



# PREVENTING THE PROGRESSION OF CNS DISORDERS

Nasdaq: CGTX • April 2024



# Forward-looking Statements

## FORWARD-LOOKING STATEMENTS

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## MARKET & INDUSTRY DATA

*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.*

# Our Value Proposition

## First-in-Class Lead Asset

CT1812 is designed to restore impaired cellular damage response functions

## Late-Stage Pipeline

Advancing mid-to-late-stage clinical trials in multiple indications in mild-to-moderate Alzheimer's disease and DLB

## Multi-billion Dollar Opportunities

Targeting multi-billion dollar diseases; under-served markets; potential first-to-market in mild-to-moderate dementia with Lewy bodies

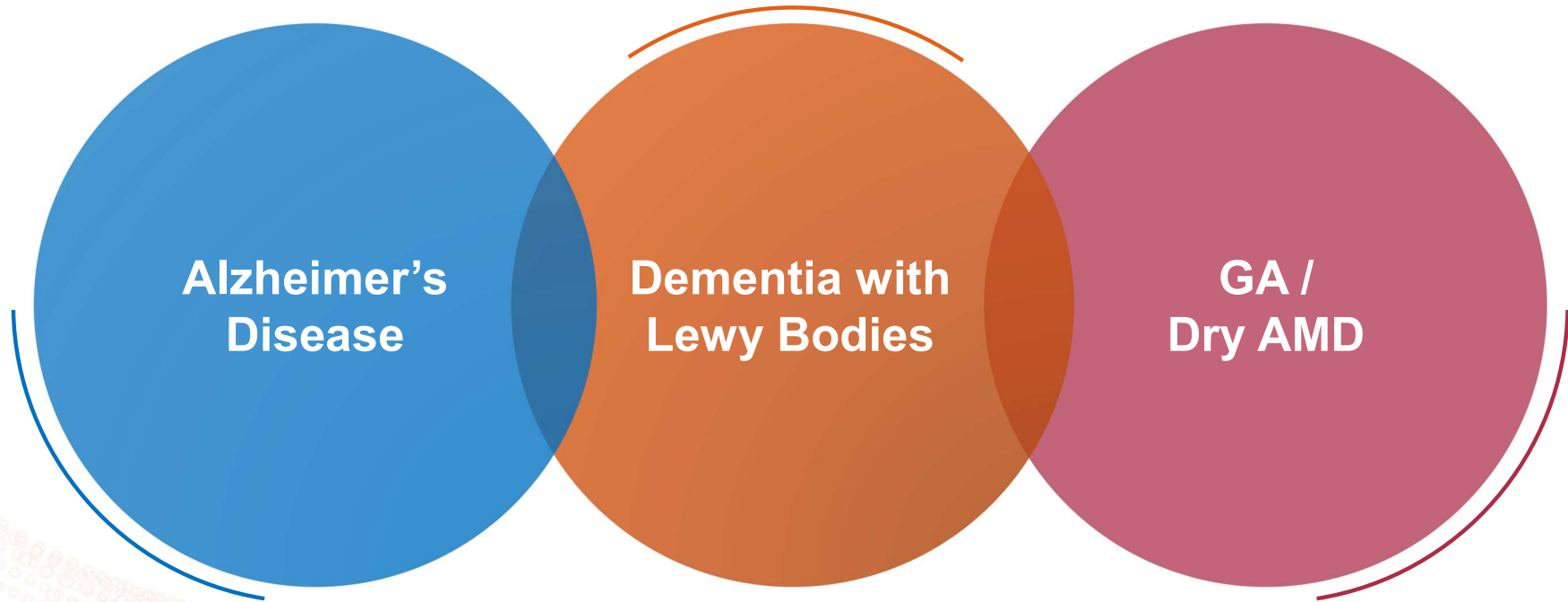
## Financially Disciplined

Major trials supported by \$171 million non-dilutive grants from NIH and others. Cash runway through May 2025

## Experienced Leadership Team

Executive team with big pharma leadership experience; R&D staff with depth of neuroscience drug development expertise

**CT1812, is an orally delivered, first-in-class, highly brain penetrant, small molecule designed to restore key cellular functions that are impaired in diseases including:**





# CT1812: First-in-class, orally dosed, highly brain-penetrant small molecule

## Oral, Once-daily Pill

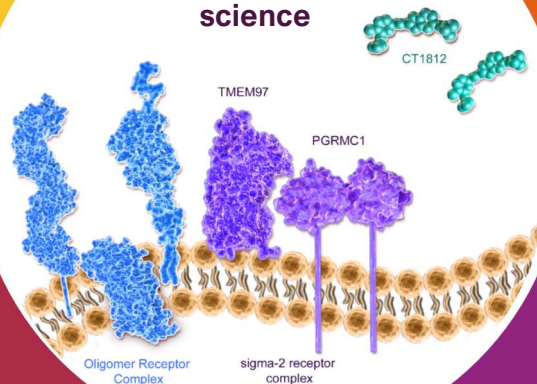
Oral, small molecule ligand of  $\sigma$ -2 receptor

High degree of CNS penetration for therapeutic target engagement

## The *Right* Target

Targeting toxic stressors: A $\beta$  and  $\alpha$ -synuclein oligomers and ROS in neurodegenerative diseases

Powerful scientific validation of  $\sigma$ -2 science



## Neuroprotective

Protects neurons; restores cellular “housekeeping” processes

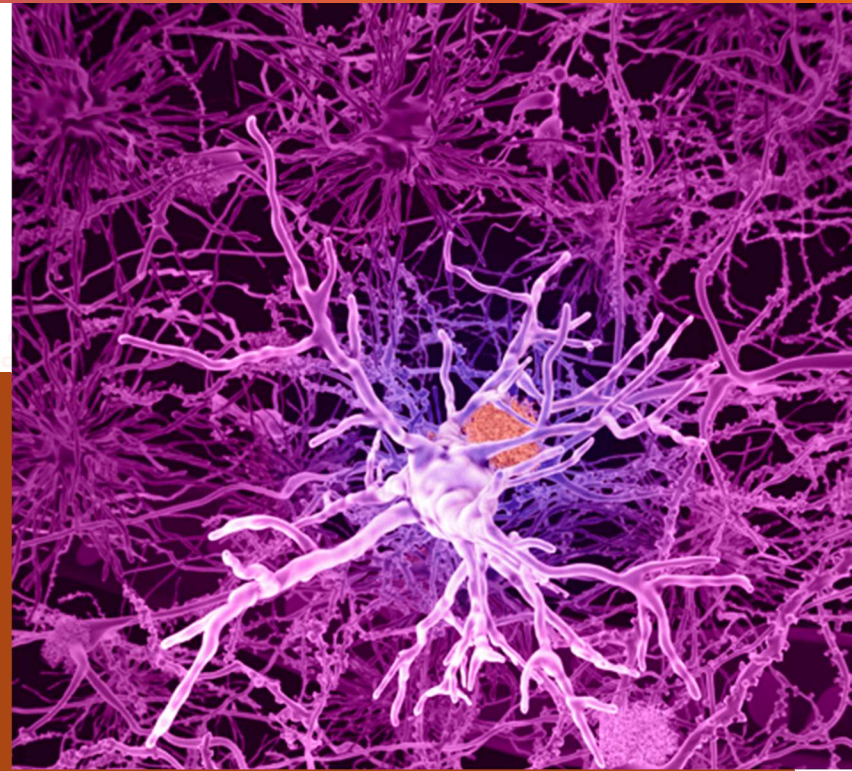
Demonstrates disease-modifying impact

## Manufacturing & IP

Scalable manufacturing from easily sourced materials

Extensive intellectual property estate

# ALZHEIMER'S DISEASE



 **COGNITION**<sup>™</sup>  
*Therapeutics*

# AD – Breakthroughs & Realities of Constraints

Mismatch between demographics, economics, access



Two approved mAbs (lecanemab, aducanumab),  
one additional drug filed for approval

- ✓ Annual cost for therapy = \$26K - \$28K/ patient
- ✓ ~\$5B cost to Medicare
- ✓ More monoclonals being studied

Constrained delivery systems  
for infused medications

- ✓ 3,600 Infusion centers in the US
- ✓ 11,900 MRI systems in the US
- ✓ 2,500 PET scanners in the US performing 2M scans/year

\* <https://hitconsultant.net/2022/12/14/report-the-state-of-cancer-centers-2022/>

# CT1812: A Novel Approach to Address Amyloid Toxicity

 **LEQEMBI™**  
(lecanemab-irmb) 100 mg/mL

 **Aduhelm®**  
(aducanumab-avwa) 100 mg/mL  
injection, for  
intravenous use

**Donanemab**

A $\beta$  monomer

Anti-oligomer mAB

Anti-protofibril mAB

Anti-plaque mAB

A $\beta$  oligomer

## **CT1812: Protects Synapses**

Small molecule ligand to the sigma-2 receptor  
Displaces A $\beta$  oligomers and prevents their  
binding to synapses

## **mABs: Lower A $\beta$ plaque**

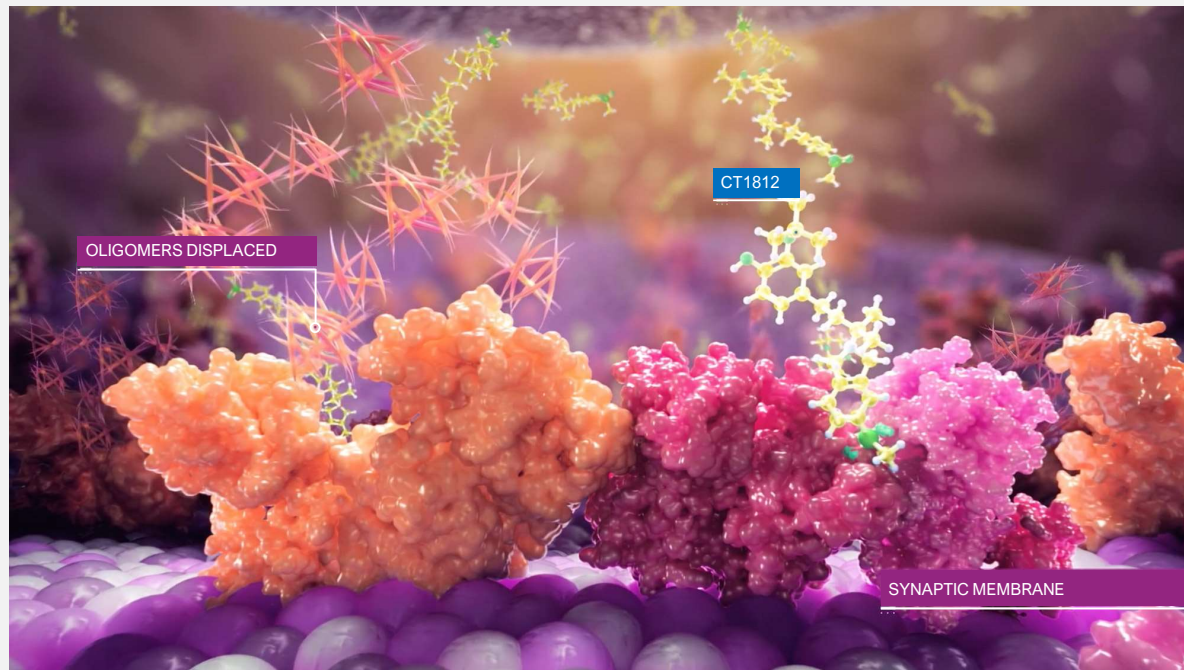
Monoclonal antibodies bind to A $\beta$  proteins  
Immunotherapeutic vaccines generate  
immune response to A $\beta$  proteins



# CT1812 – Unique Mechanism of Action for Treating AD



Age-related build-up of stressors including Aβ oligomers drive Alzheimer's disease



Aβ oligomers bind to synapses and interfere with cellular functions such as autophagy, leading to neuronal loss

CT1812 binds at σ-2, resulting in displacement of oligomers



# What We Have Learned From Clinical Trials to Date

## Endpoint of Interest:

## Result:

### Target engagement

SNAP<sup>2</sup>



Demonstrated displacement of amyloid oligomers from synapses

### Preliminary cognitive improvement

SHINE-A<sup>1</sup>



Demonstrated 3+ point difference in cognition vs placebo measured by ADAS-COG at Day 185

### Anatomical effect

SPARC<sup>3</sup>



Demonstrated effect on slowing brain atrophy

### Neurophysiology

SEQUEL<sup>4</sup>



Brain wave patterns normalized across multiple measures

1. SHINE-A cognitive and proteomic results: AD/PD 2022

2. LaBarbera, et al. Transl Neurodegener 2023

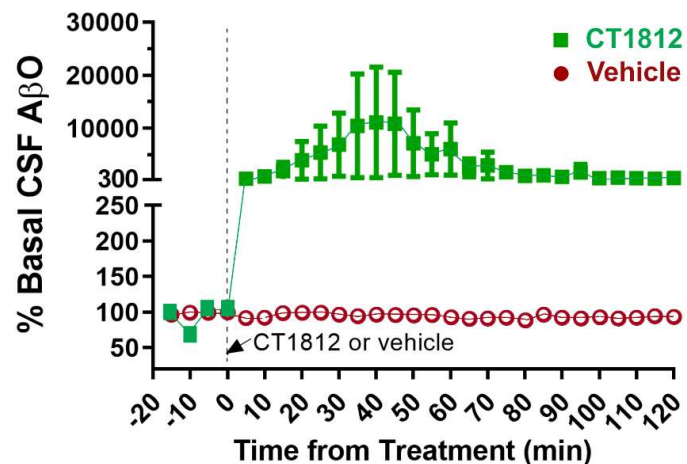
3. SPARC results published in Alz Res Therapy

4. CTAD 2023 SEQUEL imaging results presented

# Evidence of Target Engagement

## Phase 1b SNAP mirrored preclinical

MIE Measurement: *in vivo*



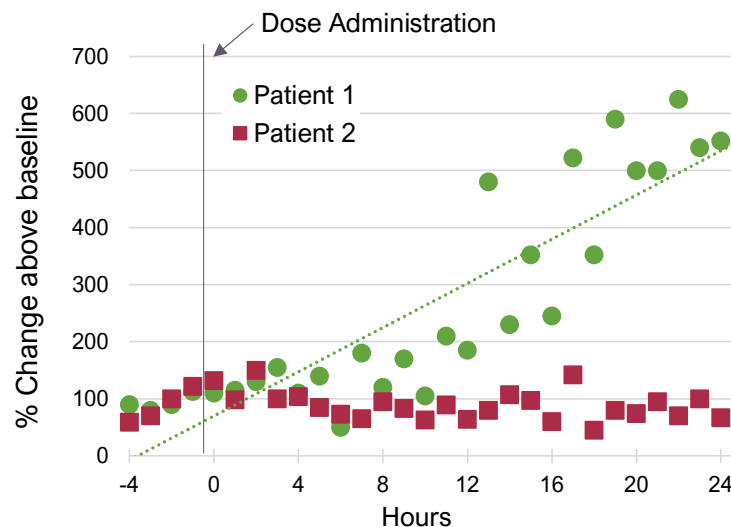
Oligomer  
Displacement  
in Mice

Replicates in  
Alzheimer's  
Patients

NOTE: Microimmuno-electrodes coated with oligomer-specific antibody detect soluble Aβ in transgenic hAPP/PS1 mice

Izzo et al. Preclinical and clinical biomarker studies of CT1812:  
A novel approach to Alzheimer's disease modification. *Alzheimer's Dement.* 2021  
Aug; 17(8):1365-1382.

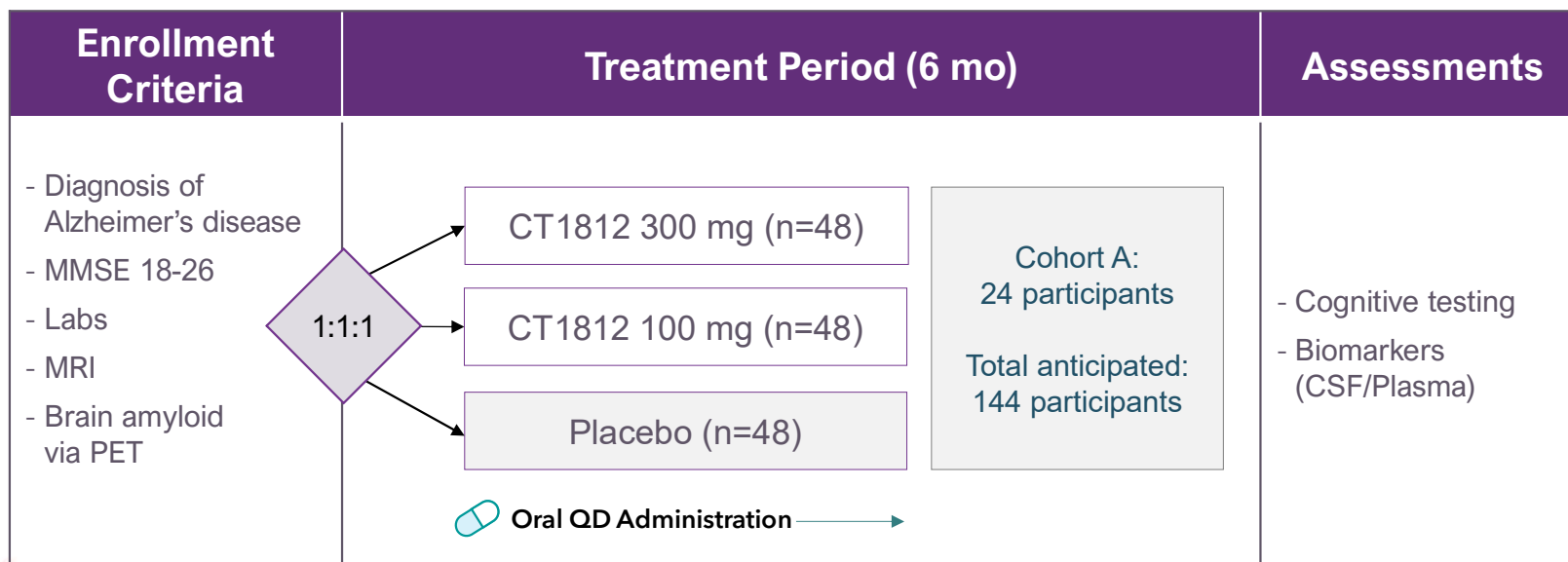
MIE Measurement: SNAP



LaBarbera et al. A Phase 1b randomized clinical trial of CT1812 to  
measure Aβ oligomer displacement in Alzheimer's disease using an indwelling  
CSF catheter. *Transl Neurodegener* 2023, 12(24).

# Phase 2 Safety and Efficacy Study in Adults with Mild-to-moderate Alzheimer's Disease

Enrollment Complete (n=153) ; Topline Expected mid-2024



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

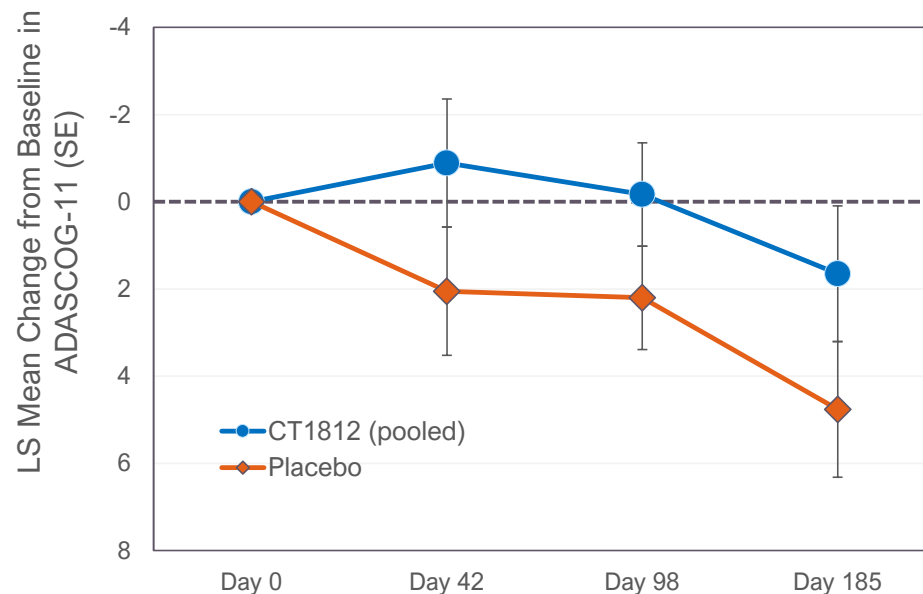


# Preliminary Clinical Evidence of Cognitive Benefit

- 3-point difference (ADAS-COG 11) at Day 185 between treated and untreated participants
  - 100mg CT1812 n=8
  - 300mg CT1812 n=8
  - Placebo n=8
- Clinically meaningful magnitude of change
- Trend towards slower cognitive decline in CT1812-treated vs placebo-treated participants

## Phase 2 SHINE Interim Analysis

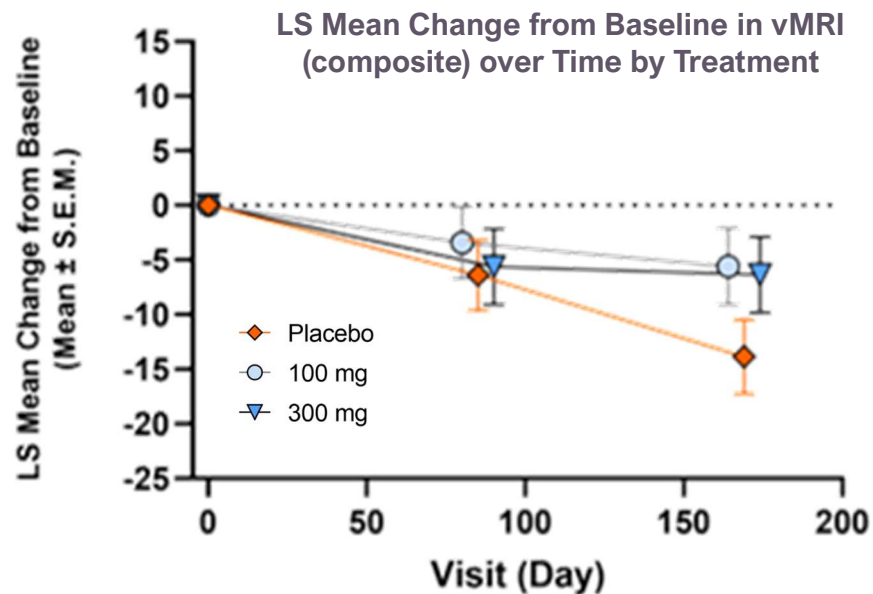
Cognitive Outcomes  
*Interim Analysis of 24 Participants*



SHINE COG0201 Study ([NCT03507790](#)) funded by NIA grant R01AG058660

# CT1812 Treatment Associated with Reduced Brain Atrophy

## Phase 2 SPARC Results



MRI Brain Volume (cm <sup>3</sup> ) 6-mo change from baseline			
	CT1812 (Pooled)	Placebo	P-value vs placebo
Hippocampus	-0.09 (0.08)	-0.40 (0.11)	0.0412
Prefrontal Cortex	-0.41 (0.95)	-4.80 (1.37)	0.0125
Pericentral Cortex	0.07 (0.53)	-2.90 (0.77)	0.0032

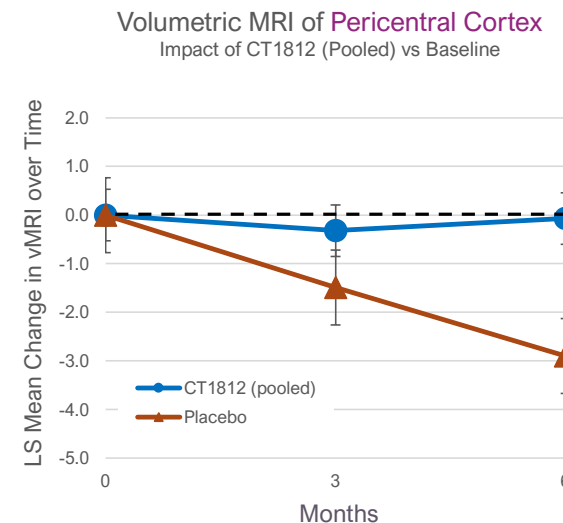
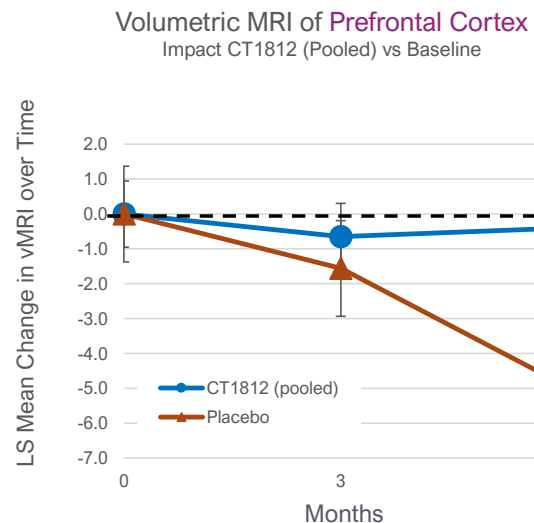
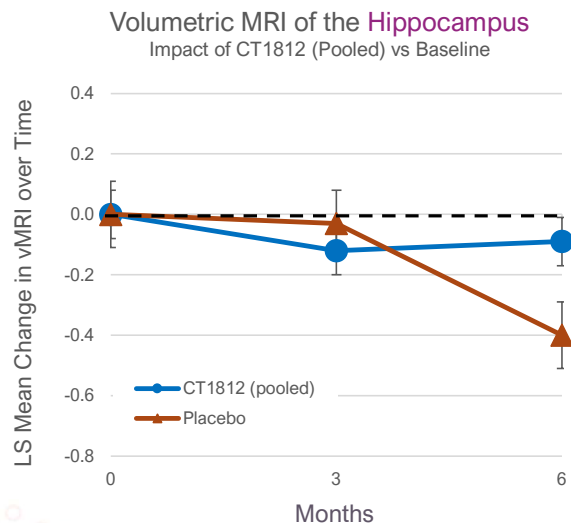
Published in *Alzheimer's Research & Therapy*:  
[doi.org/10.1186/s13195-024-01382-2](https://doi.org/10.1186/s13195-024-01382-2)

Pls Christopher H. van Dyck, M.D. at the Yale Alzheimer's Disease Research Unit and Richard E. Carson, Ph.D. at the Yale PET Center

SPARC COG0105 study partially funded by NIA grant R01AG057553

# CT1812 Treatment Associated with Reduced Atrophy in Brain Regions

## Phase 2 SPARC Results



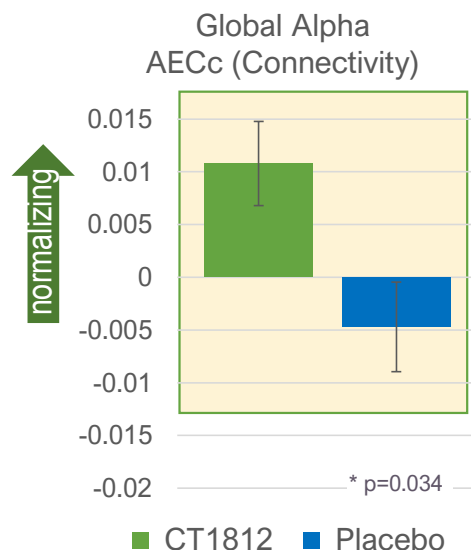
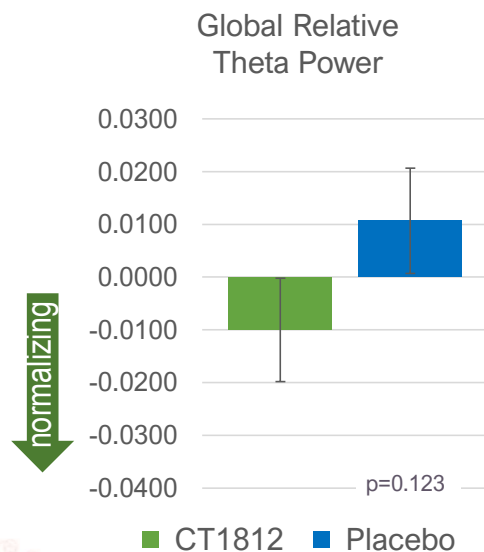
*Pls Christopher H. van Dyck, M.D. at the Yale Alzheimer's Disease Research Unit and Richard E. Carson, Ph.D. at the Yale PET Center*

*SPARC COG0105 study partially funded by NIA grant R01AG057553*

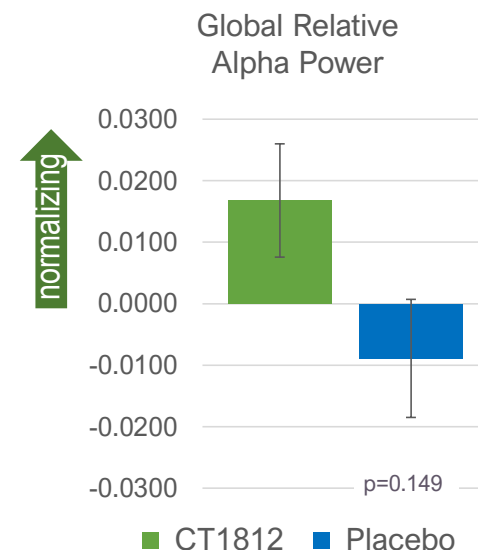
# CT1812 Normalizes qEEG Synaptic Function & Connectivity

*Positive trends in first three ranked outcomes measures*

SEQUEL Results: CTAD 2023



\* Nominally significant

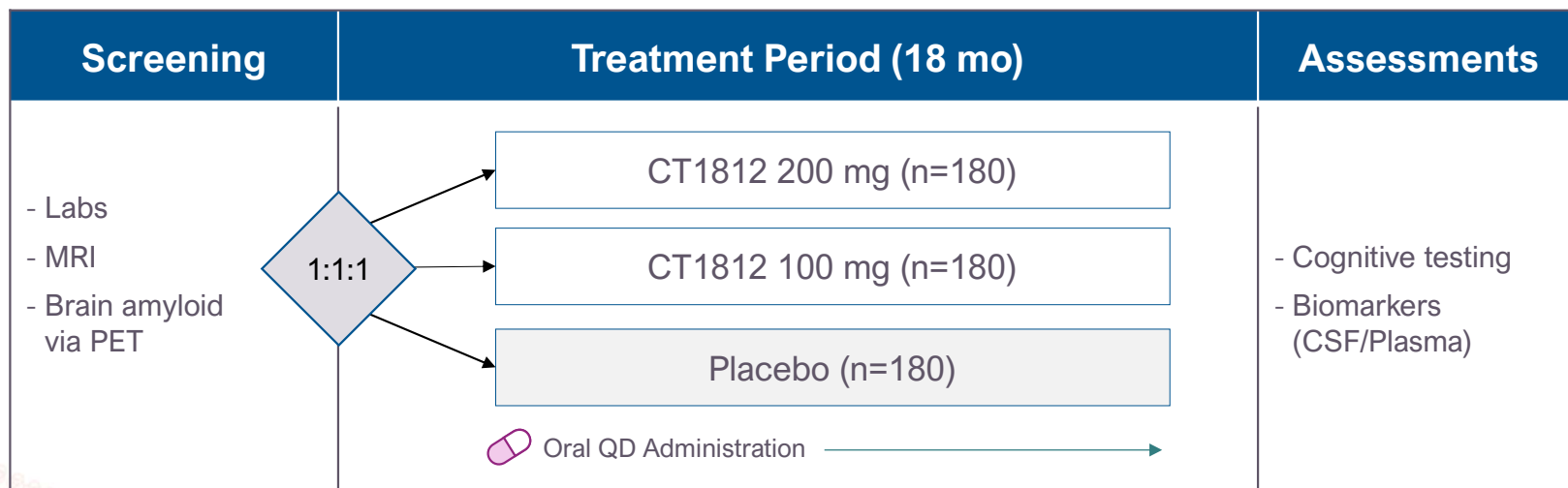




# Expanding into Early Disease with \$81M NIA Grant

*Long-term Efficacy Study in 540 Adults with Early Alzheimer's Disease*

*First Study to Collect Data on Combination Use of CT1812 and Lecanemab*



START COG0203 study (NCT05531656) supported by \$81M NIA grant (R01AG065248) in collaboration with ACTC (U24AG057437)

# KOL Perspective: Evolving Landscape in Alzheimer's Disease

Virtual Webinar April 12, 2024

## Featured Experts



**Martin J. Sadowski, MD, PhD, DSci**  
NYU School of Medicine



**Everard (Jort) Vijverberg, MD, PhD**  
The Alzheimer Center Amsterdam  
and Neuroscience Amsterdam



**Anton Porsteinsson, MD**  
Univ of Rochester Alzheimer's  
Disease Care, Research & Education

“ The drug which we know would target neurodegeneration would be any type of drug which would insulate a nerve cell from any type of insult. So for example, a drug which would protect a nerve cell from the effect of toxic oligomers. ”

*M Sadowski*

## Takeaway from the Experts

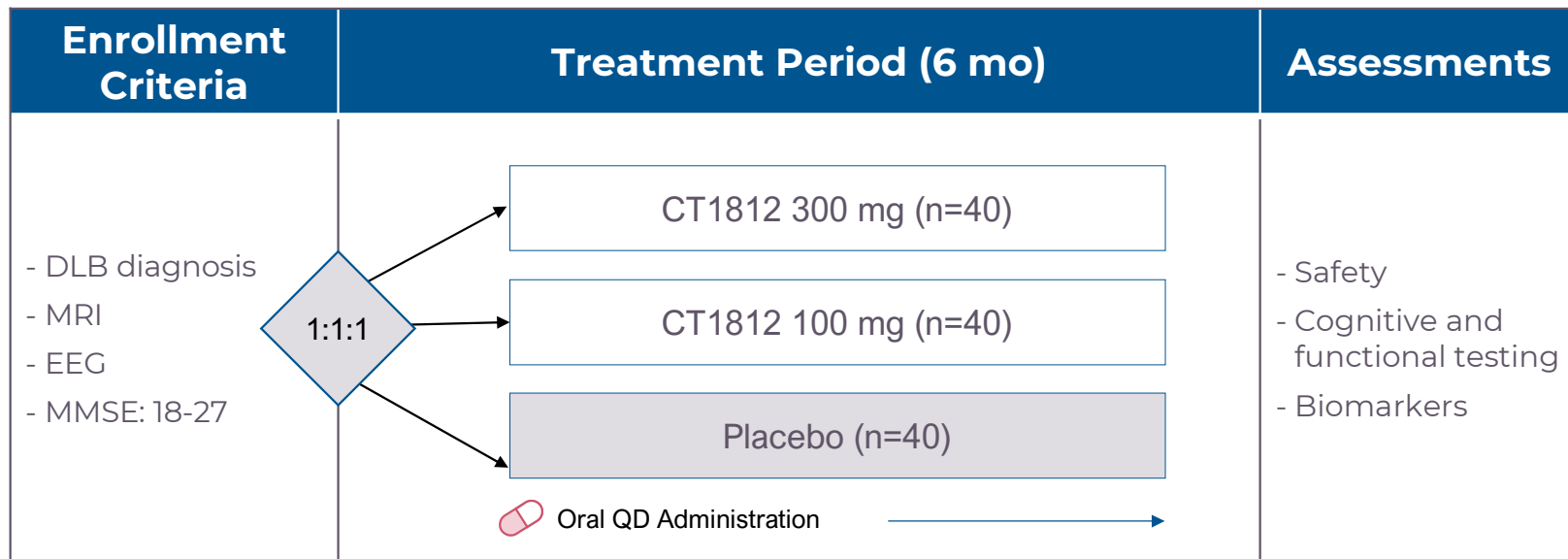
Plaque removal with A $\beta$  immunotherapies may be enhanced by the addition of agents that protect against oligomers or other stressors given in tandem or in sequence



# Studying Mild-to-Moderate DLB with \$30M Grant

Enrollment Complete (n=120)  
Topline Expected 2H-2024

*"The most common dementia  
you have never heard of"*  
- James Galvin; University of Miami



Conducted in collaboration with LBDA & University of Miami with principal investigator: James E. Galvin, MD, MPH

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

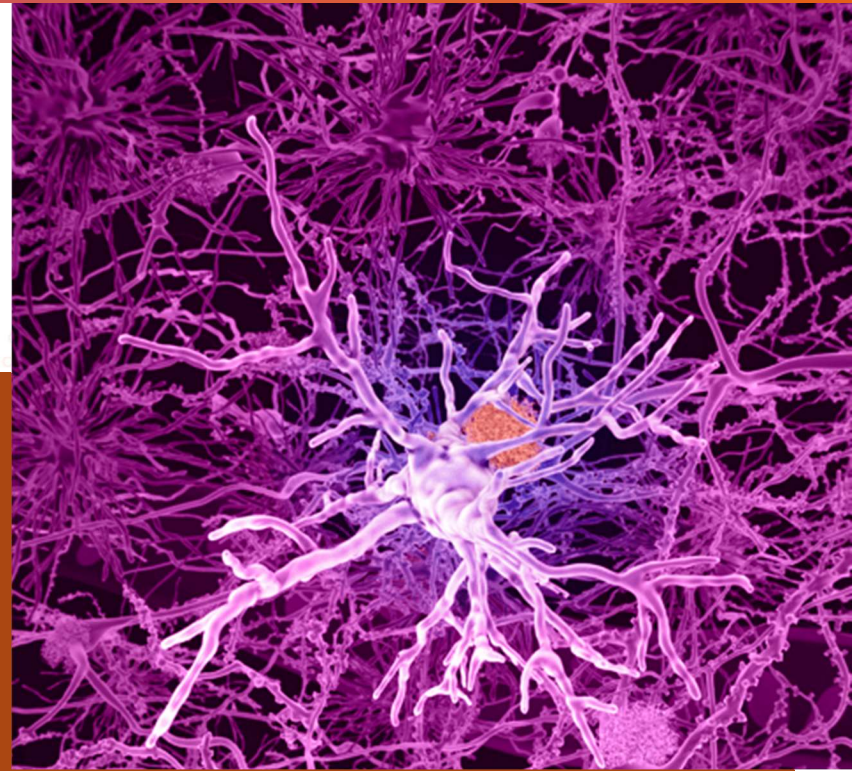
**BREAKING**

**News**

**Enrollment Target Reached: April 2024**



# Geographic Atrophy Secondary to Dry AMD





# CT1812- Oral Agent for the Treatment of Dry AMD

## Genetic Evidence

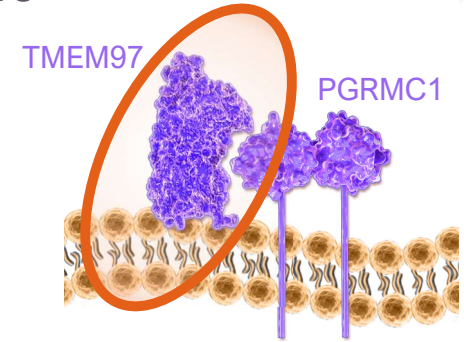
- Genetic Mutation (SNP) in TMEM97-VTN locus confers decreased risk of dry AMD
  - Further study will determine if and how SNP affects TMEM97 expression or function

## Biology

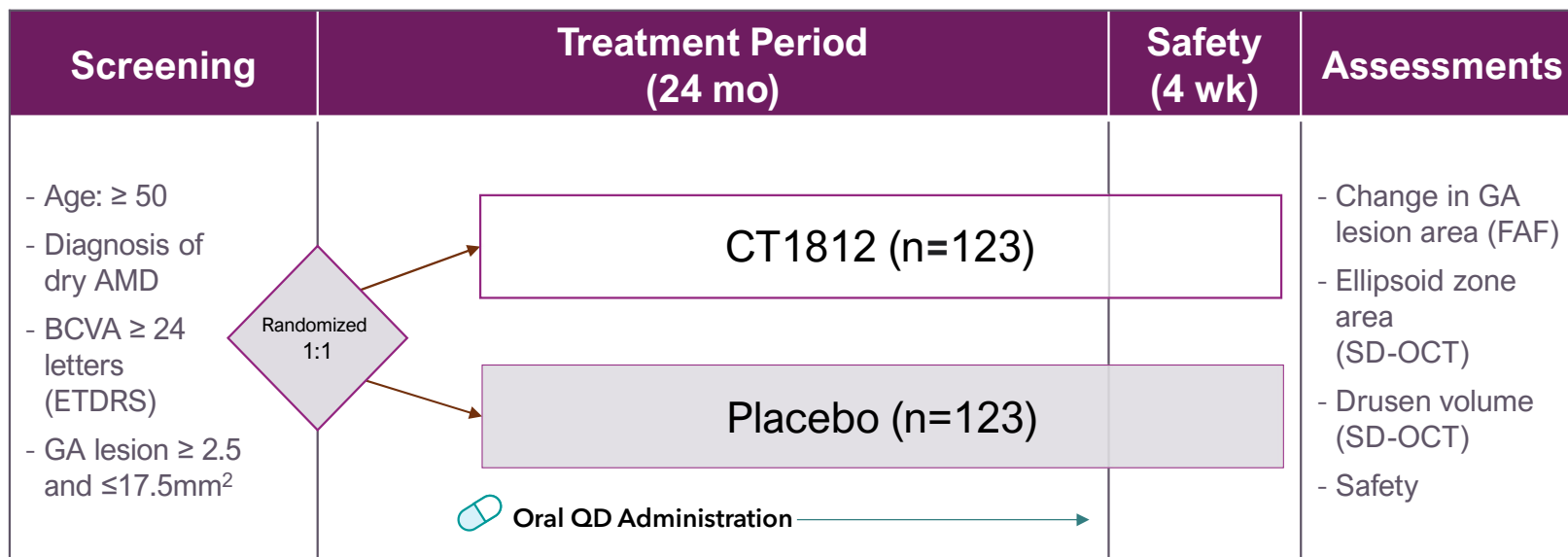
- Knocking down TMEM97 rescues retinal pigment epithelial (RPE) cells from death by oxidative stress
  - Supports role of TMEM97 in dry AMD
- Literature supports role of  $\sigma$ -2 in relevant processes: autophagy, vesicle trafficking, lipid metabolism, cellular stress

## Proteomic Studies

- Proteomics from Alzheimer's trials in patients given CT1812 showed differential movement in proteins known to be involved in dry AMD



# Phase 2 CT1812 in GA Secondary to Dry AMD



# Financial Position

## Financials as of December 31, 2023

- Cash and Cash Equivalents: \$29.9 million
- Including net proceeds from March 2024 raise of \$10.4M, expected cash runway through May 2025

## Grant funding for CT1812 studies as of Dec 31, 2023

- Preclinical through Phase 2: appx \$171.0 million
  - Approximate funding used: (\$103.5 million)
  - Remaining grant funding: **\$67.5 million**



# CT1812 – Multiple Catalysts

PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	STATUS
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## ALZHEIMER'S DISEASE

MILD TO MODERATE	COG0201 • SHINE
EARLY TO MILD	COG0203 • START

## DLB

MILD TO MODERATE	COG1201 • SHIMMER				 <b>Topline data 2H-2024</b>
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## DRY AMD

GEOGRAPHIC ATROPHY	COG2201 • MAGNIFY				<b>Actively recruiting</b>
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## COMPLETED STUDIES:

MILD TO MODERATE	Phase 2 COG0202 • SEQUEL (synaptic function)			
MILD TO MODERATE	Phase 1 COG0105 • SPARC (synaptic density)			
MILD TO MODERATE	Phase 1b COG0104 • SNAP (target engagement)			





# Thank You

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