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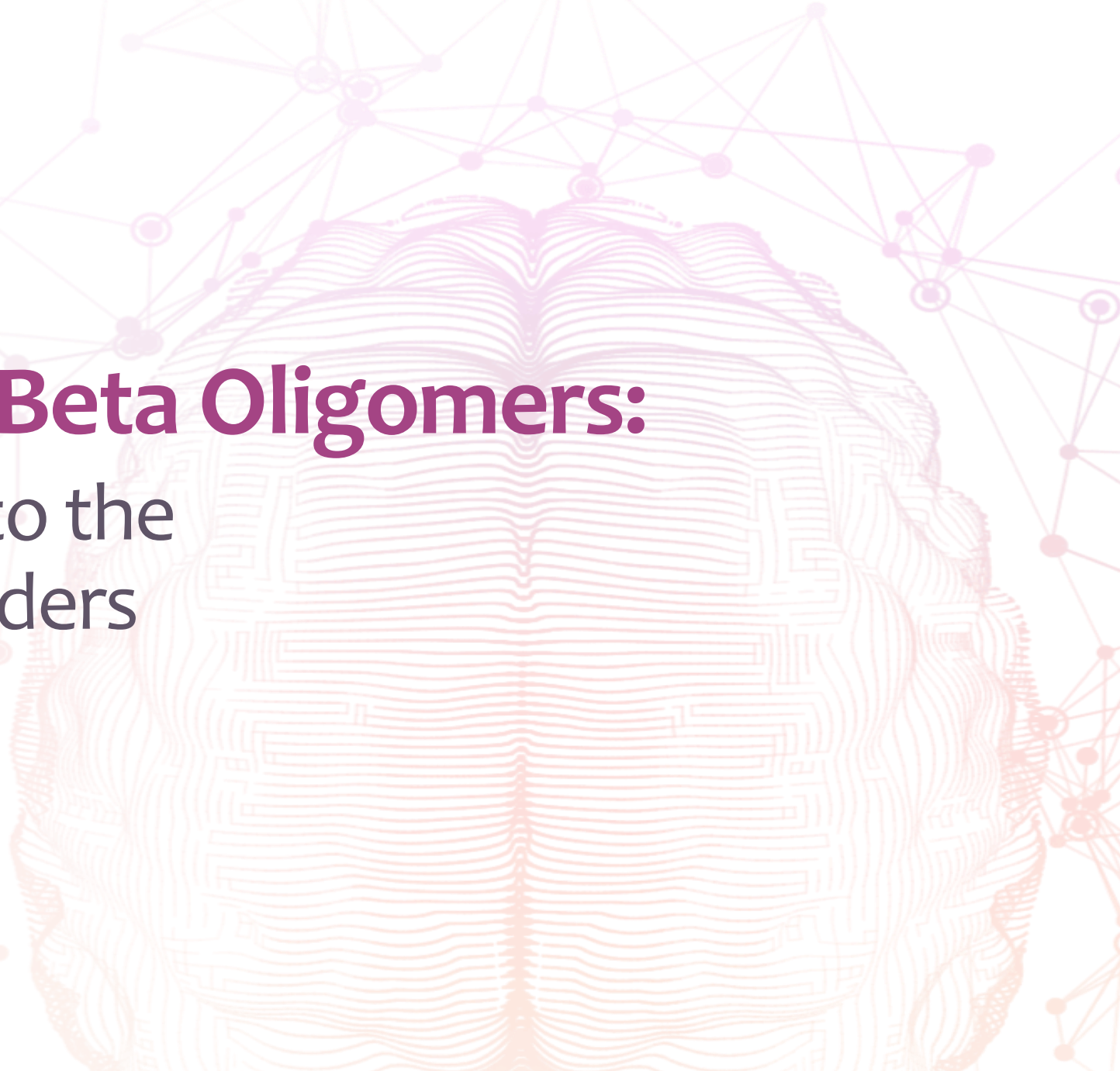
Targeting Amyloid Beta Oligomers:

A Disruptive Approach to the Treatment of CNS Disorders



September 2024

Forward-looking Statements

FORWARD-LOOKING STATEMENTS

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Cognition Snapshot

Successful Phase 2 AD Trial read out plus signal-finding studies ongoing in other indications

Alzheimer's Disease

- Pursuing 2 populations: mild-to-moderate; and early / MCI
  - ✓ Achieved goals of Phase 2 SHINE study in mild-moderate AD
  - Phase 2 START ongoing in early AD with ACTC
- Oral QD drug with no added ARIA-risk, important differentiator
- Extensive preclinical/clinical foundation supports oligomer antagonism approach

Dementia with Lewy Bodies (DLB)

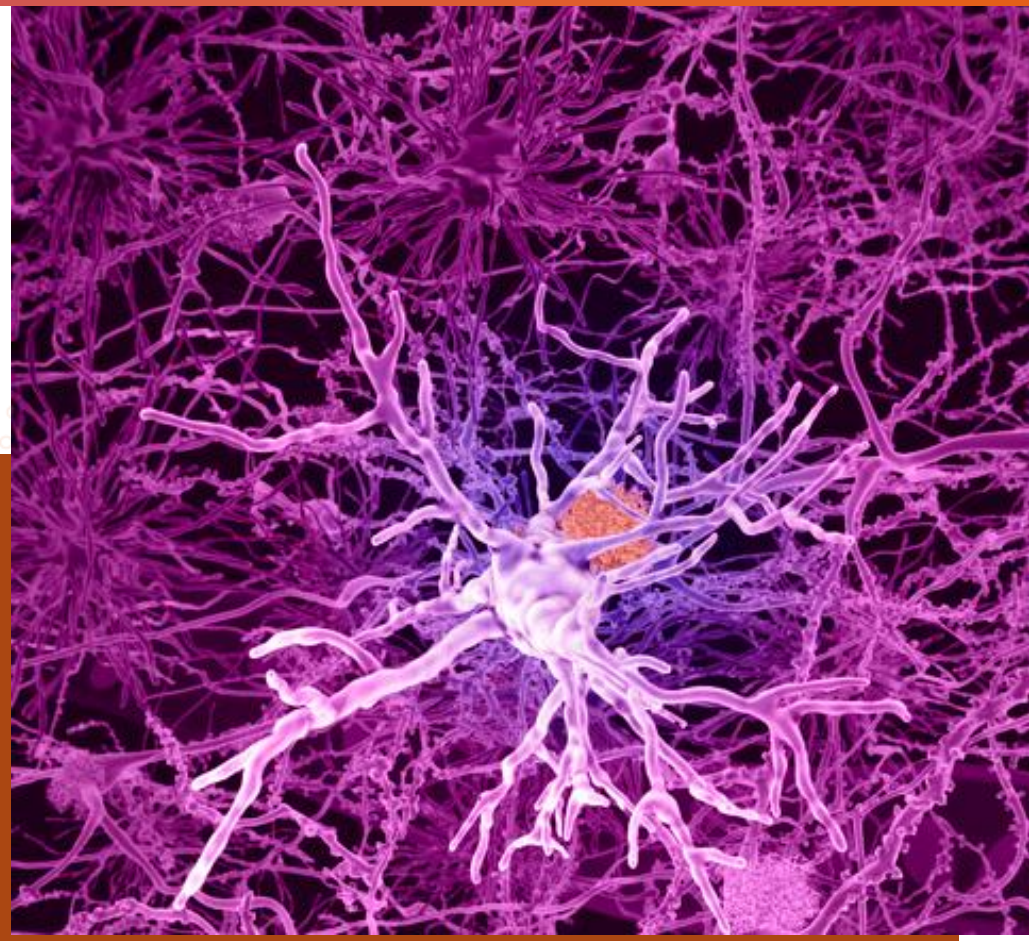
- Phase 2 signal-finding SHIMMER study in mild-to-moderate DLB completed enrollment; data ETA YE
  - Will determine CT1812's impact on constellation of symptoms
- No approved d-m treatments
- CT1812 protects against oligomers of both amyloid beta (Aβ) and alpha-synuclein (α-syn)

Geographic Atrophy Secondary to dry AMD

- Phase 2 signal-finding MAGNIFY study in geographic atrophy (GA) ongoing
  - Will determine to what extent CT1812 protection of RPE cells preserves vision
- Oral QD drug important differentiator from IVT therapies

Alzheimer's Disease

SHINE Study in Mild-to-Moderate Alzheimer's disease



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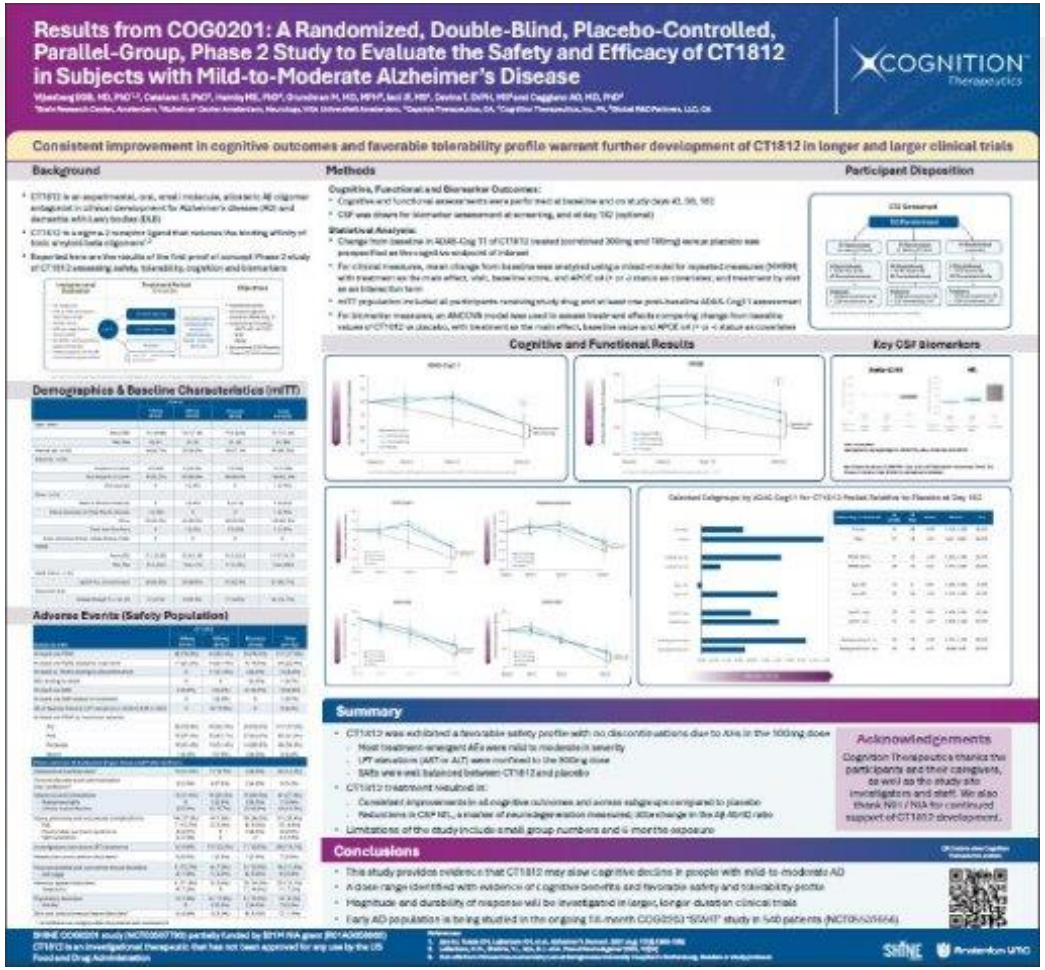
Breaking News – SHINE Phase 2 Alzheimer's Disease Study

CT1812 is Among Few Oral Candidates Showing Cognitive Impact in *Moderate* Patients

- Pooled (100 and 300mg arms) CT1812 treatment **slowed cognitive decline by 39%** on ADAS-Cog 11 vs placebo
- All key cognitive and functional outcome measures trending in favor of CT1812
- Efficacious dose with good safety profile
- Well-designed and executed study
- Supports advancing clinical development



SHINE Phase 2 Study in Adults with Mild-to-Moderate Alzheimer's Disease

Enrollment Criteria	Treatment Period 6 months	Assessments	Program Objectives

- AD diagnosis
- PET or CSF biomarker definition of AD
- MMSE 18-26
- MRI w/o significant abnormality
- No MDD, schizophrenia, bipolar disorder
- Stable regimen of AChEI or memantine permitted
	Randomized 1:1:1
	CT1812 300 mg
	CT1812 100 mg
	Placebo
	Oral QD Administration
	153 participants randomized in Australia, Netherlands, Spain, Czechia, and U.S.
		- Safety/tolerability
		- Principal cognitive measure: ADAS-Cog 11
		- Exploratory including:
		  - ADAS-Cog 13
		  - ADCS-ADL & CGIC
		  - NTB
		  - MMSE
		- Biomarkers (CSF/Plasma)
		- Plasma CT1812 exposure
			✓ Identify efficacy signal(s)
			✓ Hone safety and tolerability profile
			✓ Identify dose(s) for Phase 3

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

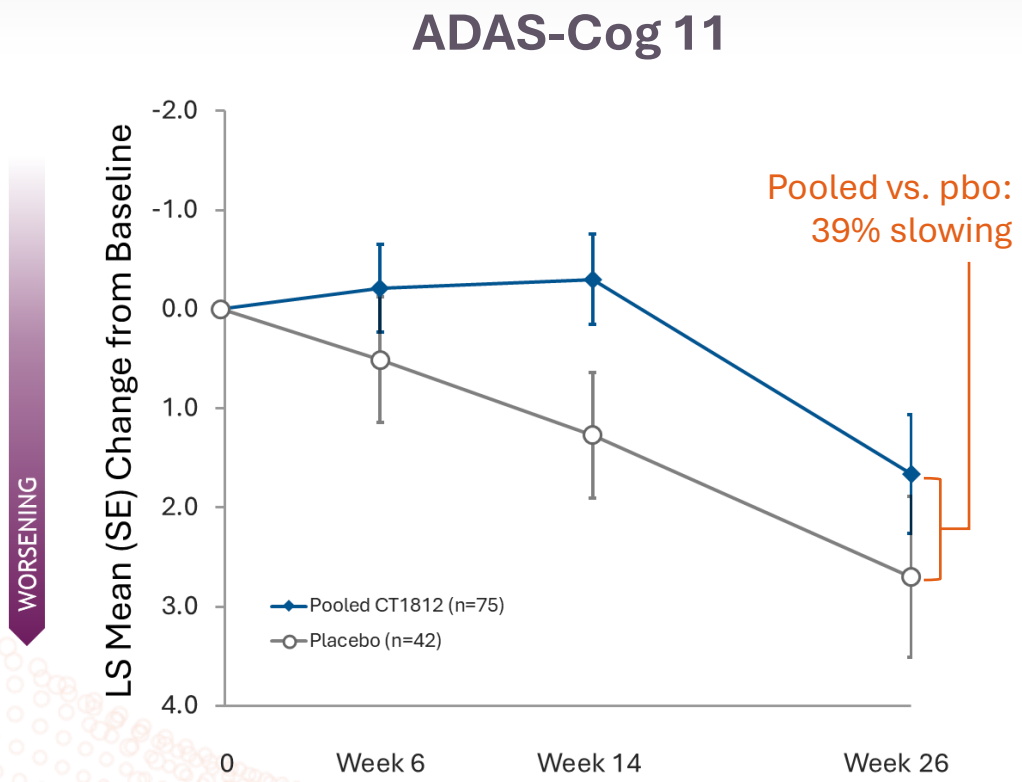
MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; PET, positive emission tomography; QD, daily; CSF, cerebrospinal fluid

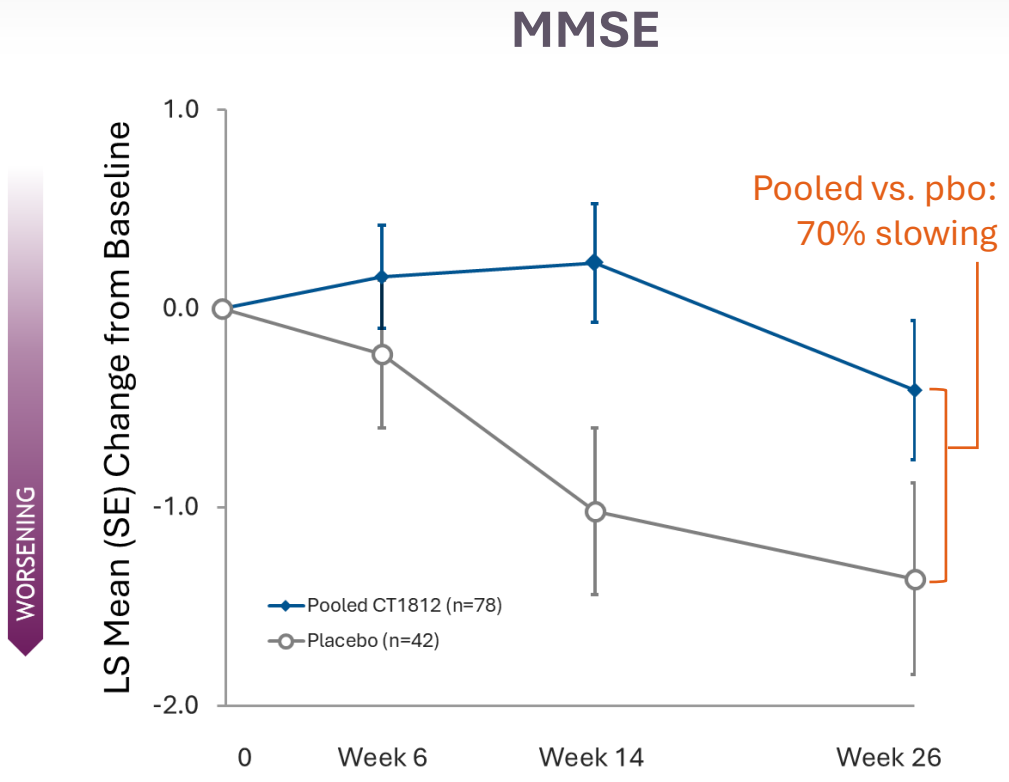
SHINE Patient Population

- PET- or biomarker-confirmed Alzheimer's disease
- Majority of participants were female (60%), Caucasian (96%), approximately 72 years of age
- Mean MMSE score upon entry: 21.37
- ~60% of patients were carriers of the ApoE4 gene
- Characteristics well-balanced between all 3 arms

SHINE Cognitive Endpoints: ADAS-Cog 11 and MMSE

Magnitude of ADAS-Cog 11 decline at 6 months similar to approved MAbs





Note: n's are at Day 182

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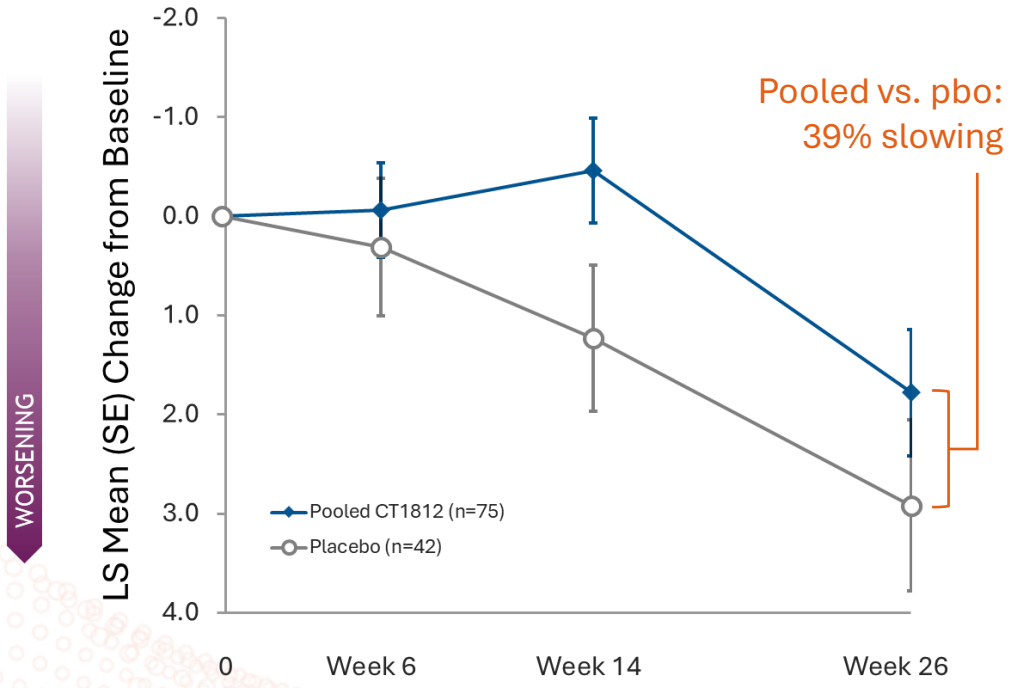
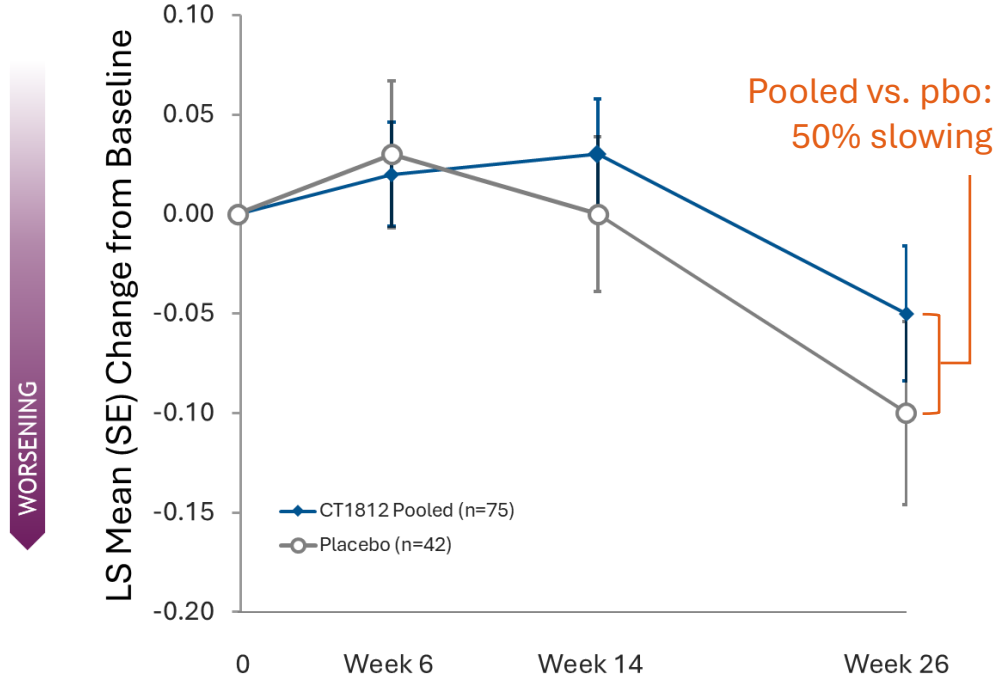
SHINE Cognitive Endpoints: ADAS-Cog 13, Cognitive Composite

Consistent results across multiple cognitive endpoints

ADAS-Cog 13



Cognitive Composite



Note: n's are at Day 182

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Summary of SHINE Safety and Tolerability findings

- CT1812 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 dose group and all the reportable liver enzyme elevations were in 300mg dose group

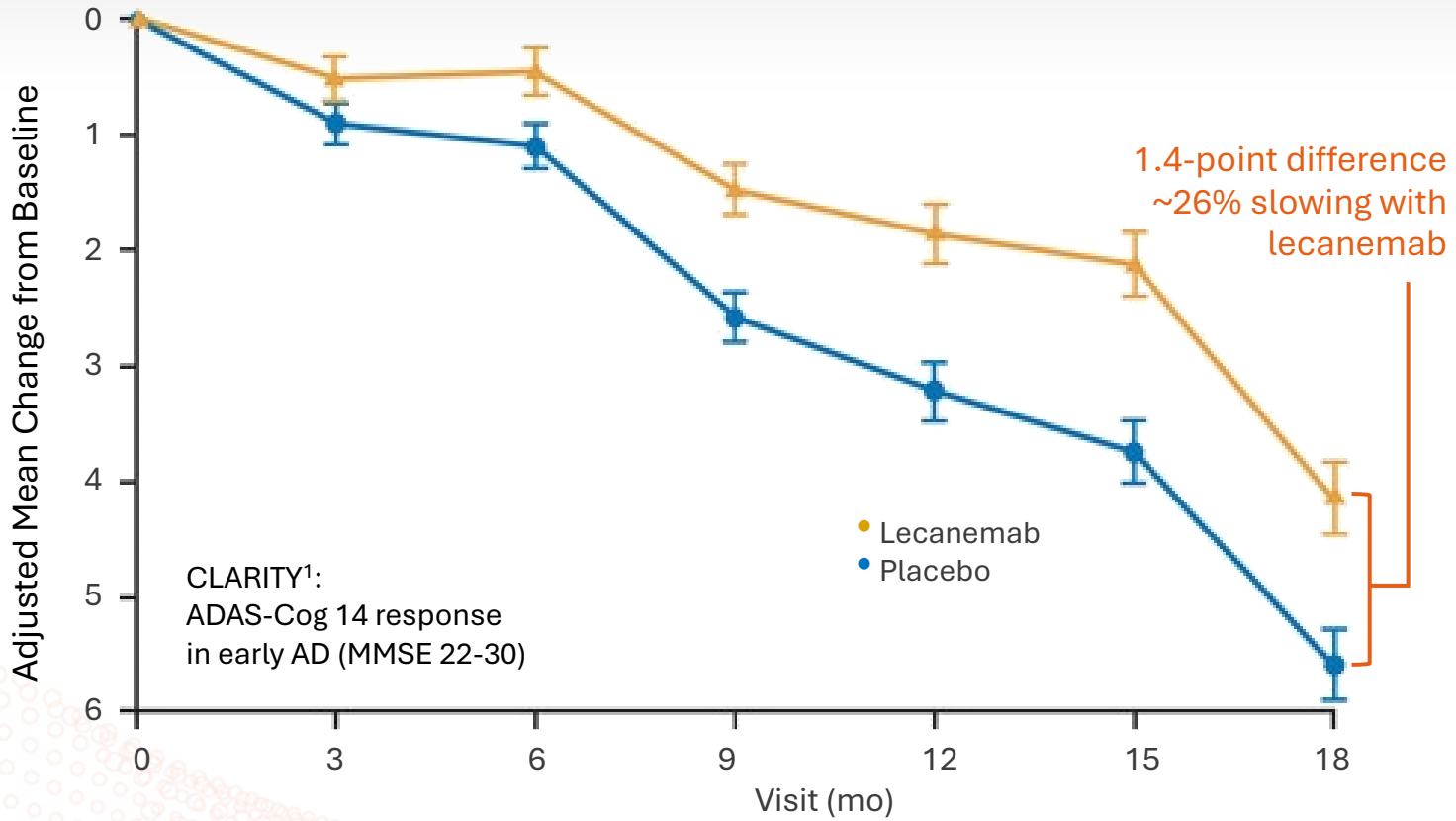
Adverse Events	
CT1812	Placebo
76.5%	78%

Serious AEs	
CT1812	Placebo
4.9%	10%

Deaths	
CT1812	Placebo
0	1 (cancer)

SHINE Response at 6 months Comparable to Approved MAbs

Once-daily pill • no ARIA • 39% slowing at 6 months vs Leqembi's 26% at 18 months



SHINE Results at 6 months
1.1 pt difference btw pooled CT1812 vs. placebo
39% slowing pooled CT1812 vs. placebo
Placebo decline in SHINE steeper w moderate AD

1. van Dyck C et al. Lecanemab in Early Alzheimer's Disease (2023) *NEJM* 388:9-21

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SHINE: Summary Exploratory Outcomes - Percent Slowing Day 182

Effect as large or larger than approved MAbs

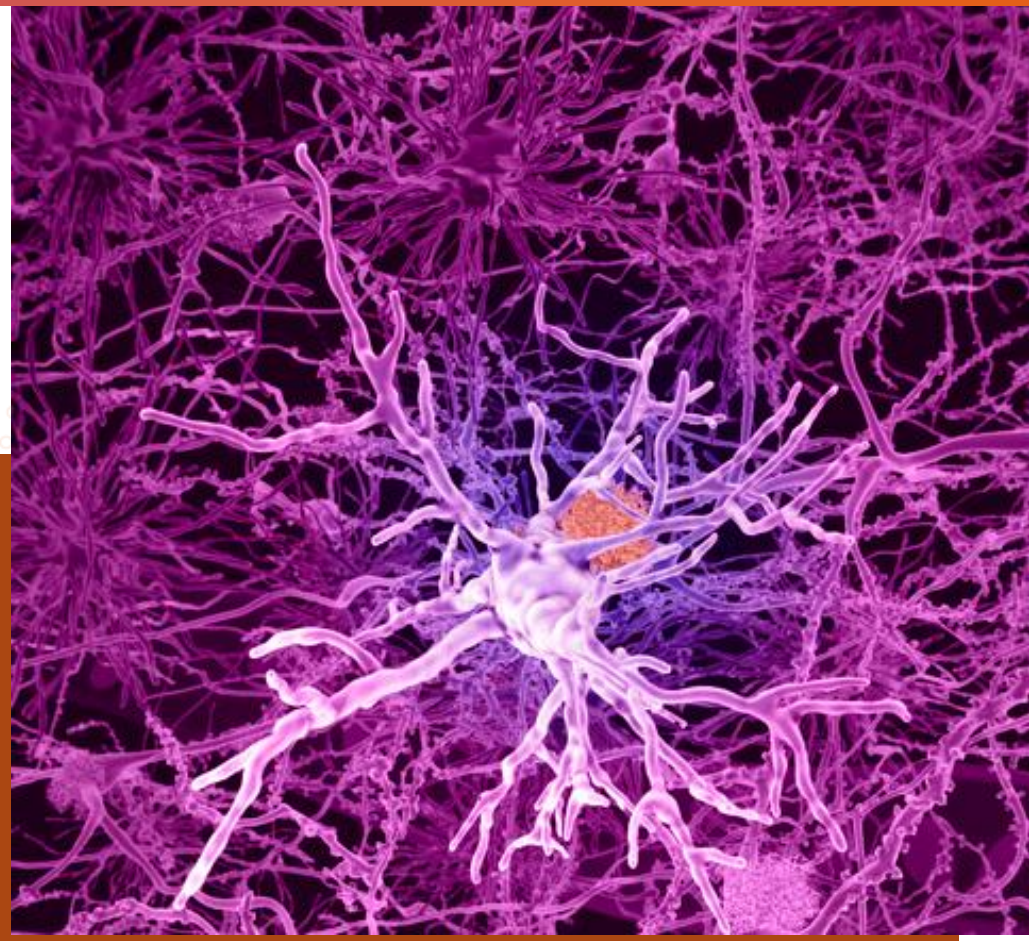
	ADAS-Cog 11	ADAS-Cog 13	MMSE	Cognitive Composite
CT1812 Pooled[1]	39%	39%	70%	50%
Lecanemab[2] (at 18mo)	--	26% (ADAS-Cog 14)	--	24% (ADCOMS)
Donanemab[3] (at 18 mo)	--	20% (ADAS-Cog 13)	16% (MMSE)	22% (iADRS)

Note: data shown for benchmarking only; no head-to-head studies have been conducted

1. Percentages reflect mean changes from baseline compared to placebo
2. van Dyck C et al. Lecanemab in Early Alzheimer's Disease (2023) *NEJM* 388:9-21
3. Sims JR et al. Donanemab in Early Symptomatic Alzheimer Disease (2023) JAMA. 2023;330(6):512-527

SHINE: Corroborated by Experts

Results of a Commissioned Survey of 51 neurologists



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CT1812 Market Opportunity

Insights from a Survey of Neurologists

Survey Design:

- 51 neurologists from academic, community or private settings who treat over 13,000 Alzheimer's patients annually were surveyed
- None were involved in CT1812 clinical trials

Current Options for Alzheimer's Disease:

- Two recently approved monoclonal antibodies: lecanemab and donanemab
- Acetylcholinesterase (AChE) inhibitors: donepezil, galantamine, and rivastigmine
- NMDA receptor antagonist: memantine

Market Opportunity:

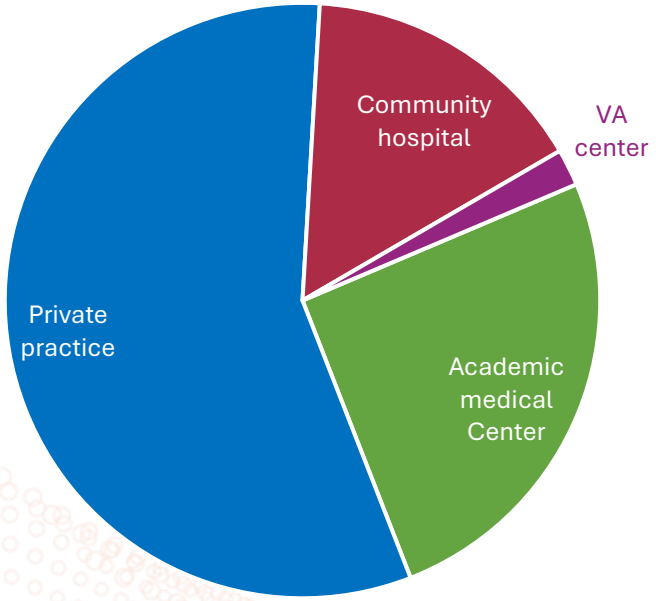
- 7 M in the U.S. & 55 M worldwide have Alzheimer's*

** Alzheimer's Disease Facts and Figures 2024*

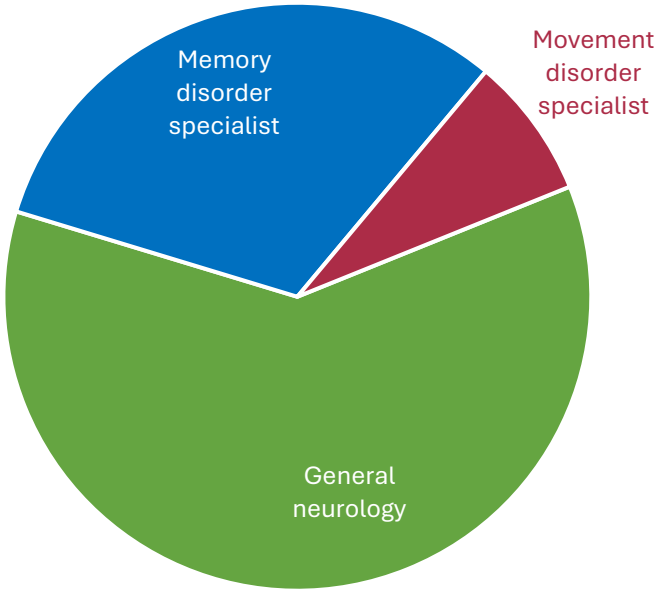
SHINE Data Feedback from Neurologists

Surveyed diverse group of 51 neurologists who treat over 13,000 AD patients annually

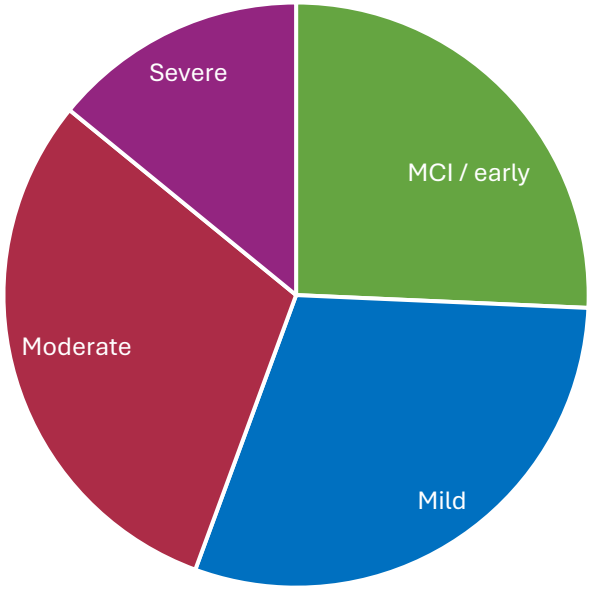
Cross Section of Practice Setting



Cross Section of Specialties



Cross Section of Patients (MMSE)



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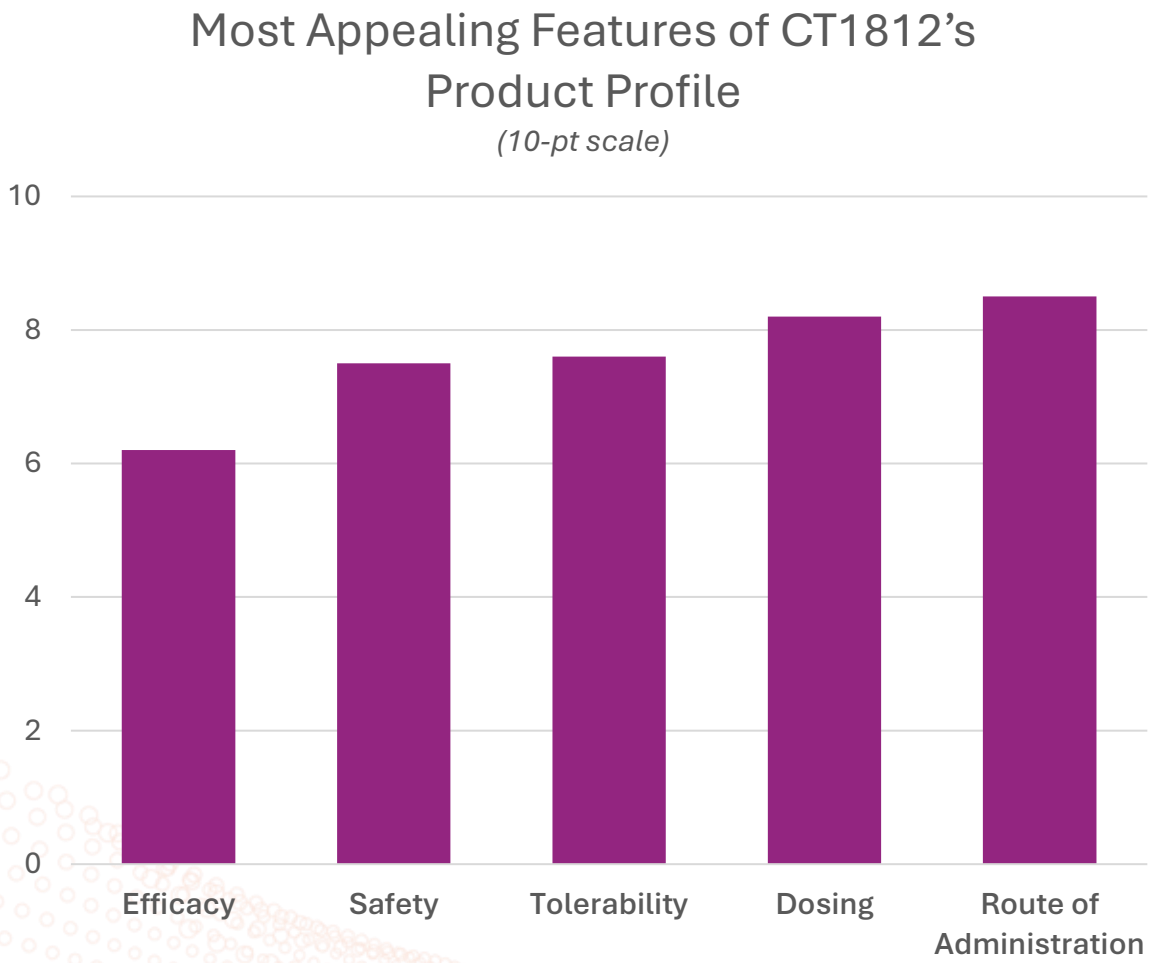
CT1812's Safety and Oral Delivery Appealed to Neurologists



"Ease of dosing as oral medication"

"Oral medication without ARIA risks"

"Pill form is always welcome over an IV infusion"

"Does not require infusion or intensive monitoring"

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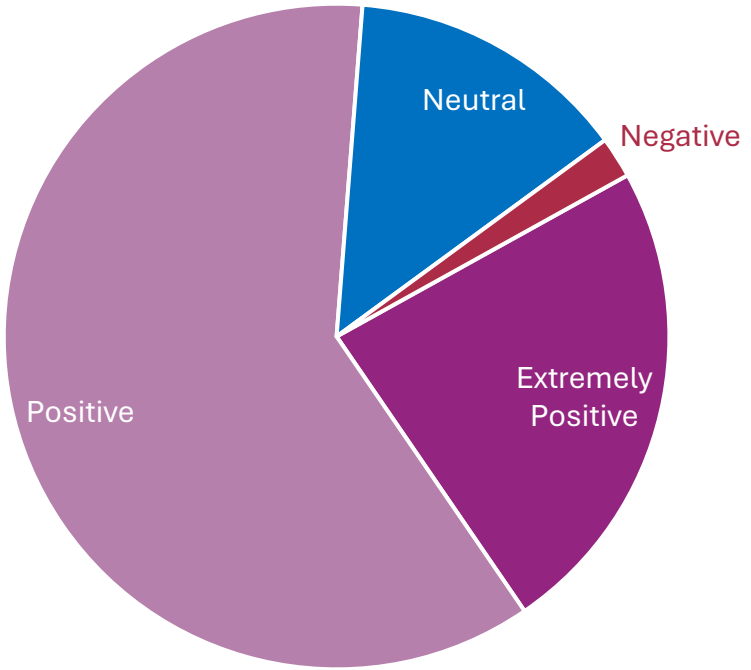
Neurologists Enthusiastic About SHINE Results

Oral, once-daily treatment with cognitive benefit and no increased ARIA risk

- The absence of symptomatic ARIA was seen as important (rated 8.4 out of 10)
- 86.3% of respondents felt CT1812's cognitive benefit (ADAS-Cog, MMSE, Cog Composite) was at least as good if not better than lecanemab
- 78.5% felt CT1812's functional benefit (ADCS-ADL and -CGIC) was at least as good if not better than lecanemab
- Efficacy rated 6.2 out of 10 possibly due to limited trial duration and number of participants in SHINE

Overall Characterization of SHINE Results



Appx 84% felt SHINE was positive or extremely positive

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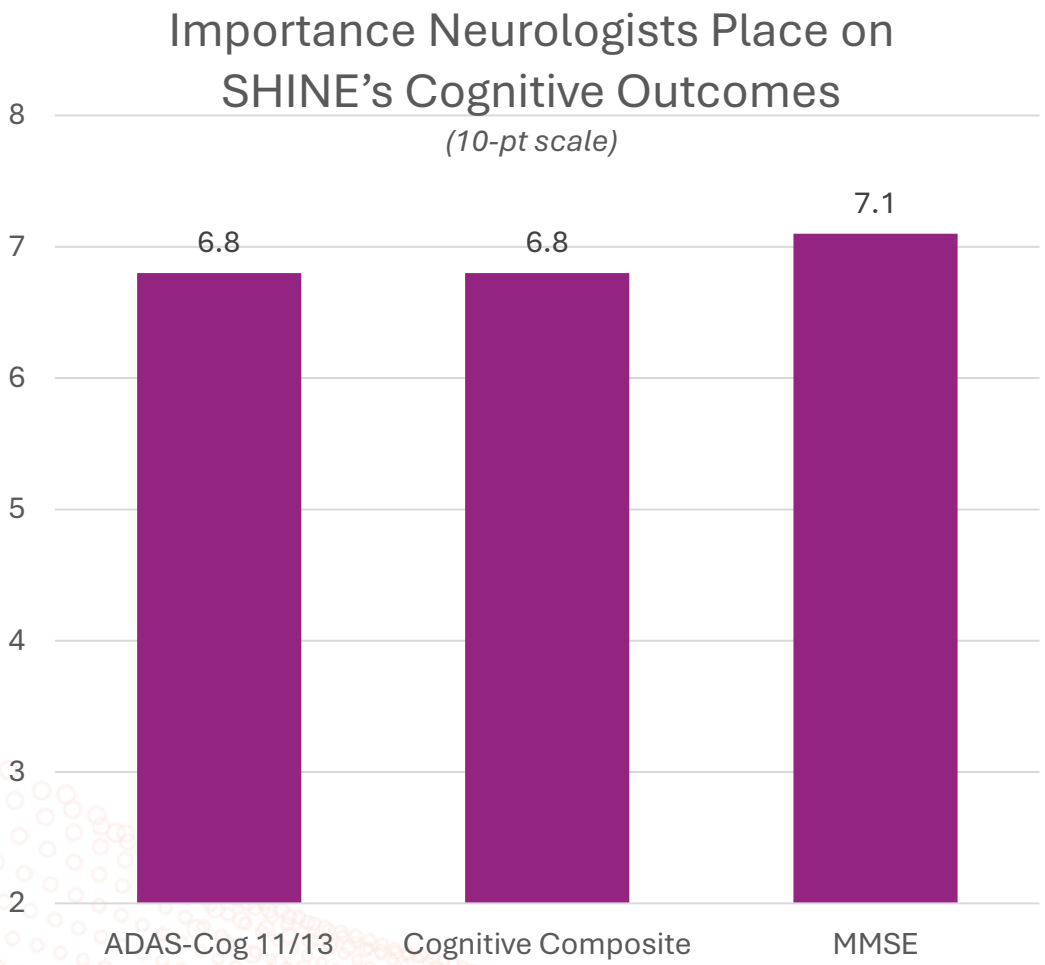
Efficacy Findings in Particular were Viewed as Significant



- Importance on cognitive outcomes echoed in open discussion of the most attractive aspects of the SHINE results
  - *"Consistent improvement in all clinical outcomes"*
  - *"Efficacy as good as, or better, than currently promoted anti-amyloid antibodies"*
  - *"Effective on slowing cognitive decline as an oral medication"*
  - *"Good improvement in mental status measures over 26 wks"*

Next Steps: Larger Studies with Longer Duration

Neurologists surveyed see a path forward for CT1812

In discussion of next steps for CT1812, neurologists expressed interest in:

- Treatment effect in combination with and/or head-to-head against anti amyloid drugs
- Treatment effect in combination with and/or head-to-head against AChEi + Namenda
- Larger placebo-controlled studies to see longer-term safety and clinical impact
- Potential in more patients with greater disease severity
- Mechanistic explanation for early effect

If Approved, Neurologists Would Consider CT1812

Monotherapy and combination uses appealed to clinicians

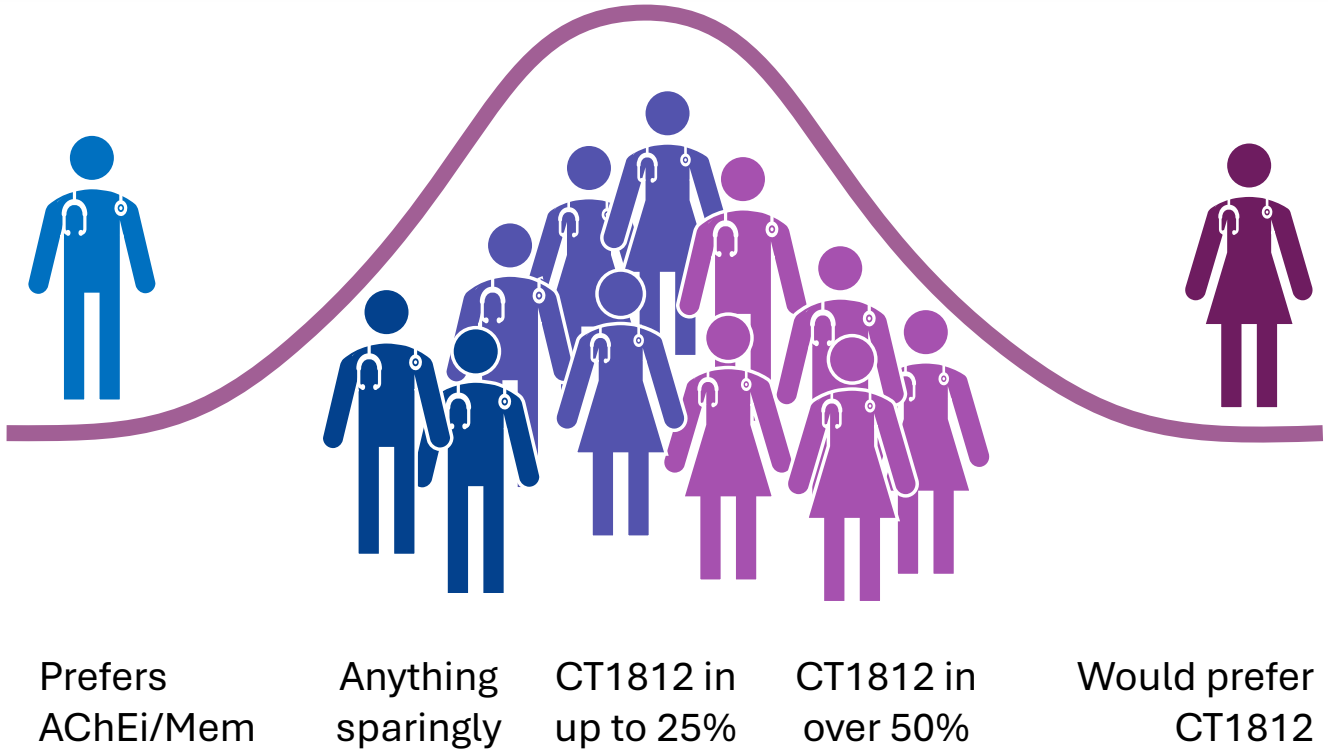
- What percentage of your mild patients would you consider candidates for CT1812?

62.8%

- What percent of your moderate patients would you consider candidates for CT1812?

58.4%

98% of Respondents Would Prescribe CT1812



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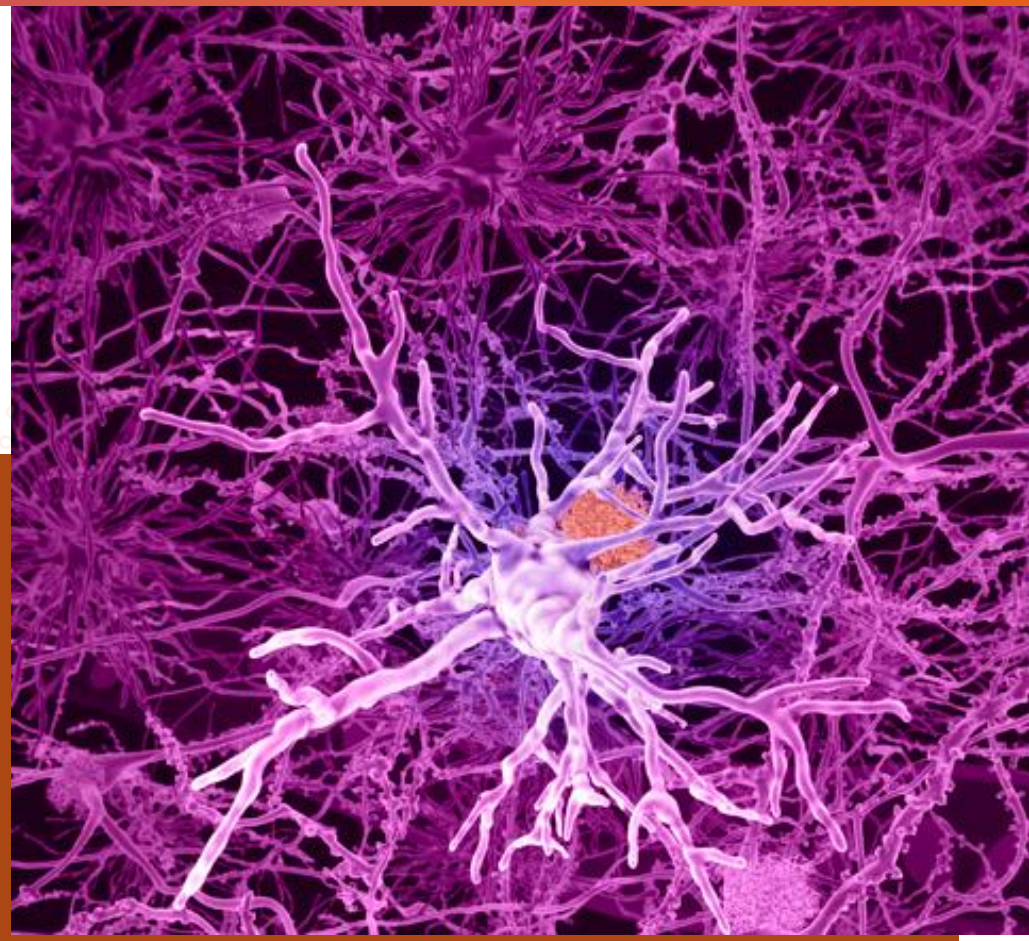
Alzheimer's Disease

START Study in early Alzheimer's disease



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START - A 540-Person Study in Early AD

First study to allow lecanemab as background therapy in combination with CT1812

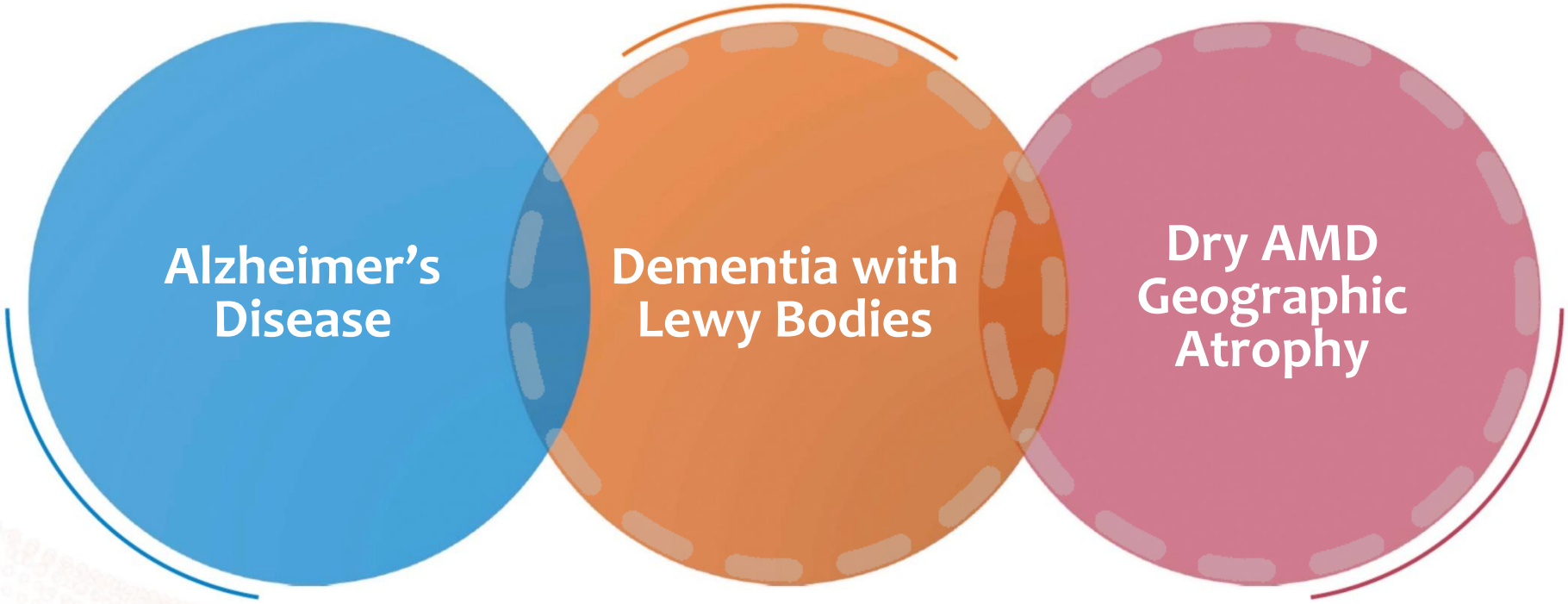
Enrollment Criteria	Treatment Period 6 months	Assessments	Program Objectives

- 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
	CT1812 200 mg
	CT1812 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

MCI, mild cognitive impairment; CDR-SB, Clinical Dementia Rating Scale Sum of Boxes; ADAS-Cog, Alzheimer's Disease Assessment Scale–Cognitive; ADL, activities of daily living; QD, daily; NIA, National Institute on Aging; ACTC, Alzheimer's Clinical Trials Consortium

CT1812 is Also Being Investigated in two Additional Indications



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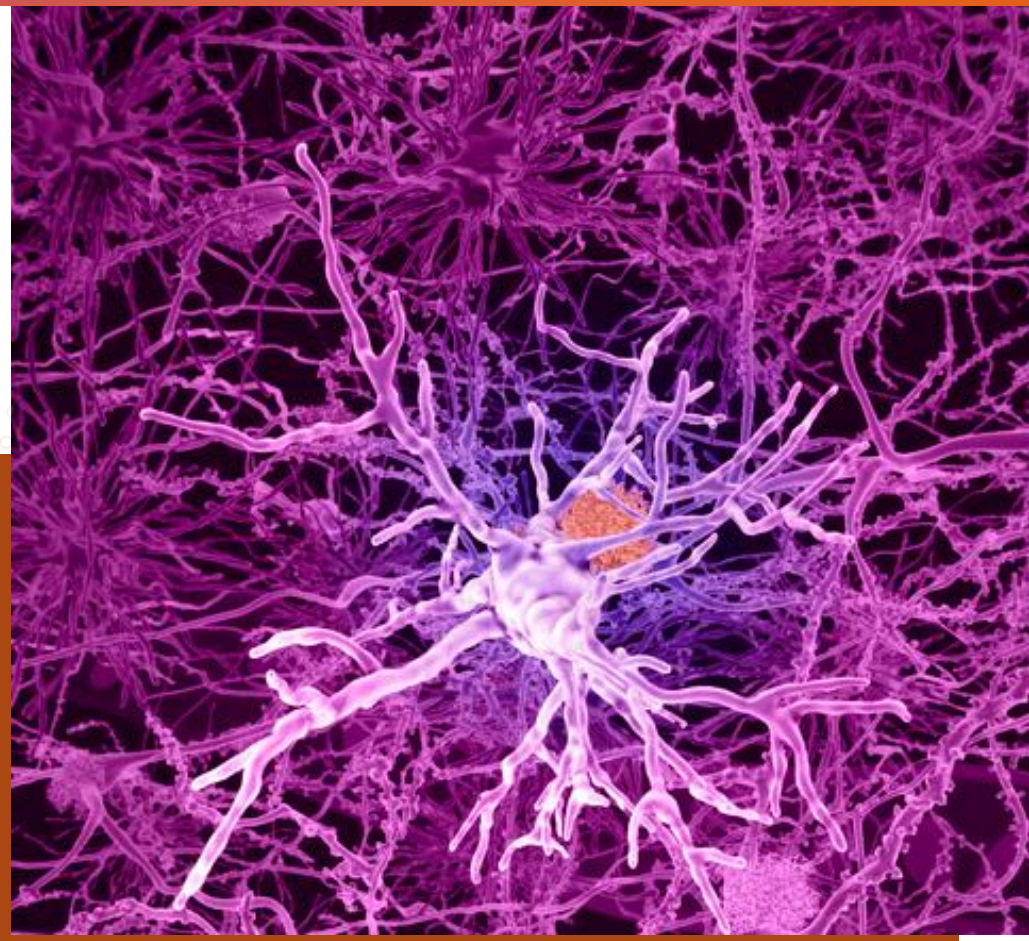
Dementia with Lewy Bodies

"The most common dementia you've never heard of"



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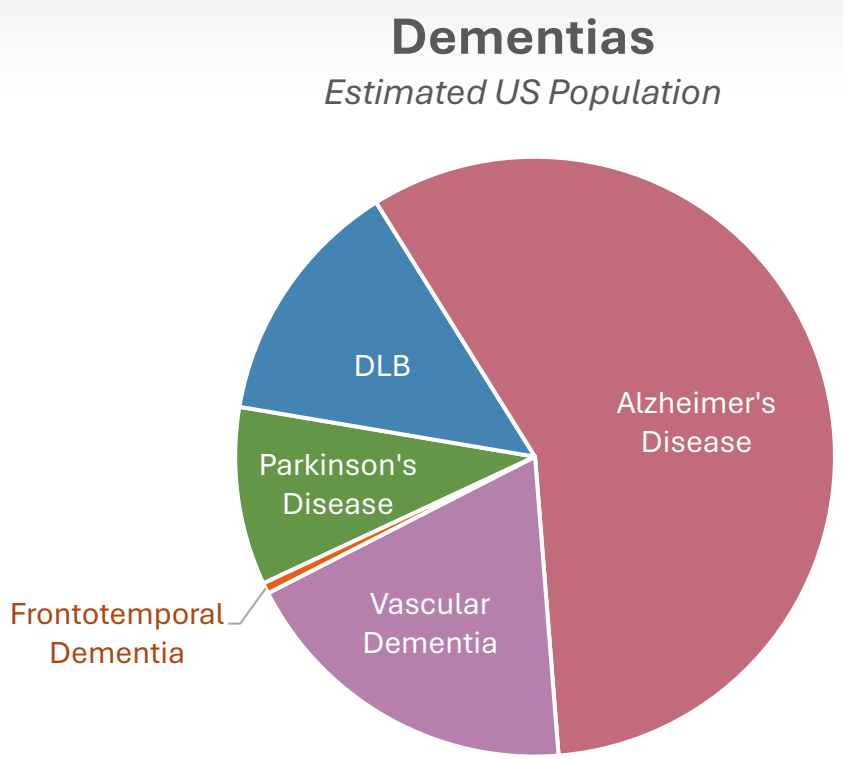
Lewy Body Dementias are Second only to AD in Prevalence

- In the U.S. an estimated 1.4 million people[1] have dementia with Lewy bodies (DLB)
- It is estimated that 50-80% of patients with DLB have Aβ as well as α-synuclein[2] pathology
- Core symptoms of DLB include:
  - Progressive cognitive decline
  - Fluctuating cognition with variations in attention
  - Impaired visuospatial perception
  - Recurrent visual hallucinations
  - REM sleep disorder



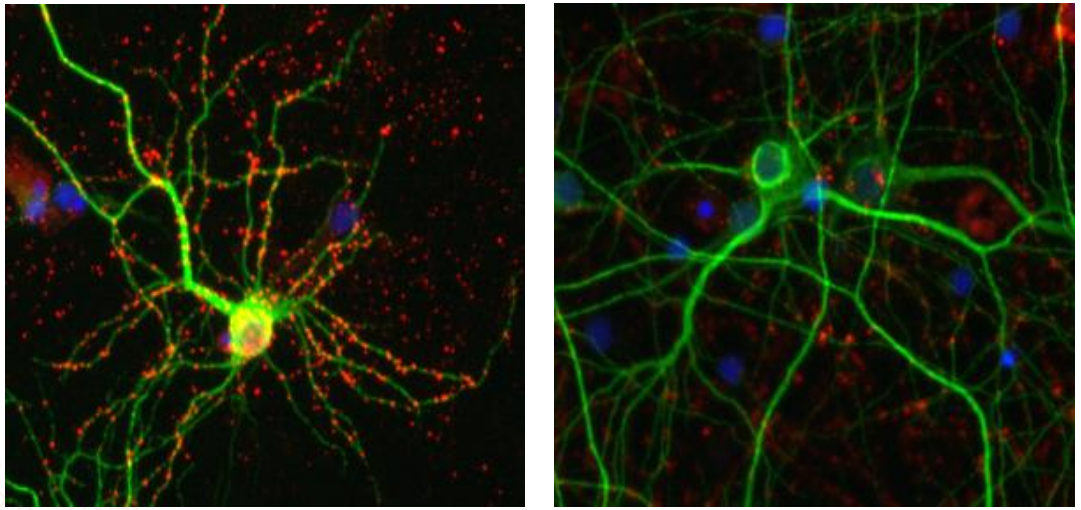
1) Lewy Body Dementia Association. About LBD. Available from: https://www.lbda.org/about-lbd
2) Int J Mol Sci. 2023 Jun; 24(12): 10215. doi: 10.3390/ijms241210215

Evidence Supports CT1812 Potential in DLB

Protection of neurons from α-synuclein oligomers

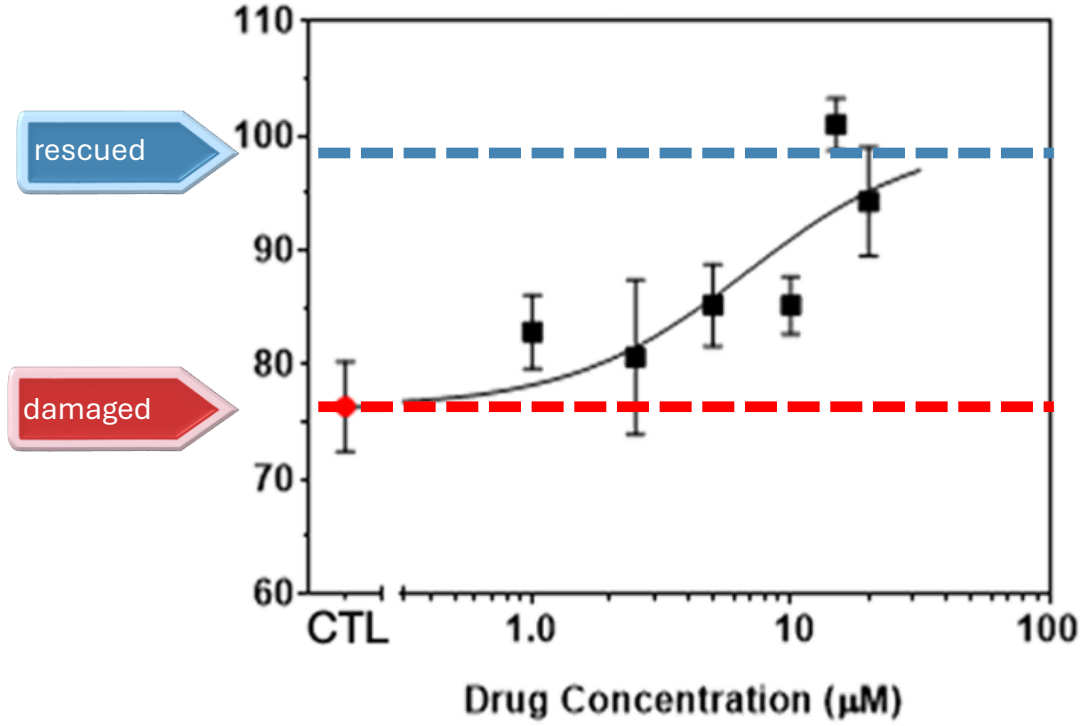
α-synuclein oligomers

α-synuclein oligomers + CT1812



α-Synuclein oligomers in red

Neurons rescued from α-synuclein oligomer-induced damage



Limegrover CS, et al. J Neurosci Res. 2021. doi: 10.1002/jnr.24782

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SHIMMER Study Brings Together Experts and New Tools to Explore Efficacy of CT1812

- Until recently, DLB could only be confirmed upon autopsy, making clinical research difficult
- SHIMMER was designed to have the best chance available to detect signals of improvement
  - Cognition partnered with experts at U Miami Miller School of Medicine and LBDA
  - Using validated clinical[1] and diagnostic[2] tools

CORE CLINICAL FEATURES OF DLB	
Domain	**Features**
Cognitive	Visual tracking and attention
	Visuospatial and perception
	Episodic memory deficits that improve with cued recall
	Timed attention tasks
	Executive tasks
	Construction tasks
	Verbal and psychomotor initiation
	Cognitive fluctuations
Movement	Bradykinesia
	Rigidity (with or without cogwheeling)
	Festinating gait
	Postural instability with falls
	Rest, postural, or action tremor
Behavioral	Well-formed visual hallucinations (eg, little people, furry animals)
	Delusions (eg, Capgras or misidentification)
	Depression
	Anxiety
	Apathy
	Hallucinations in other modalities
	REM sleep behavior disorder
Autonomic/ constitutional	Orthostatic hypotension
	Loss of smell
	Constipation
	Sialorrhea/rhinorrhea
	Sexual dysfunction
	Urinary incontinence
	Hyperhidrosis
	Seborrheic dermatitis

1) *Lewy Body Composite Risk Score (LBCRS)*
2) *α-Synuclein seeding amplification assay*

SHIMMER Study in Dementia with Lewy Bodies

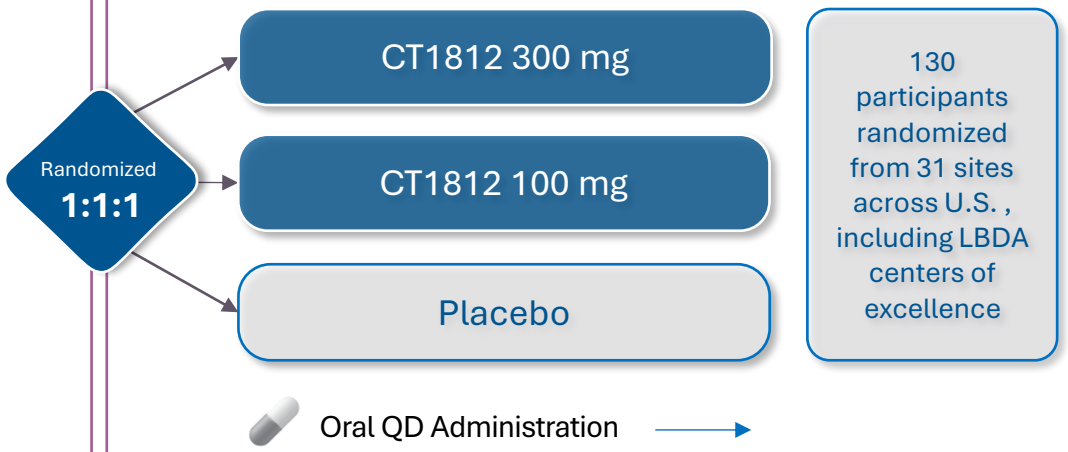
Topline YE 2024

Conducted in collaboration with experts at LBDA and University of Miami

Enrollment Criteria

- Age 50-85
- DLB diagnosis
- MRI
- MMSE: 18-27

Treatment Period
6 months



130 participants randomized from 31 sites across U.S. , including LBDA centers of excellence

Assessments

- Safety/tolerability
- Global CGIC
- Cognition
  - MoCA, MMSE, CDR
- Function
  - UPDRS III
  - ADL
- Behavior
  - Epworth Sleep
  - Fluctuations
- Biomarkers

Program Objectives

- ✓ Identify efficacy signal(s)
- ✓ Confirm safety and tolerability profile
- ✓ Identify dose(s) for Phase 3
- ✓ Explore impact on behavioral symptoms of sleep and fluctuations

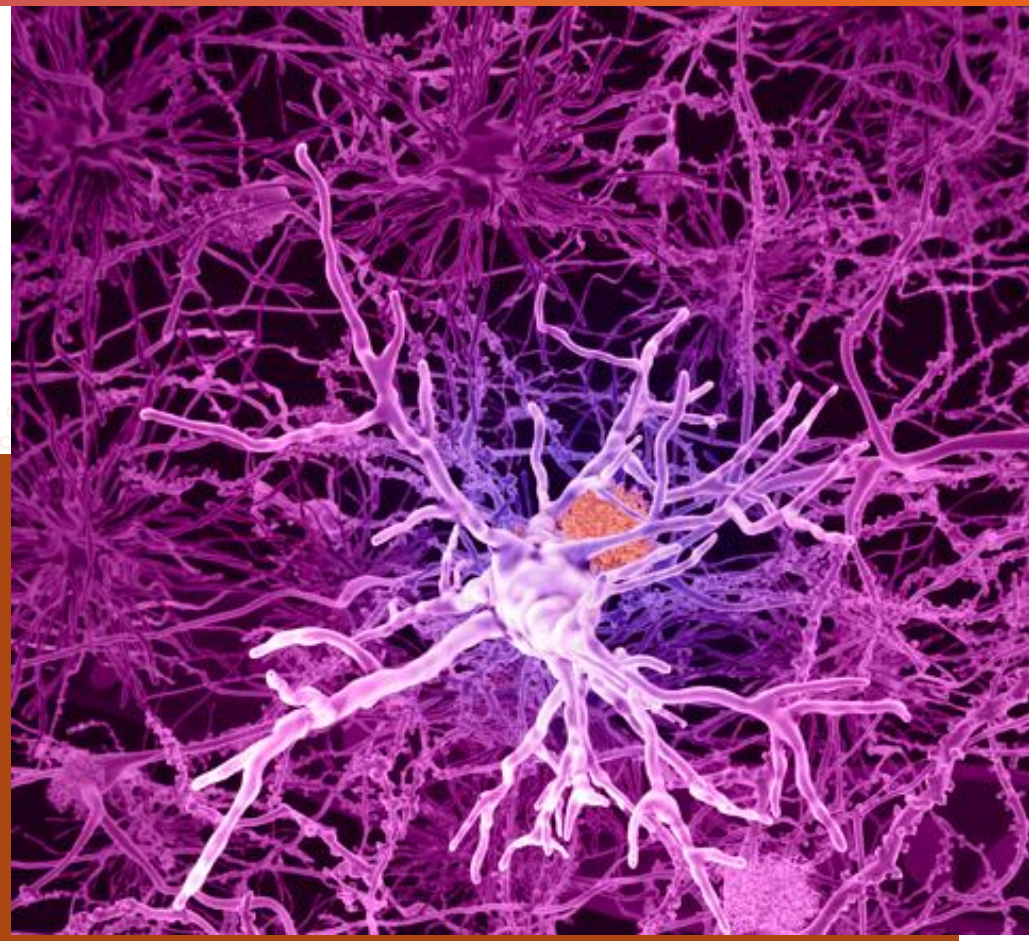
SHIMMER COG1201 study (NCT05225415) partially funded by $30M NIA grant R01AG071643

DLB, Dementia with Lewy Bodies; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; QD, daily; NIA, National Institute on Aging; LBDA, Lewy Body Dementia Association

SHIMMER COG1201 COGNITION Therapeutics

Geographic Atrophy

Damage to the macula resulting from advanced dry age-related macular degeneration (dry AMD)



COGNITION™ Therapeutics

Rationale for CT1812 in Dry AMD/Geographic Atrophy

Opportunity: crosses blood-retinal barrier to reach retina without an injection

What is dAMD/GA	Geographic atrophy (GA), the most advanced form of dry AMD, effects ~5M people WW and is associated with significant vision loss
Unmet Need	Complement inhibitors require injections into eye(s)
Pathophysiology	Death of retinal pigment epithelium (RPE) cells drives loss of photoreceptors (neurons required for sight) *In vitro* evidence supports CT1812 rescue of RPE cells
MAGNIFY	Proof-of-concept Phase 2 study in adults with GA

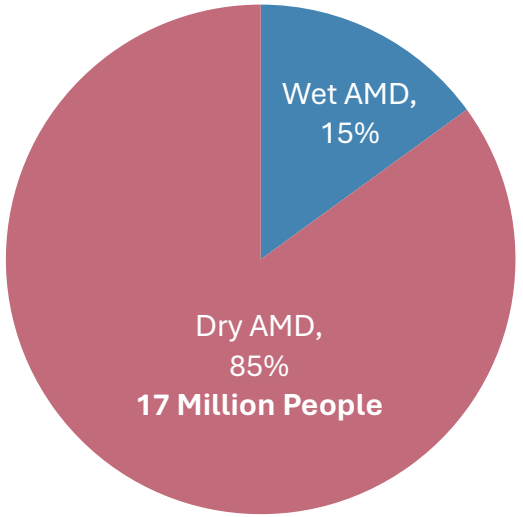
COGNITION™ Therapeutics

Dry AMD and Geographic Atrophy

Leading cause of severe vision loss in people over 50 (AAO)

- AMD is leading cause of blindness over 50 yr[1]
- Dry AMD is a progressive condition accounting ~90% of all AMD cases
  - Advanced dry AMD, or GA, affects approximately two million people in the U.S.
- Only two drugs are approved for dry AMD[2]
  - Until 2023, dietary supplements were SoC
  - For reference, wet AMD market is $7 billion worldwide

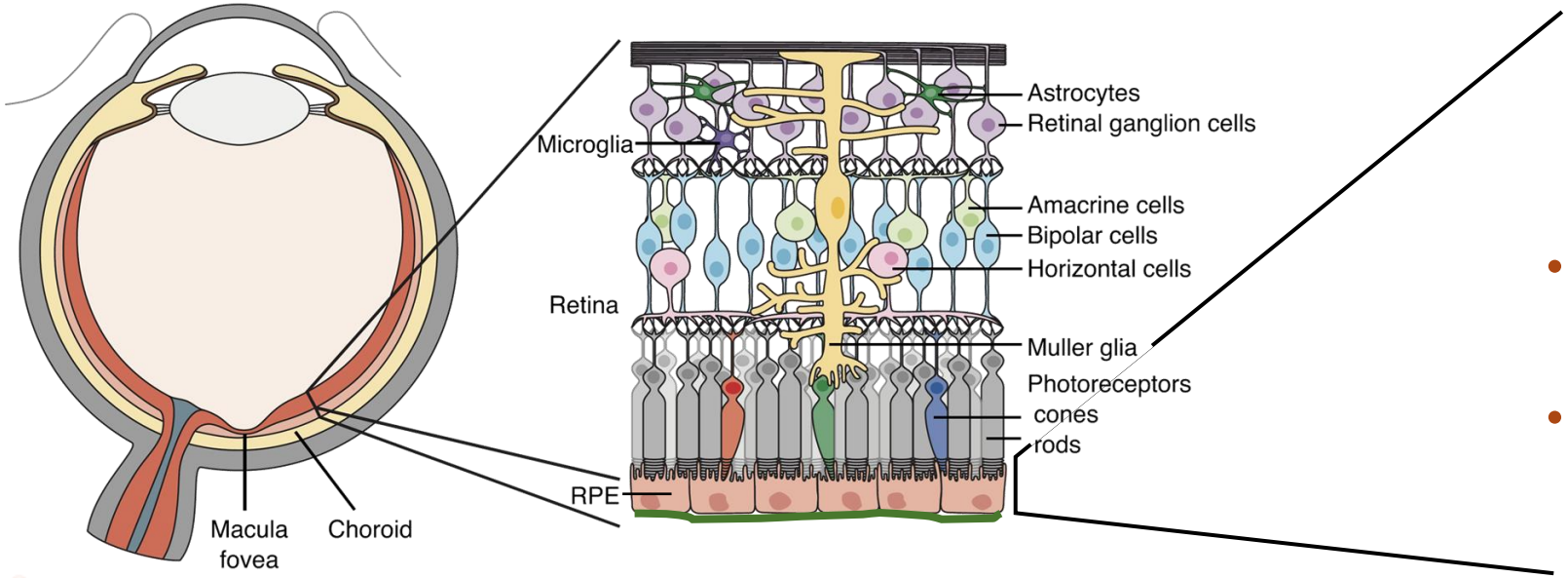
20 million people in North America have AMD[3]



1) American Academy of Ophthalmology
3) Izervay (avacincaptad pegol) & SYFOVRE™ (pegcetacoplan injection)
3) BrightFocus Foundation. Age-Related Macular Degeneration: Facts & Figures

COGNITION™ Therapeutics

CT1812 Protects RPE Cells and the Photoreceptors they Support

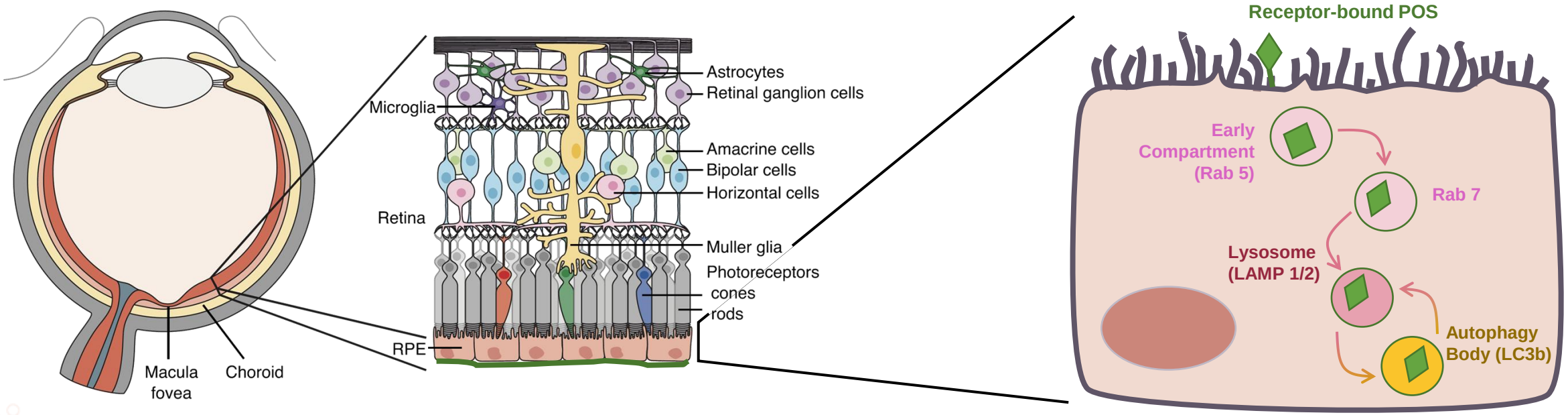


- Photoreceptors – specialized neurons necessary for sight – require support from retinal pigment epithelial (RPE) cells that are damaged in dry AMD
- CT1812 has been shown to rescue RPE cells *in vitro*
- CT1812's potential to preserve vision through this mechanism is being tested in Phase 2

Figure modified from Orozco et al., Cell Reports 2020

Cellular and Molecular Pathogenesis of Dry AMD (dAMD)

CT1812 restores trafficking and degradation of POS



In dry AMD, RPE cells are unable to successfully recycle photoreceptor outer segments ( ) through the autophagy process

Figure modified from Orozco et al., Cell Reports 2020

MAGNIFY Trial in dAMD/GA

Potential first oral drug for geographic atrophy

Enrollment Criteria	Treatment Period 6 months	Assessments	Program Objectives
- Age: ≥ 50 - Diagnosis of dry AMD - BCVA ≥ 24 letters (ETDRS) - GA lesion ≥ 2.5 and ≤17.5mm2	Randomized 1:1 CT1812 200 mg Placebo Oral QD Administration Recruiting 246 adults with GA secondary to dry AMD	- Change in GA lesion area (FAF) - Ellipsoid zone area (SD-OCT) - Drusen volume (SD-OCT) - Safety	✓ Identify efficacy signal(s) ✓ Assess potential to treat two eyes simultaneously ✓ Confirm safety and tolerability profile at 200mg dose

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

Completed Studies Support Potential in Mild-to-Moderate AD

Ongoing Trials Expand CT1812 into New Indications

COG0203 - START

Early-to-mild Alzheimer's disease
Actively recruiting

COG1201 - SHIMMER

Mild-to-moderate DLB
Topline data YE2024

COG2201 - MAGNIFY

GA secondary to dry AMD
Actively recruiting

SHINE

- 153 participants
- Consistent slowing cognitive decline (ADAS-Cog 11 and 13, MMSE, Cog Composite)
- Trends in functional benefit

SEQUEL[1]

- 16 participants
- Normalization of brain waves across EEG measures
- Significant improvement in AEC-c and relative theta in central region

SPARC[2]

- 23 participants
- Preservation of brain atrophy via volumetric MRI
- No change in SV2A treated or pbo

SNAP[3]

- 3 participants
- Rapid displacement of Aβ oligomers via CSF
- Replication of preclinical findings via MEI

1) Vijverberg E et al. J Prev Alzheimers Dis (2024) 2) van Dyck, CH et al. Alz Res Therapy 16, 20 (2024) 3) LaBarbera, KM et al. Transl Neurodegener 2023, 12(24)

The Promise of CT1812

- **First-in-class** Aβ oligomer antagonism via sigma-2 receptor
- **Consistent efficacy** in Alzheimer's disease studies
  - ARIA unlikely to occur based on MoA
- **Potential first-to-market for DLB**
- **Potential first oral for dAMD/GA**
- **Well tolerated safety** profile anticipated
- **Oral** administration
  - No need for IV therapy, a key limitation of immunotherapeutics
  - No surveillance imaging required
  - Greater convenience and access

Current Financial Position

As of June 30, 2024

Cash and cash equivalents — $28.5 M

Expected cash runway into 2Q 2025

Grant funding for CT1812 studies

Preclinical through Phase 2	~$171 M
Approximate funding used	($113.7 M)
Remaining grant funding	$57.3M

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Thank You

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