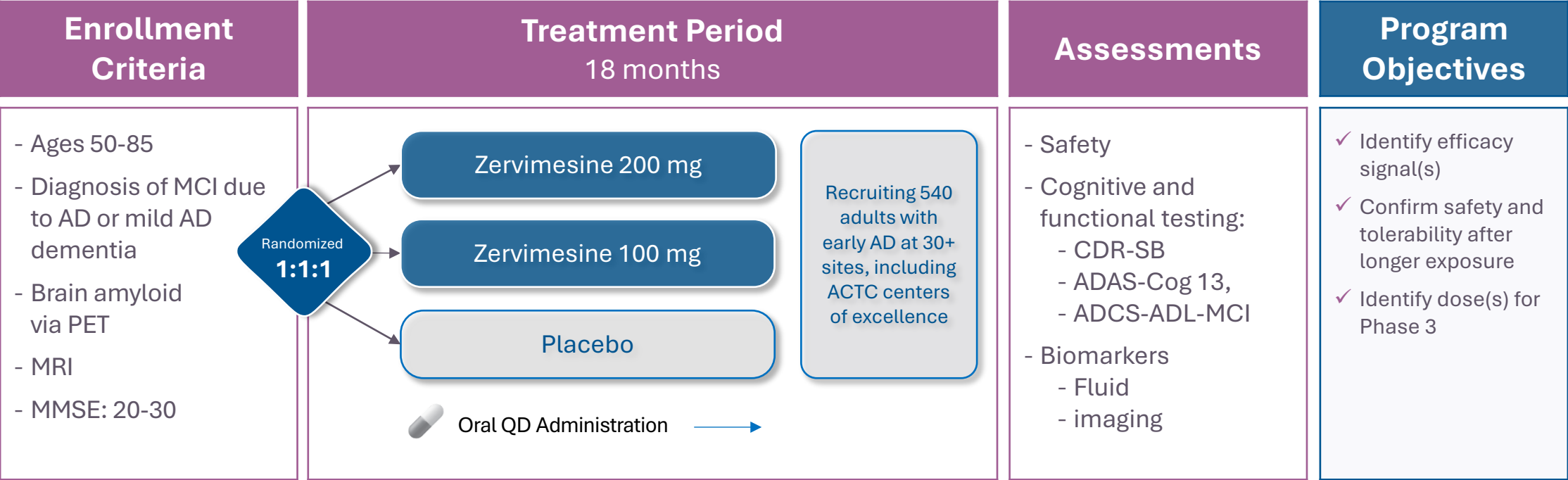
Plasma p-tau217 biomarker identifies strong zervimesine-treatment responder group

- Zervimesine has favorable safety and tolerability profile
 - Similar percentages of AEs in pooled treated and placebo groups
- All cognitive and functional measures trended in favor of zervimesine
- Large cognitive impact observed in below-median plasma p-tau217 subgroup
- Will assess optimal plasma p-tau217 cut-point for future studies

Next steps: Requested End-of-Phase 2 meeting with FDA to establish protocol for Phase 3 in population defined by plasma p-tau217

START - A 540-Person Study in Amyloid-positive Early AD

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



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

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



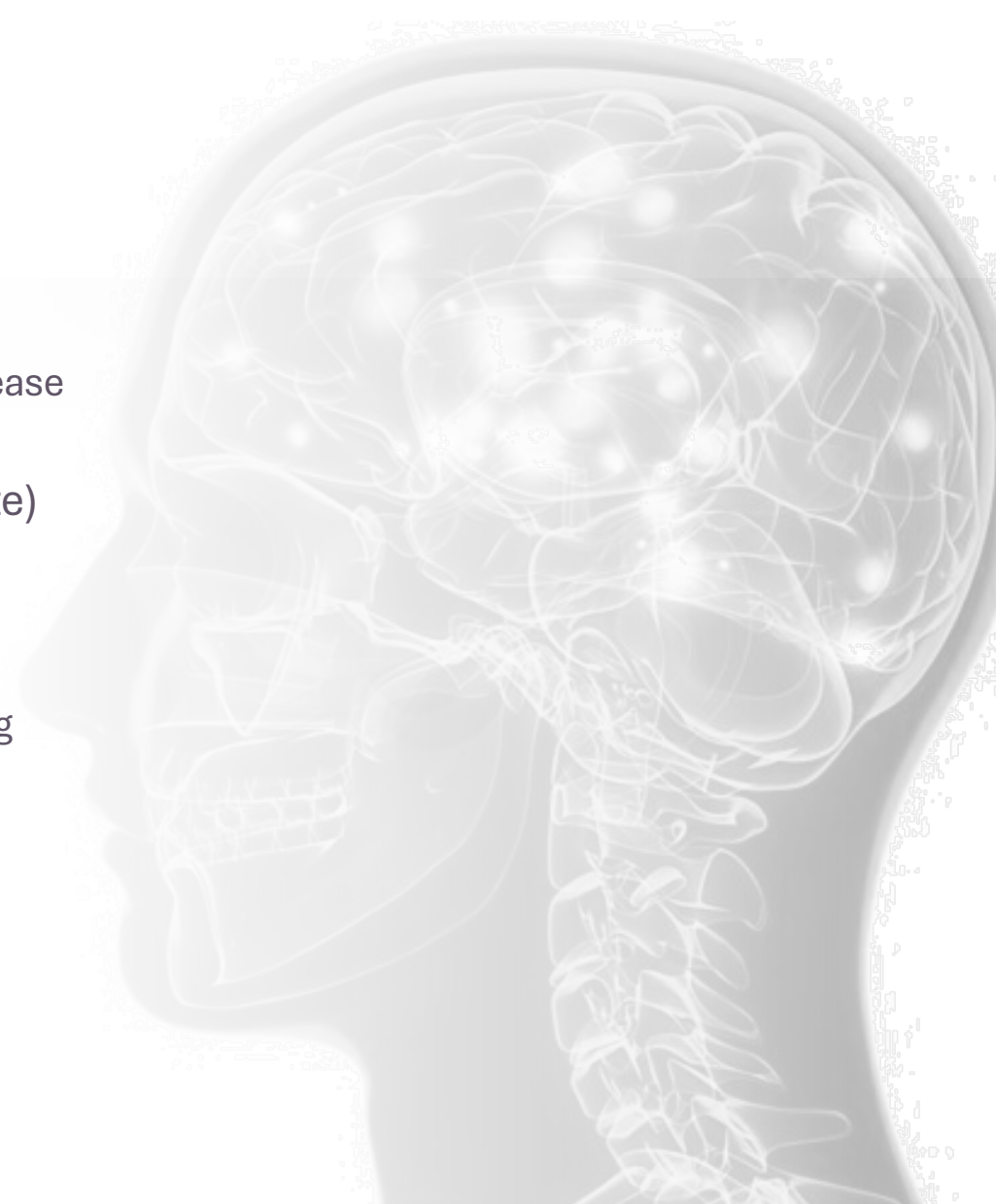
Geographic Atrophy

Slowing of GA growth
rate and area

Executive Summary

First-in-class oligomer antagonist with compelling efficacy data

- **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
- **Generally 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



Current Financial Position

As of quarter ended June 30, 2025

Cash and cash equivalents \$11.6 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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