



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

*November 2025*

# Forward-looking Statements

## FORWARD-LOOKING STATEMENTS

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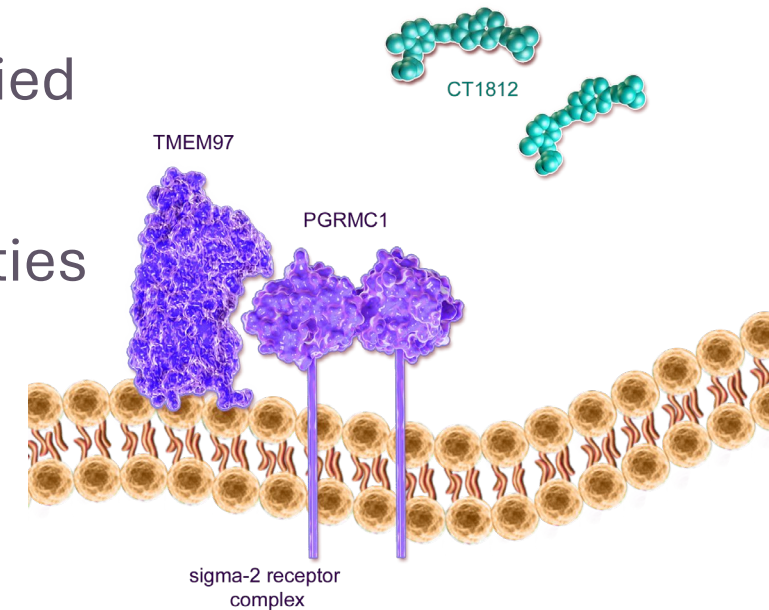
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*Projections, estimates, industry data and information contained in this presentation, including the size of and growth in key end markets, are based on information from third-party sources and management estimates. Although we believe that these third party-sources are reliable, we cannot guarantee the accuracy or completeness of these sources. Our management’s estimates are derived from third-party sources, publicly available information, our knowledge of our industry and assumptions based on such information and knowledge. Our management’s estimates have not been verified by any independent source. All of the projections, estimates, market data and industry information used in this presentation involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such information. In addition, projections, estimates and assumptions relating to us and our industry’s future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including, but not limited to, those described above, that could cause future performance to differ materially from our expressed projections, estimates and assumptions or those provided by third parties.*

# Novel MoA Discovered Through Founder's Screening Assay

## Zervimesine Interrupts Binding of Toxic Oligomers

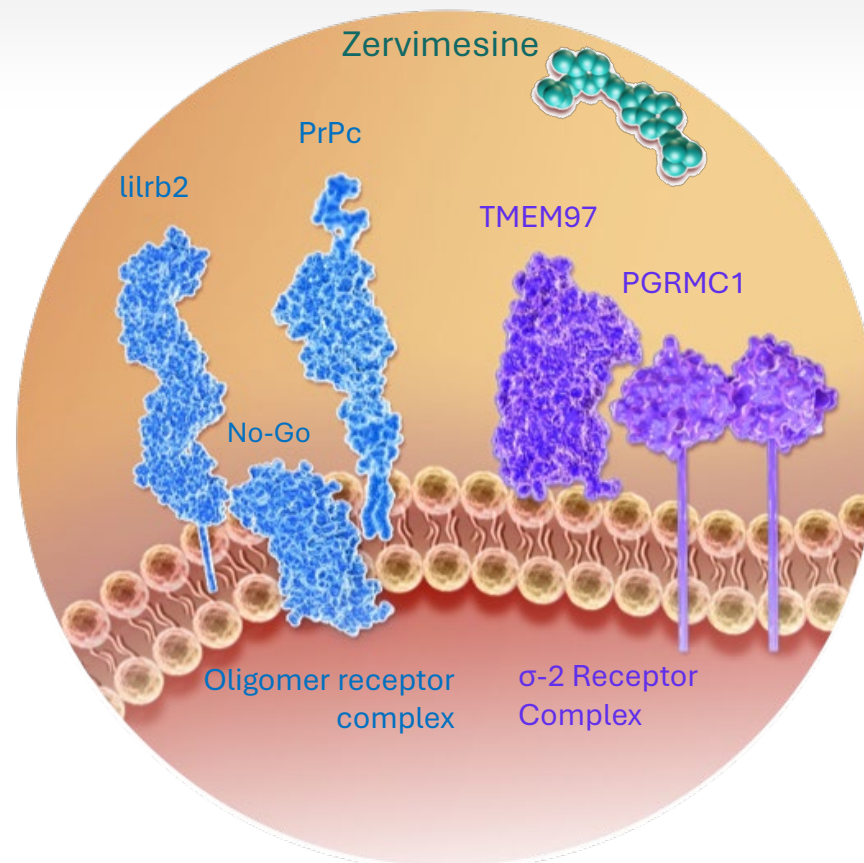
- Phenotypic *in vitro* screen to select molecules that protect neurons from toxic oligomers
- Screened 10,000 compounds through this assay and identified 5 unique chemical series
- Zervimesine readily crossed BBB with good drug-like properties
- Early work led to NIH grants, which funded through Phase 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	
<b>Completed Studies</b>				
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

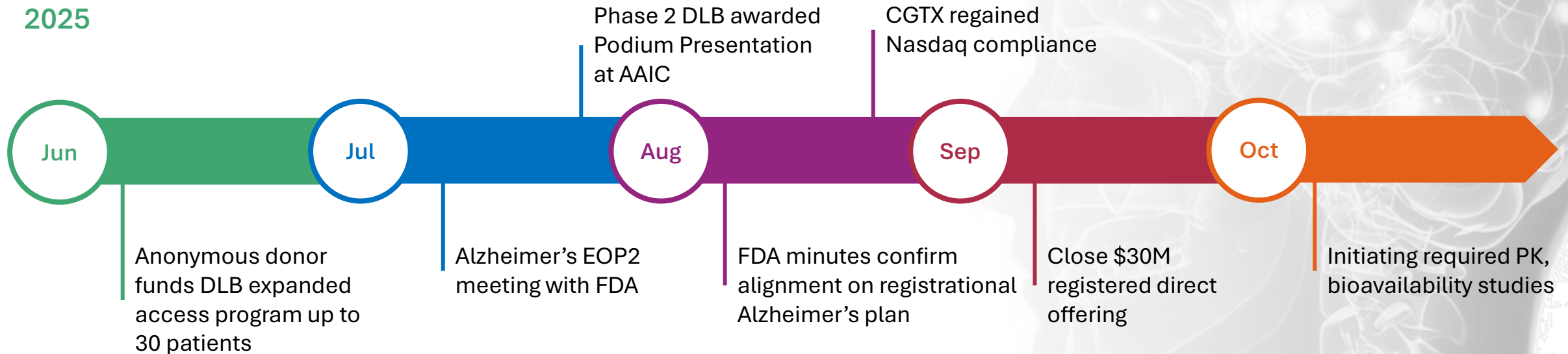
- Phase 2 SHINE Study: Efficacy across cognitive measures in mild-to-moderate Alzheimer's disease
- Phase 2 SHIMMER Study: behavioral, functional, cognitive, movement benefit in mild-to-moderate DLB
- Phase 2 MAGNIFY Study: slower lesion growth in geographic atrophy secondary to dry AMD

# 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

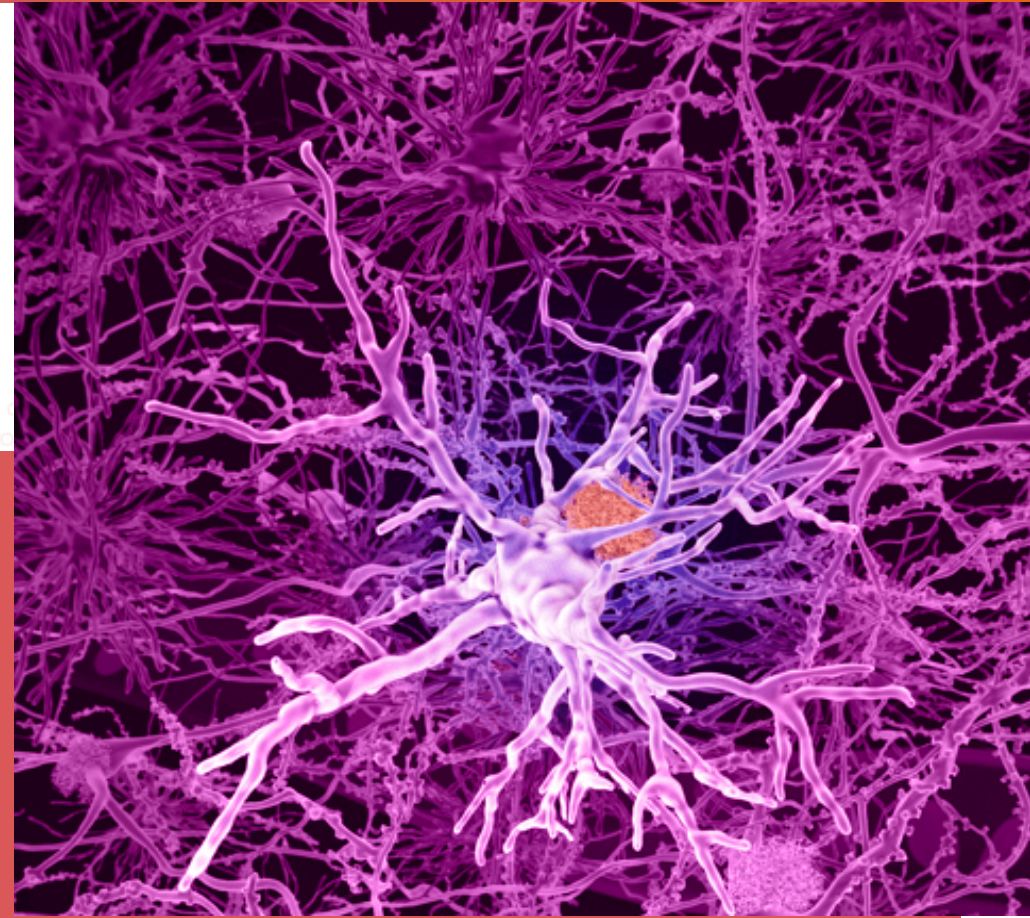
# CGTX Company Summary: With Recent Raise, Advancing Towards Late-stage Studies Following EOP2 FDA Meeting





# Alzheimer's Disease

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



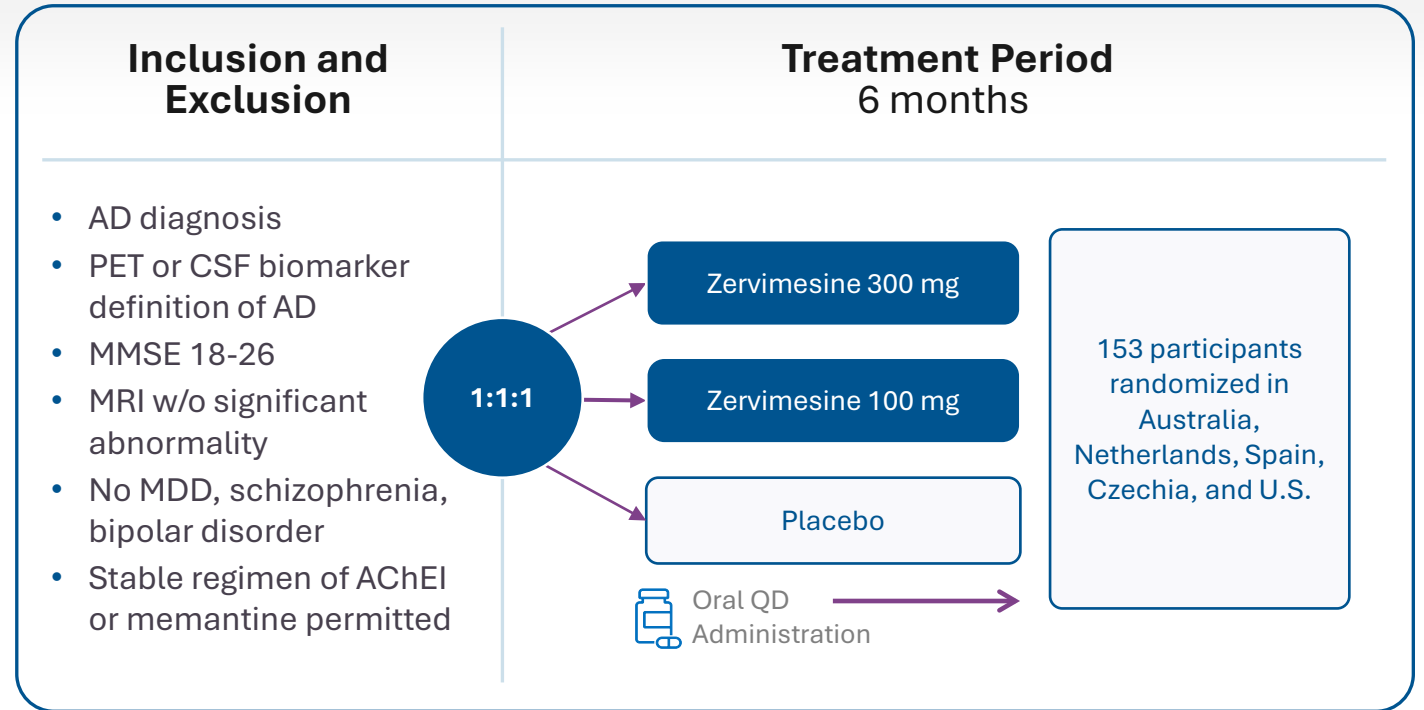


# SHINE: Phase 2 PoC in Mild-to-Moderate Alzheimer's Disease

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

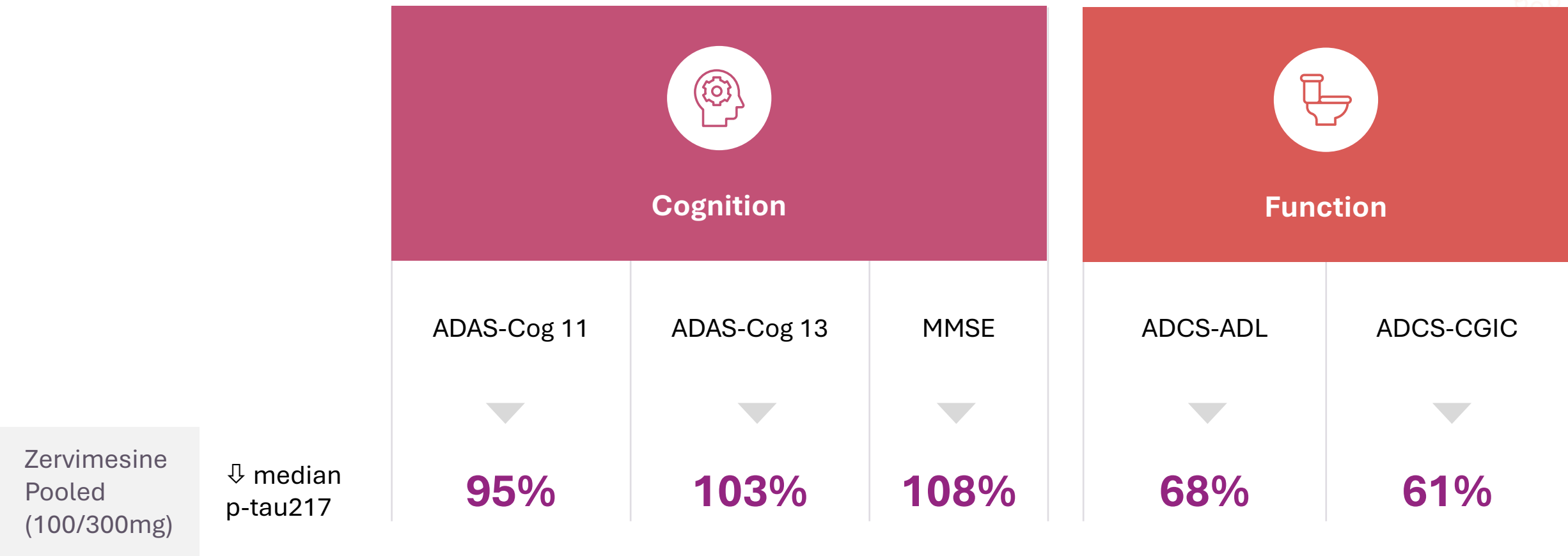


SHINE COG0201 study (NCT03507790) partially funded by \$31M NIA grant R01AG058660

**SHINE**  
COG0201

# Up to 108% Percent Slowing on Assessments

Strong, consistent efficacy signals across measures



# Tau Burden in Amyloid-related AD Clinical Trials

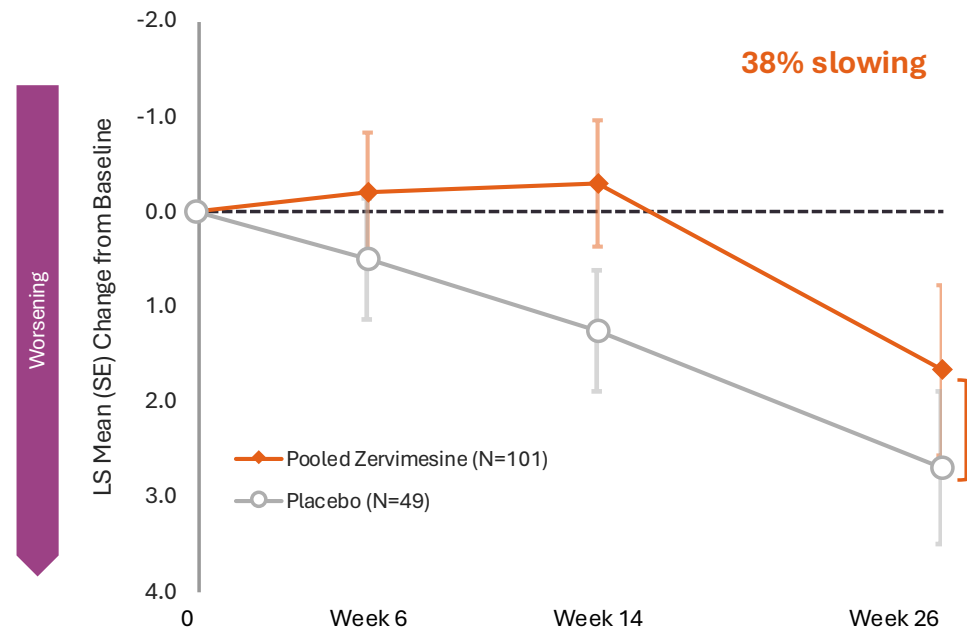
Baseline plasma p-tau217: a predictive biomarker of response to therapy

- 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 $\beta$  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

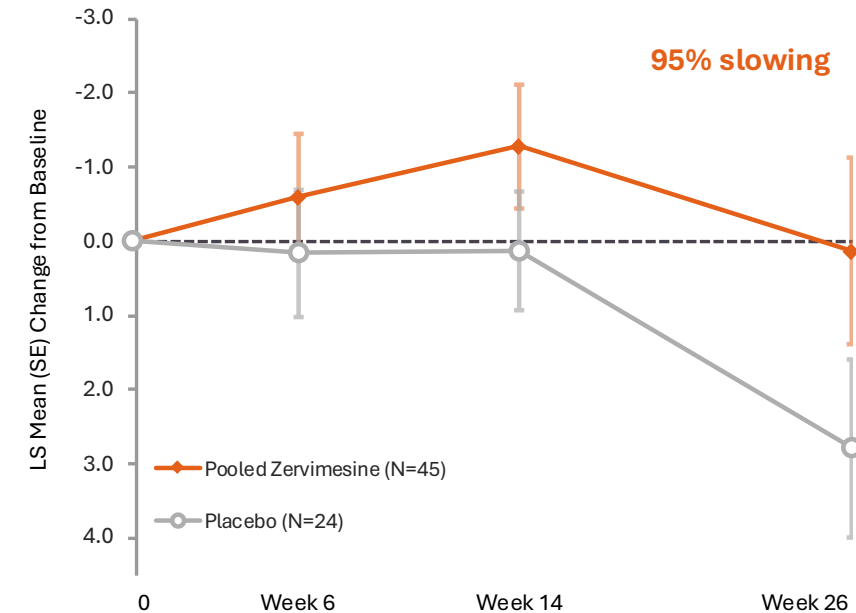
Preservation of ADAS-Cog 11 in participants below median plasma p-tau217†

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



P-value (pooled v pbo)	0.363	0.046	0.310
Observed treatment difference pooled v pbo: 1.03 pt			

Below median p-tau217 (n=69)



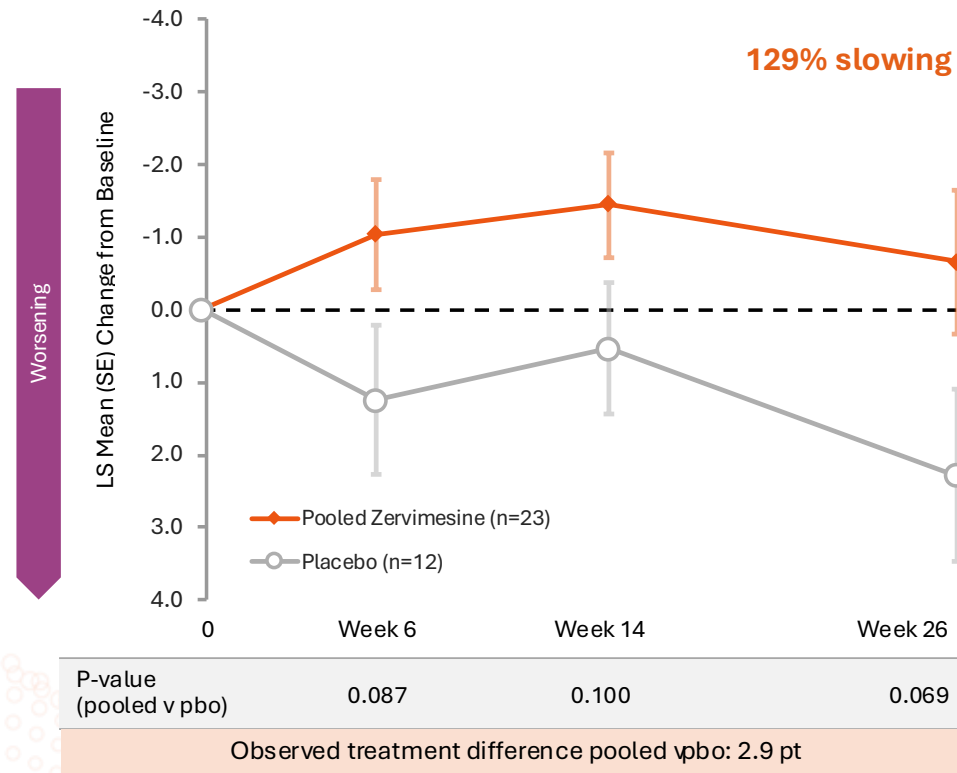
P-value (pooled v pbo)	0.470	0.163	0.080
Observed treatment difference pooled v pbo: 2.66 pt			



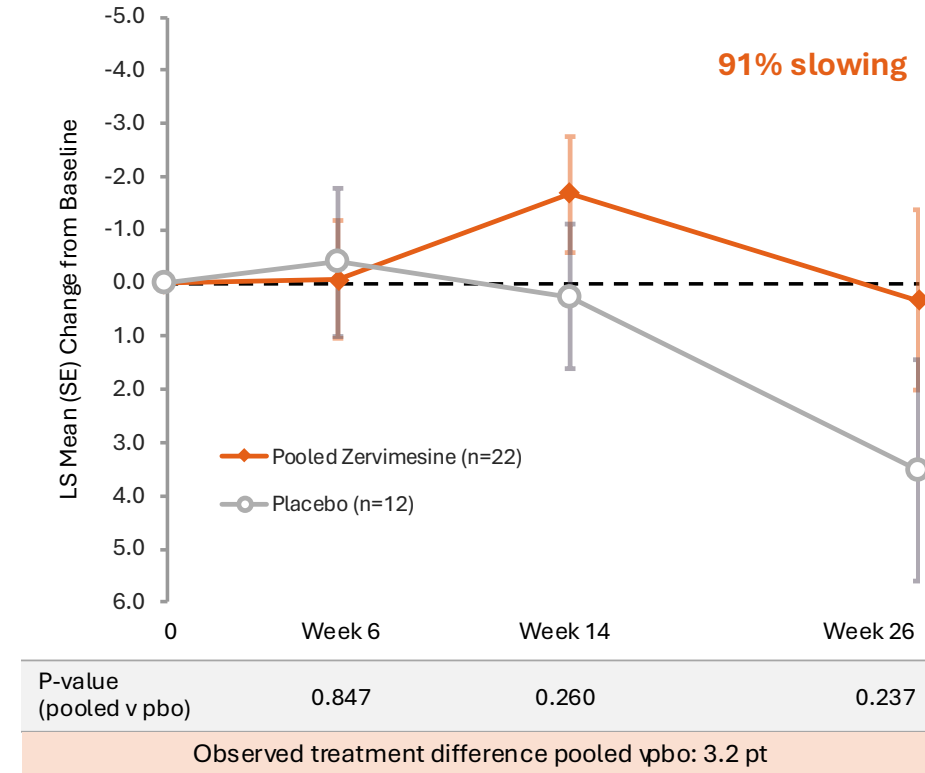
# Consistent Treatment Impact in Participants with Lower p-tau217 Across Baseline MMSE scores

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

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

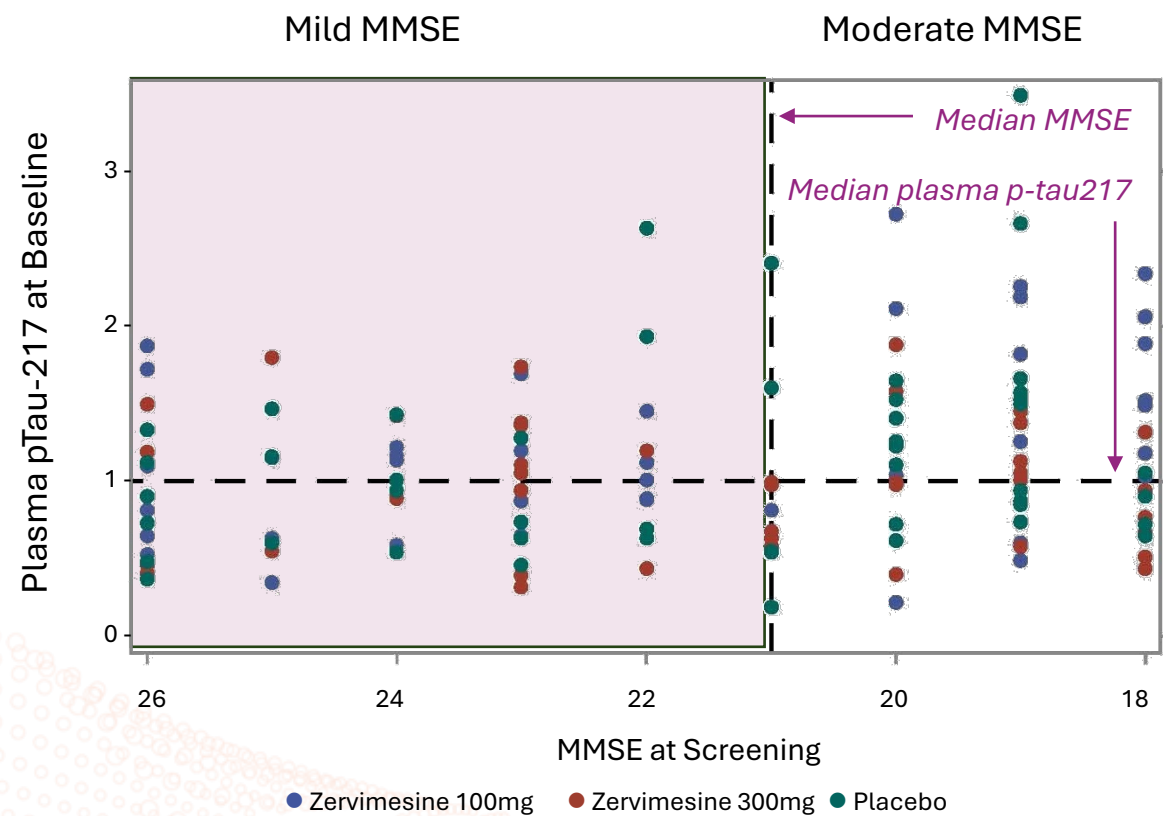


Zervimesine-Treated **Moderate** (MMSE 18-21) Participants



# 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

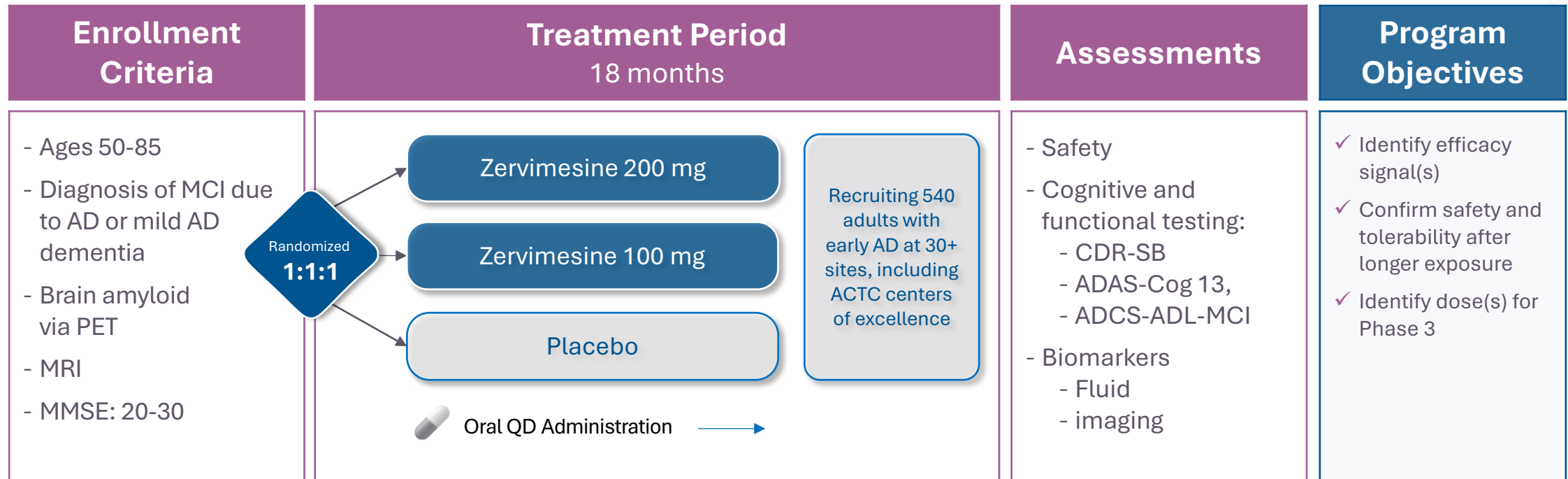
# FDA Confirms Phase 3 Plan in Alzheimer's Disease

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



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



## Dementia Programs:

Strong clinical signals in the two primary causes of dementia:

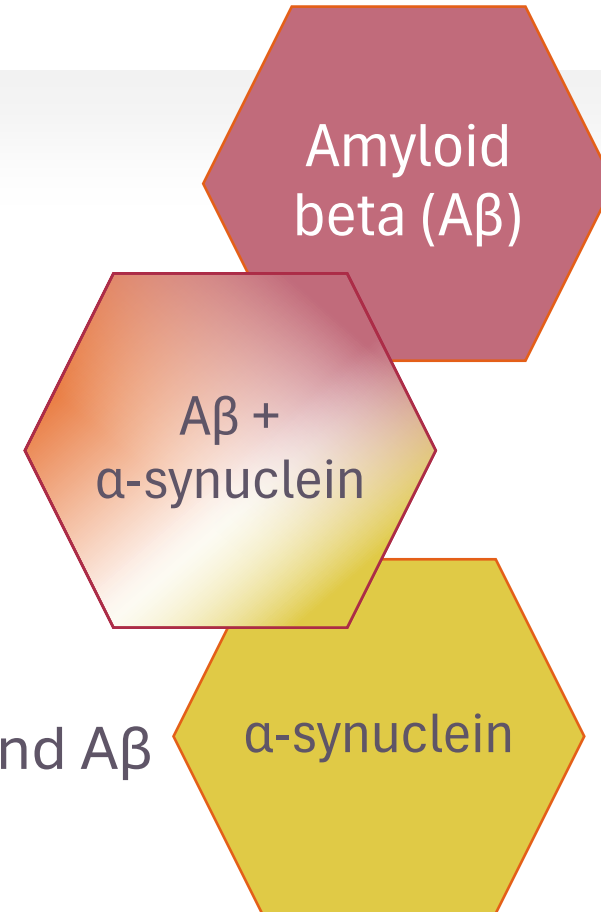
- Dementia with Lewy Bodies (DLB)
- Mild-to-Moderate Alzheimer's Disease



# AD and DLB: 2 Diseases with Overlapping Pathology

Primary treatment goal – slow the progression of cognitive decline

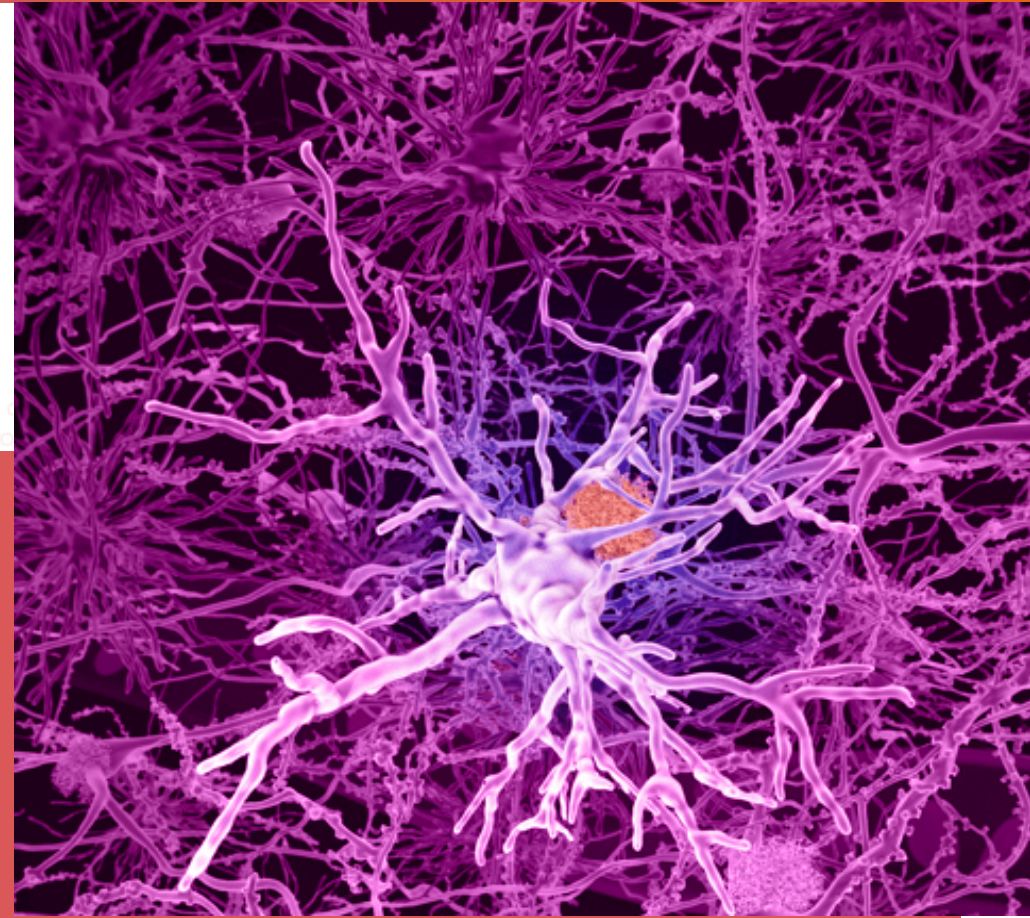
- A $\beta$ : closely associated with Alzheimer's pathogenesis
- $\alpha$ -synuclein: closely associated with Lewy body dementias
- Co-pathology is common
  - Up to 80% of DLB patients have BOTH  $\alpha$ -synuclein and Amyloid beta (A $\beta$ )<sup>1</sup>
  - Appx 50% of Alzheimer's patients have BOTH A $\beta$  and  $\alpha$ -synuclein<sup>2</sup>
- Zervimesine has shown protective function against  $\alpha$ -synuclein and A $\beta$





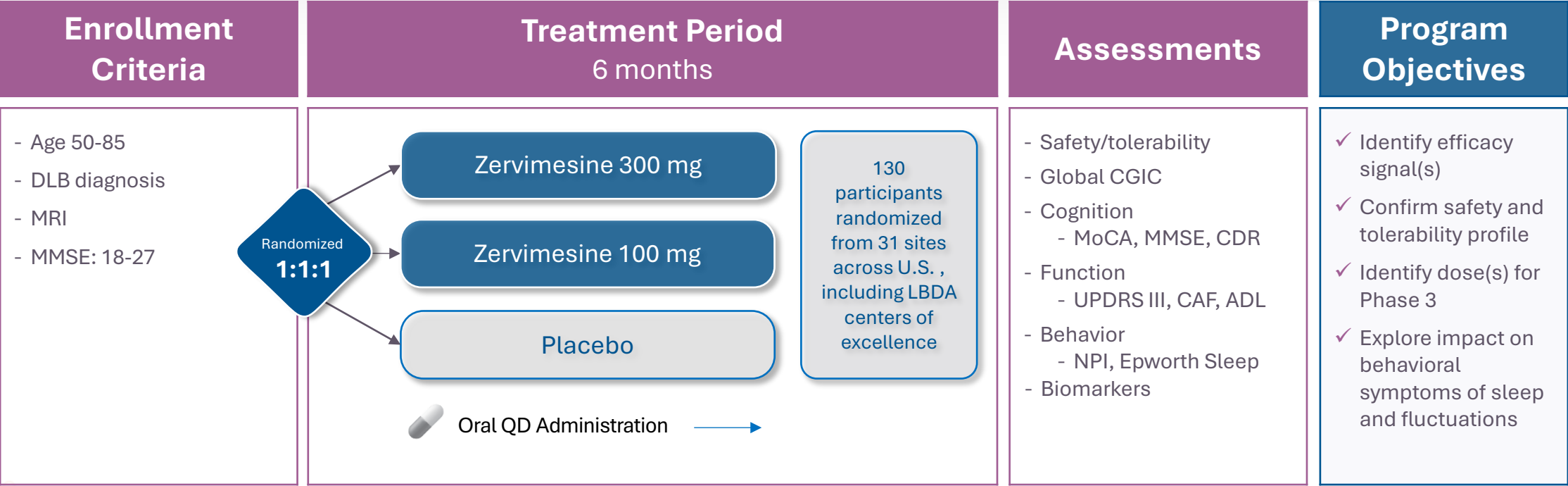
# Dementia with Lewy Bodies (DLB)

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

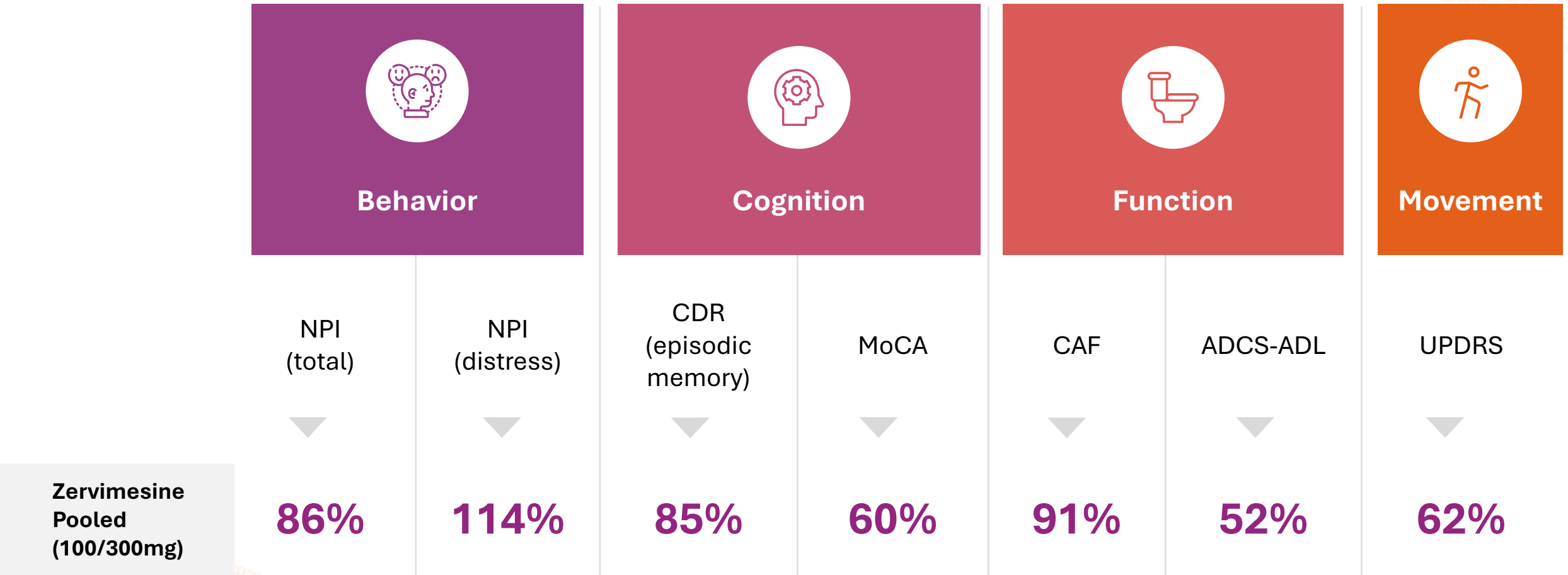


SHIMMER COG1201 study (NCT05225415) partially funded by \$30M NIA grant R01AG071643



# Up to 91% Percent Slowing on Assessments

Strong clinical signals across major DLB symptoms relative to placebo

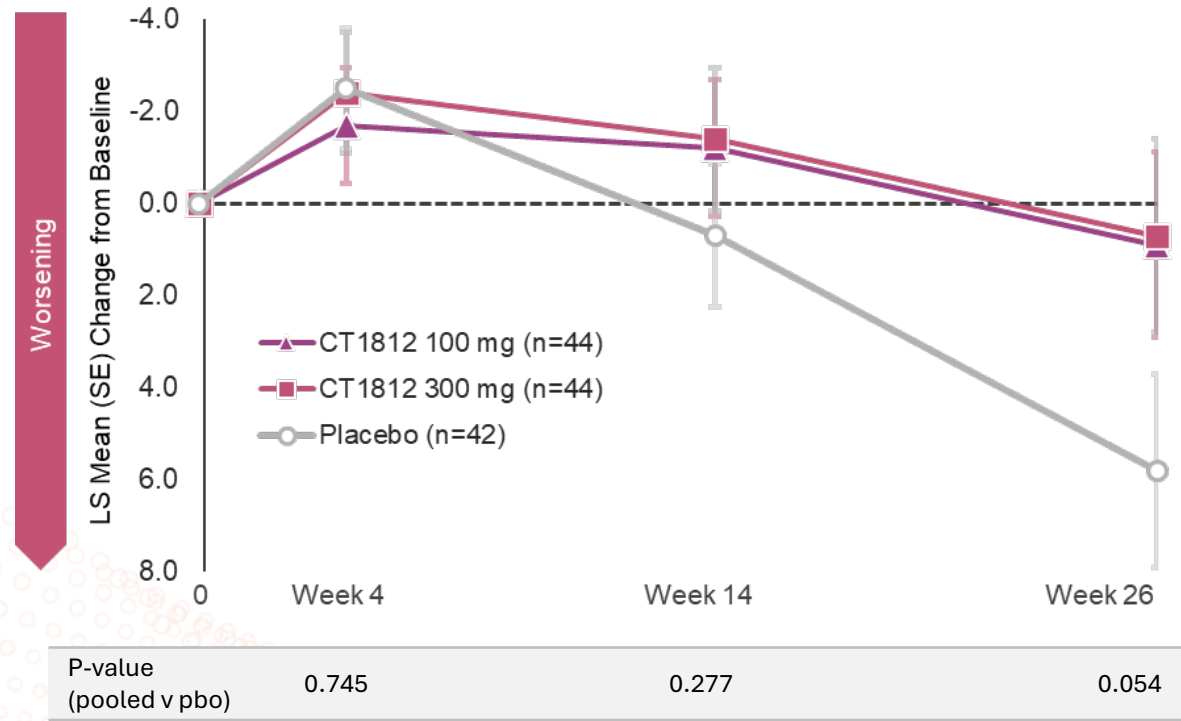


# Zervimesine Showed Dramatic 86% Impact on Neuropsychiatric Measures

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

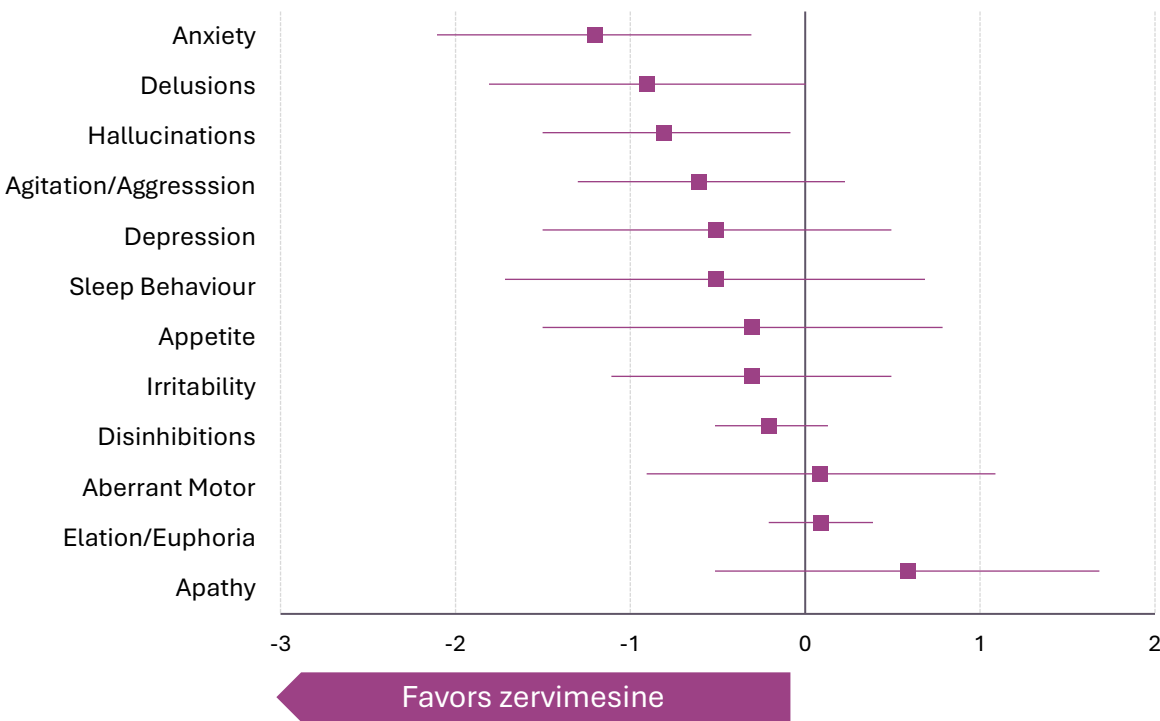
## NPI

NPI Total Score (A-L)



## NPI favor Treatment with Zervimesine

LS Mean Difference from Placebo 95% CI



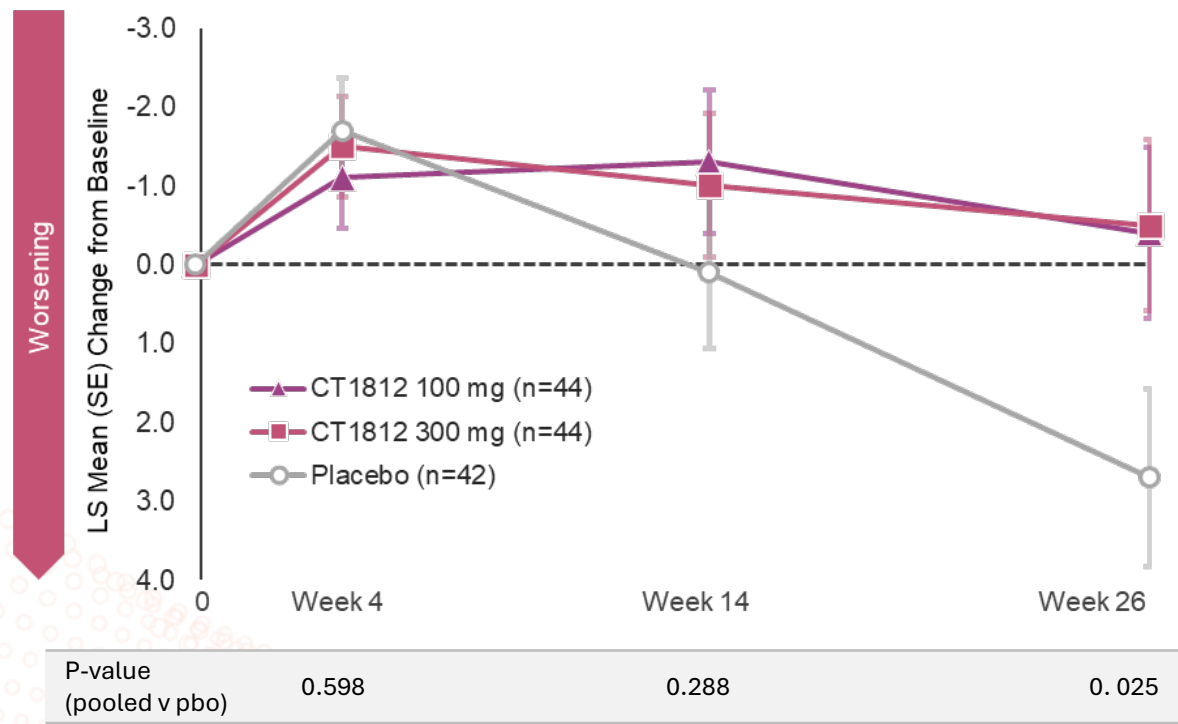
# Because Participants Improved in Hallucinations, Delusions & Anxiety, Caregivers were Notably Better

New tool created to measure caregiver burden in DLB

## NPI Distress

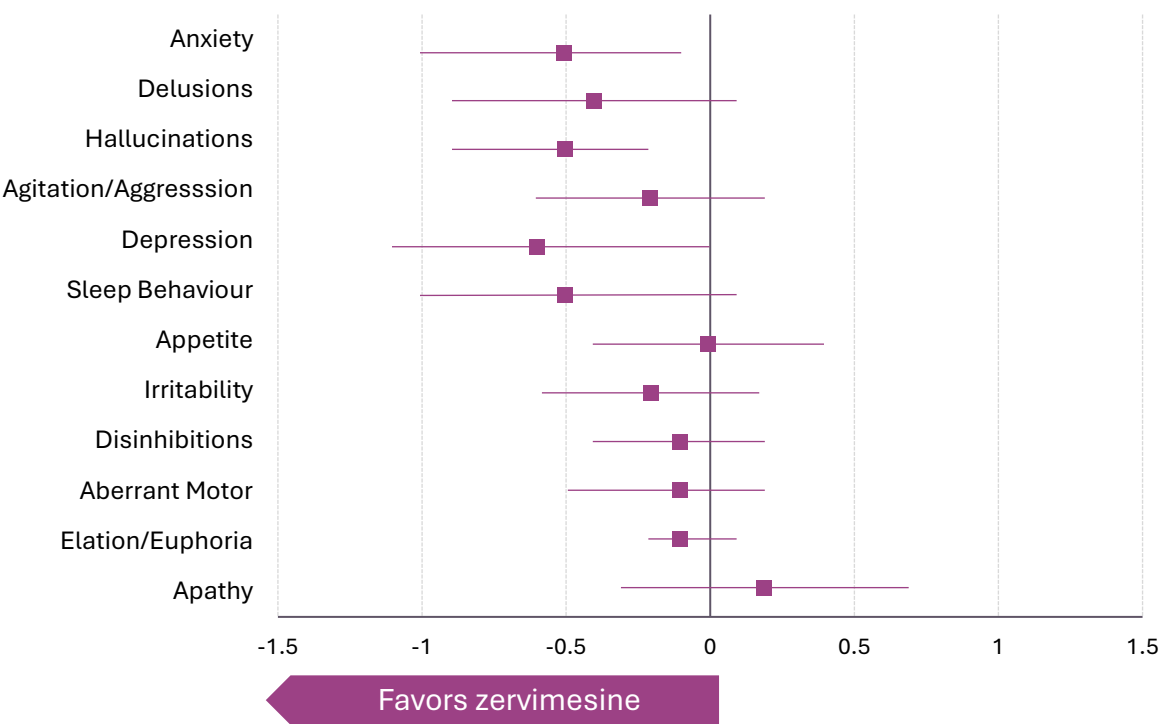
NPI Total Score (A-L) Caregiver Distress

114% Slowing



## NPI Distress favors Treatment with Zervimesine

LS Mean Difference from Placebo 95% CI

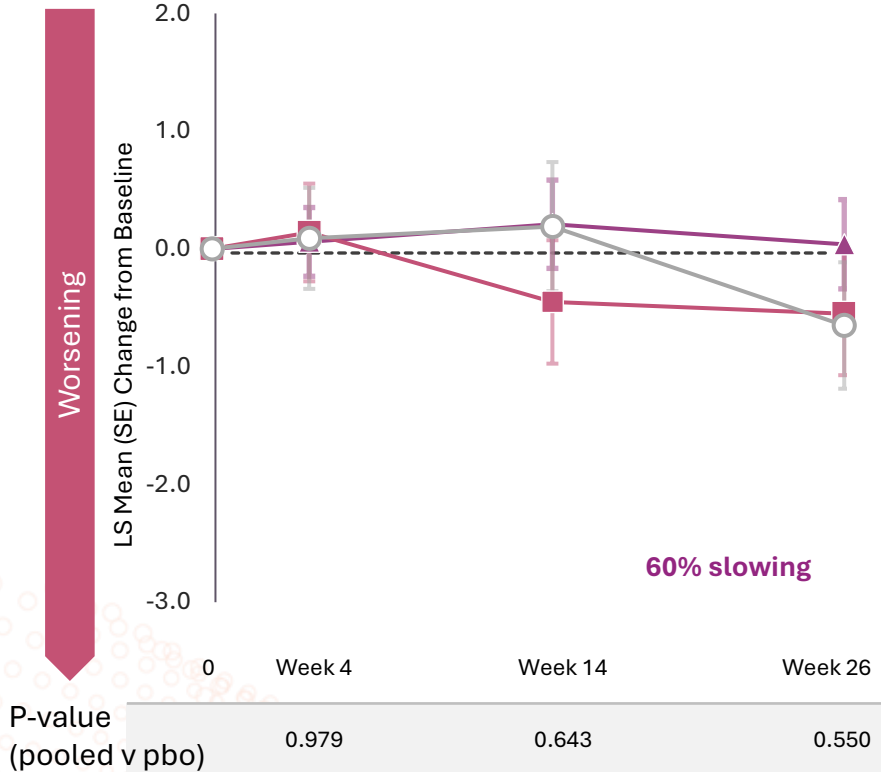


# Up to 91% Slowing of Cognitive Decline Across Assessments

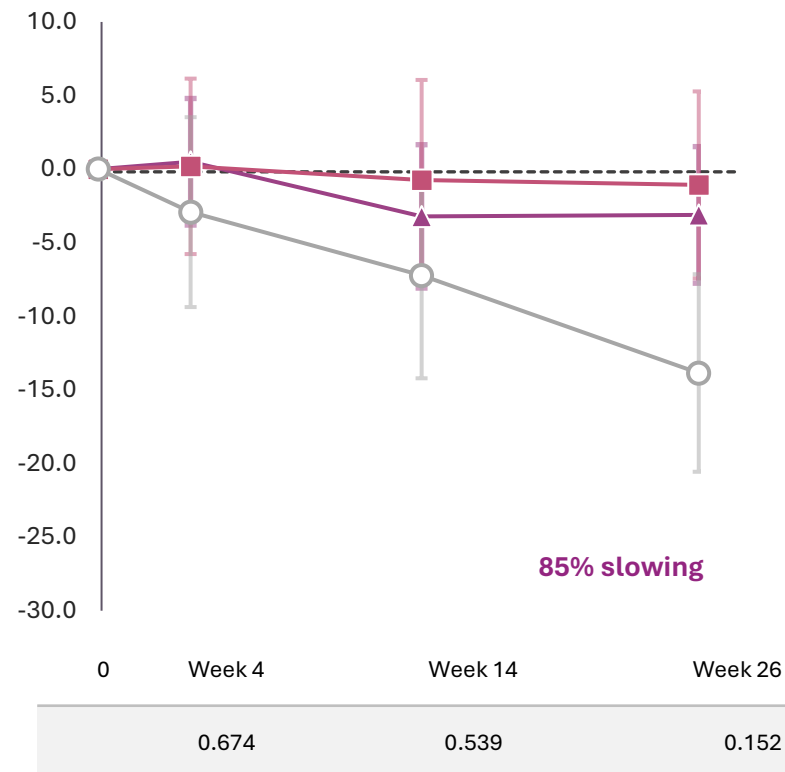
Zervimesine improved patients' attentiveness and problem solving

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

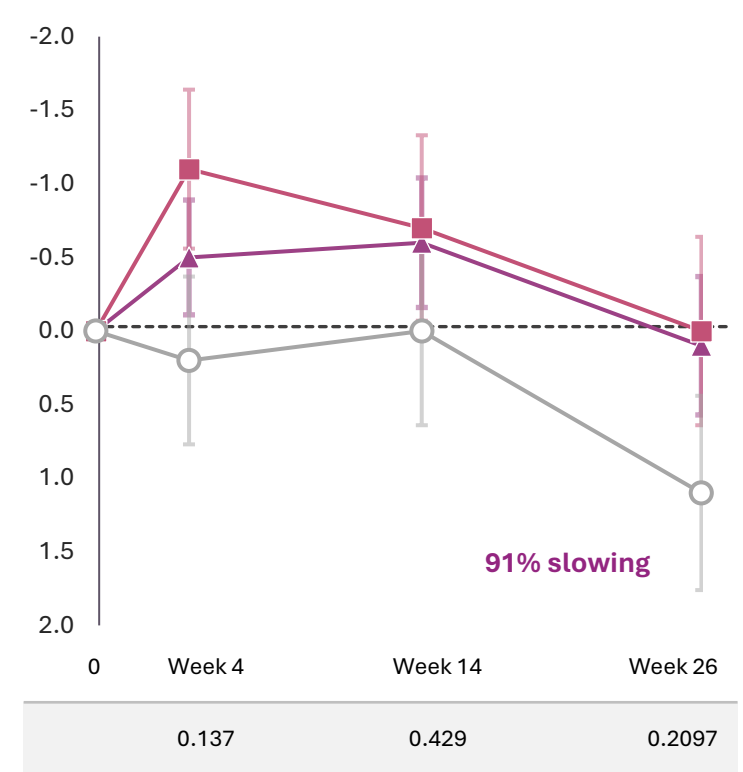
MoCA (ITT)



CDR - Episodic Memory (ITT)



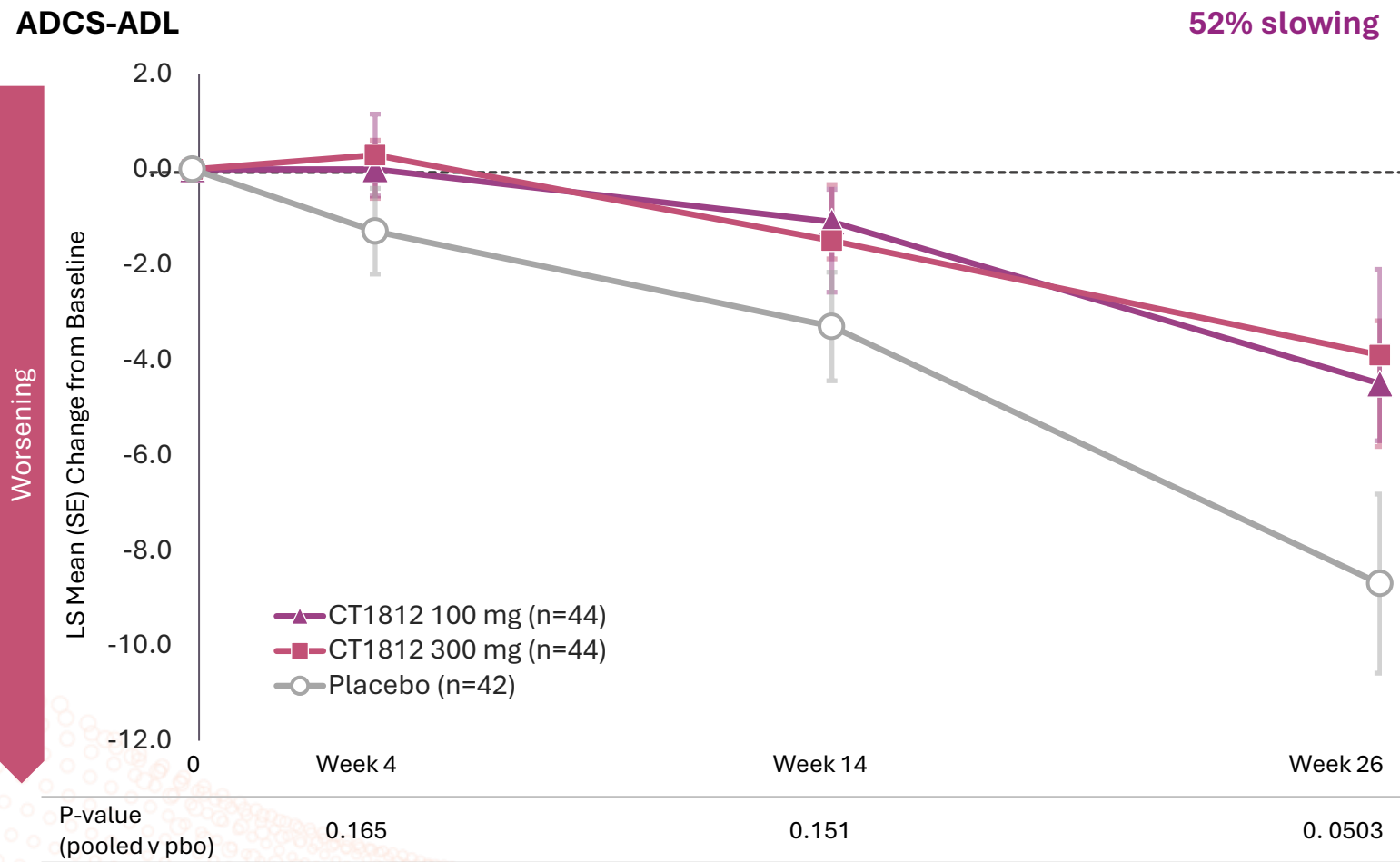
CAF (Fluctuations) (ITT)





# People on Zervimesine Maintained Self-care

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



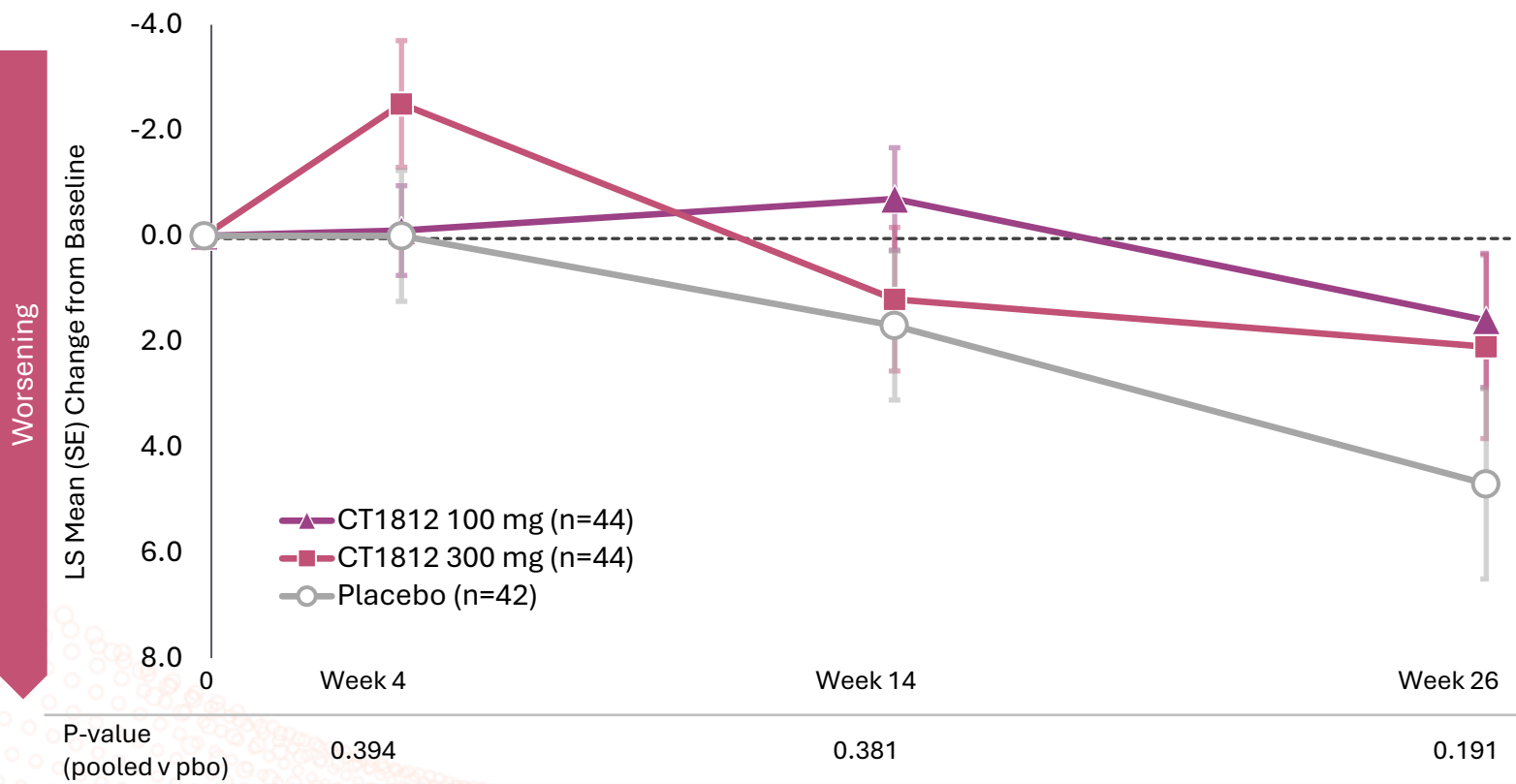
- Bathing
- Toileting
- Dressing
- Conversing
- Grooming
- Shopping
- Feeding
- Writing

# 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

# 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  $\geq 3x$  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 <sup>†</sup>
CT1812	94.3%	10.3%	2 (2.2)%
Placebo	88.1%	19.0%	1 (2.4)%

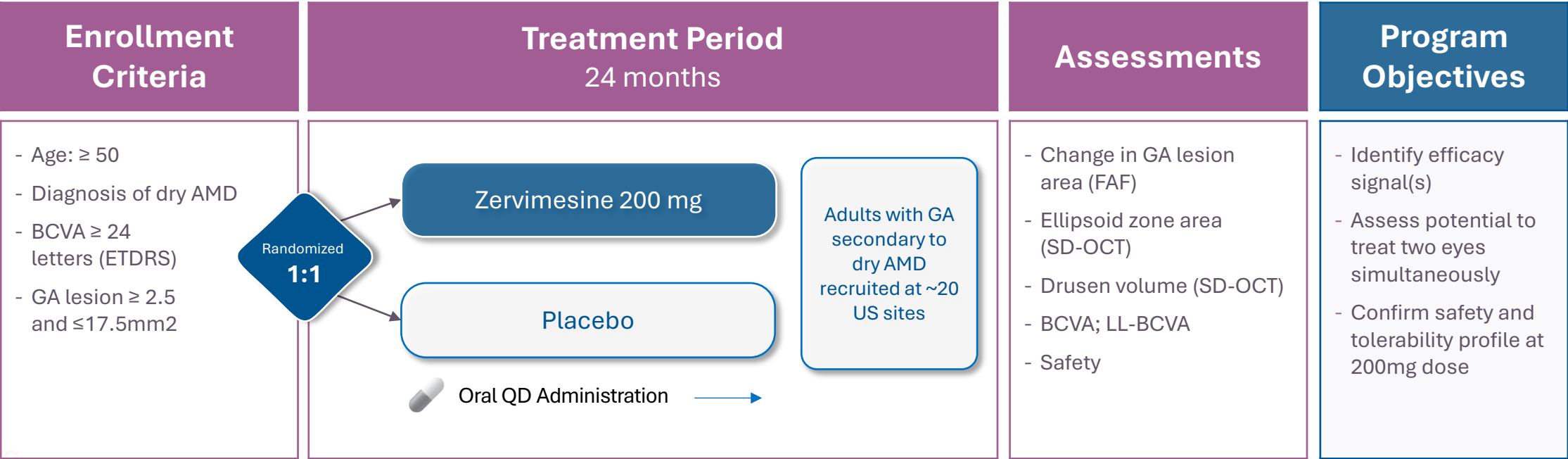
# MAGNIFY Topline Results

GA lesion growth slower with  
zervimesine treatment



# MAGNIFY Trial in Dry AMD/GA

Zervimesine: oral drug development candidate for geographic atrophy



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
- Safety profile consistent with AD/DLB studies

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



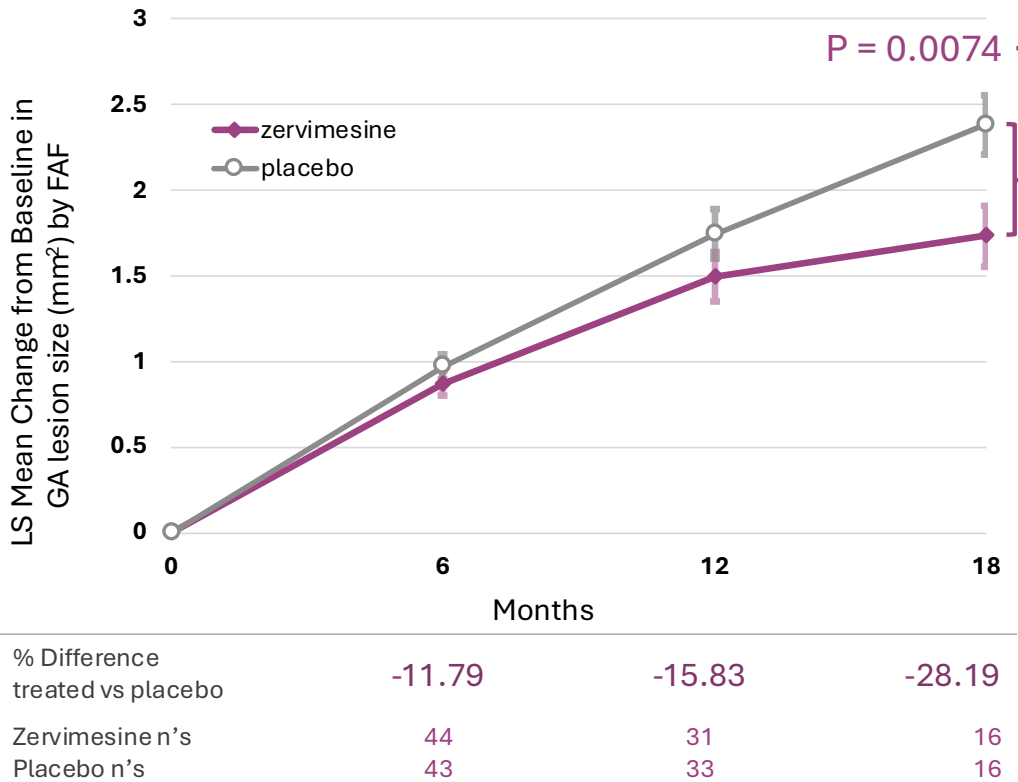
Slope Analysis<sup>1</sup>

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

Percent Difference  
from Placebo

29%  
(P=0.054)

Mean Area by Time<sup>1</sup>



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



Compared to Published Results<sup>1,2</sup>:

## IZERVAY Avacincaptad pegol (2mg)<sup>1</sup>

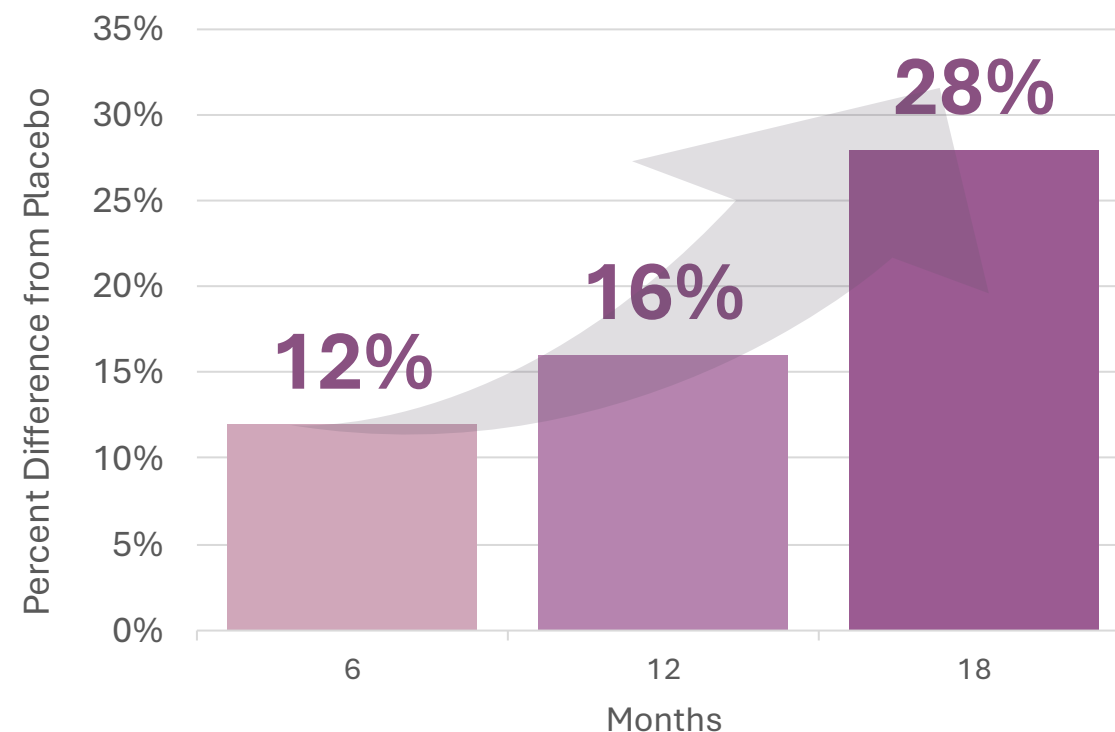
- Gather1 at 18 months – 35%
- Gather2 at 12 months – 18%
- Gather2 at 24 months – 14%

## SYFOVRE Pegcetacoplan (15mg)<sup>2</sup>

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

## Topline MAGNIFY Results<sup>3</sup>

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 September 30, 2025

**Cash and cash equivalents** \$ 39.3 M

### Grant funding for zervimesine studies

Preclinical through Phase 2 ~\$171 M

Approximate funding used (\$135 M)

Remaining grant funding \$36 M







# Thank You

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