COGNITION™ Therapeutics

Results from the Proof-of-Concept Phase 2 ‘SHINE’ Study of CT1812 in Mild-to-Moderate Alzheimer’s Disease

July 29, 2024

Forward-looking Statements

FORWARD-LOOKING STATEMENTS

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Alzheimer's Disease and CGTX

THE CHALLENGE

Despite 35 years of research based on the Amyloid Cascade Hypothesis, there are only **TWO** approved therapies and major unmet needs persist for the rapidly growing population of people with Alzheimer's disease

THE OPPORTUNITY

Strong scientific evidence supports the Amyloid Oligomer Hypothesis, ie, that oligomers—not plaques—are the **MOST NEUROTOXIC** form of amyloid beta that underlie cognitive decline

CGTX SOLUTION

Lead asset is CT1812: An investigational oral small molecule that potently antagonizes amyloid oligomers via a unique mechanism of action

- ✓ **Completed: Phase 2 POC SHINE trial in Mild-to-Moderate Alzheimer's disease population**
- ✓ Phase 2 POC dementia with Lewy body trial to read out 2H2024
- ✓ Currently running early Alzheimer's disease trial START (N=540)
- ✓ Phase 2 POC trial in geographic atrophy secondary to dry AMD ongoing

Agenda for SHINE Study Presentation

- Development History of CT1812
- Results of Cognitive and Functional Measures
- Safety and Tolerability
- Exploratory Biomarker Findings
- Commentary – Dr. Martin Sadowski
- Questions and Answers

Today's Speakers

Study investigator and industry thought leader

Everard (Jort) Vijverberg, MD, PhD

Staff Neurologist and CNS Trial Specialist, Amsterdam Alzheimer Center at Amsterdam Neuroscience, the Research Institute for Neuroscience of Amsterdam UMC

Martin J. Sadowski, M.D., Ph.D.

Professor of Neurology, Psychiatry, Biochemistry and Molecular Pharmacology at NYU
Director of the Alzheimer Drug Trial Program

CT1812 Background

Brief history of CT1812 development

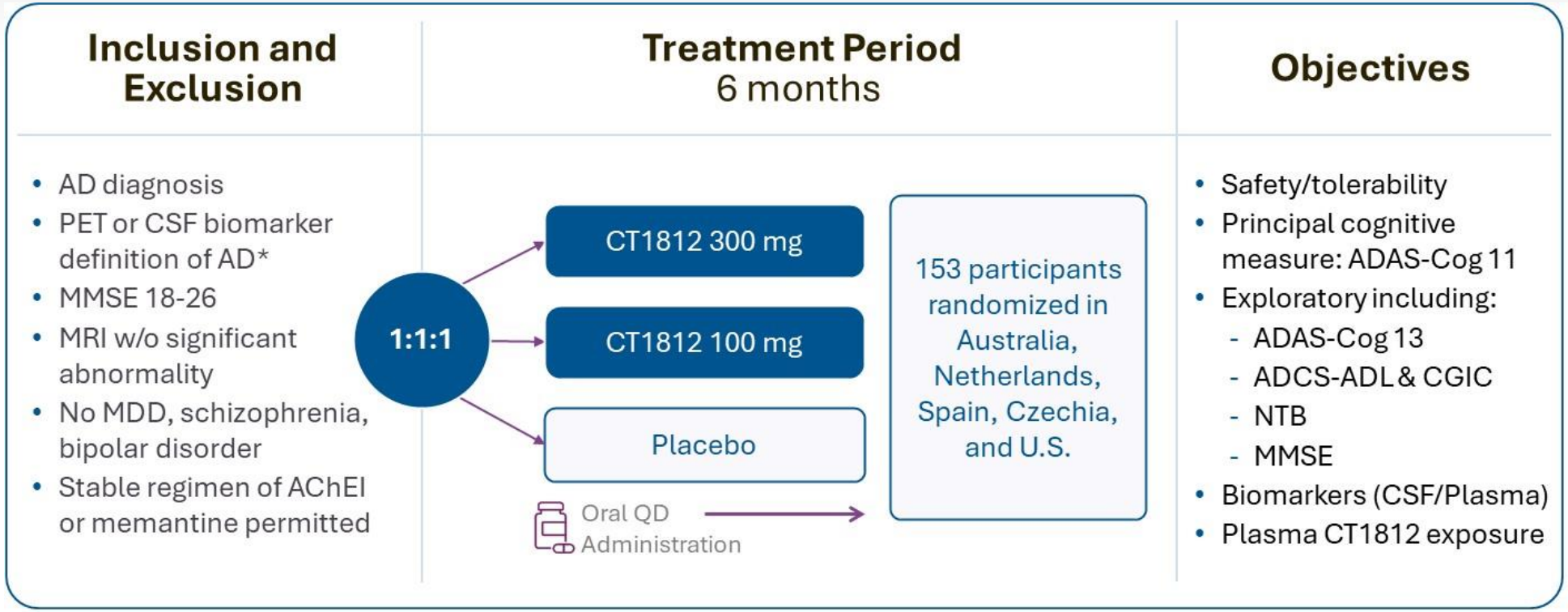
- Candidate identified by Cognition Therapeutics team via a screen established to identify molecules that protect neurons from the toxicity of Aβ oligomers
- Long history of Cognition research and publications has demonstrated that CT1812 can reduce the binding affinity of Aβ oligomers
- All intellectual property is wholly owned by Cognition Therapeutics
- Multiple trials completed
- COG0201 SHINE is the first phase 2 proof-of-concept study of CT1812 in mild-to-moderate Alzheimer's disease

Summary of COG0201 SHINE Results

Compelling evidence to advance into next phase of study

- COG0201 SHINE: FPI October 2018, LPO May 2024
- Favorable treatment differences versus placebo with both 100mg and 300mg dose groups on all key cognitive outcome measures
- CT1812 treatment resulted in slowing progression across outcome measures
  - The magnitude of effect is comparable to approved MAbs
  - Overall change in ADAS-Cog 11 was about 1 point at six months
- Adverse events were well balanced between treatment groups
- All liver enzyme elevations occurred at the higher 300mg dose
- These results support dose selection for future trials
  - 100mg dose had comparable efficacy to 300mg dose with no discontinuations due to AEs
  - No new safety signal

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



* *Cut-offs from Clinical Neurochemistry Lab at Sahlgrenska University Hospital in Gothenburg, Sweden or study protocol*

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

SHINE COG0201

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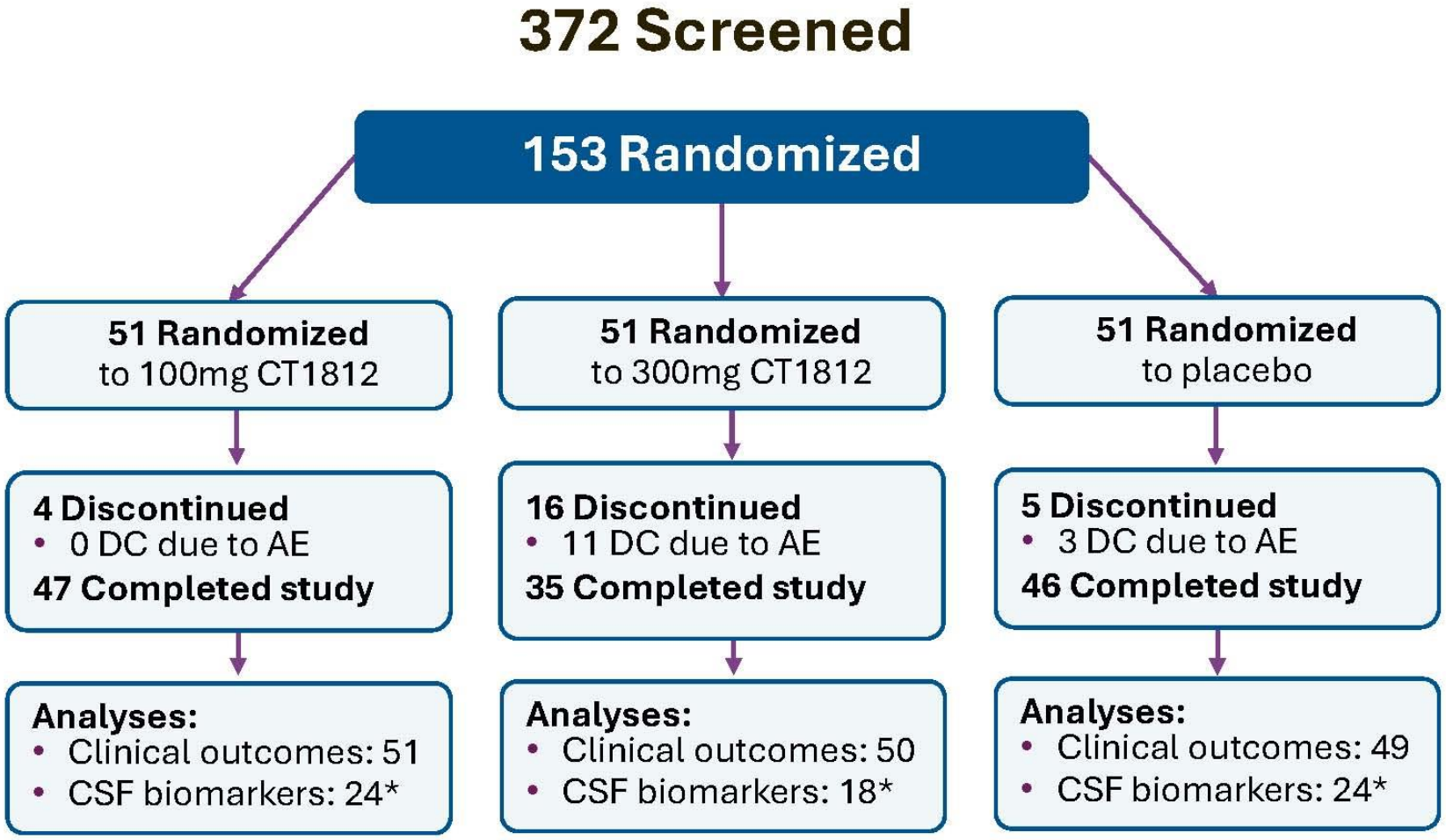
COG0201 SHINE Participant Disposition



* Varies by assay according to biospecimen availability

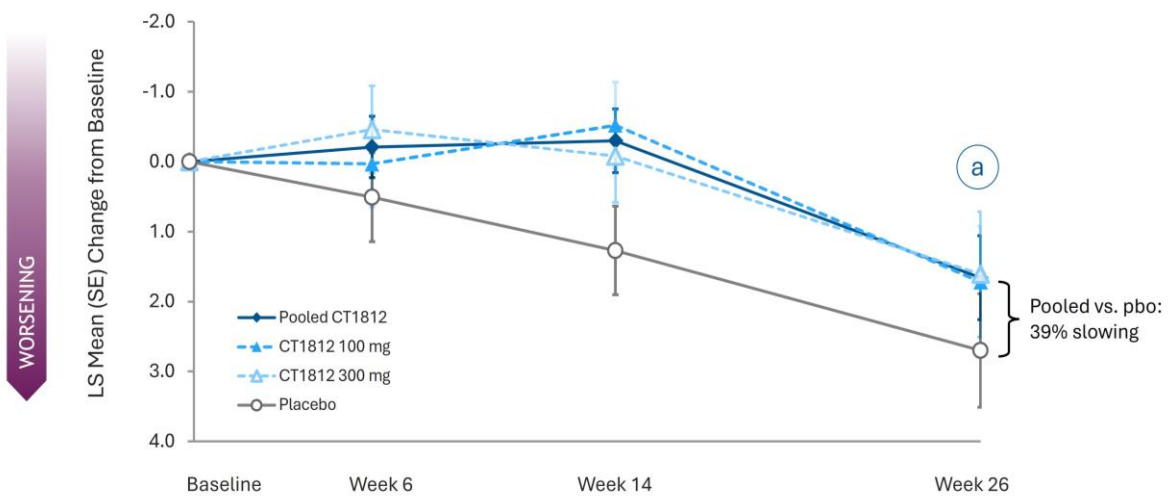
COG0201 SHINE Baseline Characteristics

	CT1812		Placebo (N=49)	Total (N=150)
	100mg (N=51)	300 mg (N=50)		
Age - years				
Mean (SD)	72.4 (6.96)	74.1 (7.20)	71.6 (8.06)	72.7 (7.43)
Min, Max	53, 81	57, 85	51, 85	51, 85
Female sex - n (%)	34 (66.7%)	28 (56.0%)	28 (57.1%)	90 (60.0%)
Ethnicity - n (%)				
Hispanic or Latino	4 (7.8%)	6 (12.0%)	1 (2.0%)	11 (7.3%)
Not Hispanic or Latino	47(92.2%)	43 (86.0%)	48 (98.0%)	138 (92.0%)
Not reported	0	1 (2.0%)	0	1 (0.7%)
Race – n (%)				
Black or African-American	0	1 (2.0%)	2 (4.1%)	3 (2.0%)
Native Hawaiian or Other Pacific Islander	1 (2.0%)	0	0	1 (0.7%)
White	50 (98.0%)	48 (96.0%)	46 (93.9%)	144 (96.0%)
More than One Race	0	1 (2.0%)	1 (2.0%)	2 (1.3%)
Asian, American Indian, Alaska Native, Other	0	0	0	0
MMSE				
Mean (SD)	21.5 (3.38)	20.8 (3.48)	21.8 (3.03)	21.37 (3.31)
Min, Max	17.0, 29.0	13.0, 27.0	17.0, 29.0	13.0, 29.0
Background med (AChEI/memantine) - n (%)				
Yes	33 (64.71%)	32 (64.0%)	29 (59.18%)	94 (62.67%)
No	18 (35.29%)	18 (36.0%)	20 (40.82%)	56 (37.33%)
ApoE status – n (%)				
ApoE4 Pos. (homo/hetero)	30 (58.8%)	30 (60.0%)	31 (63.3%)	91 (60.7%)
Education level				
Grades through 11 – no. (%)	7 (13.7%)	8 (16.0%)	7 (14.3%)	22 (14.7%)

Cognitive Endpoints: ADAS-Cog 11 and MMSE

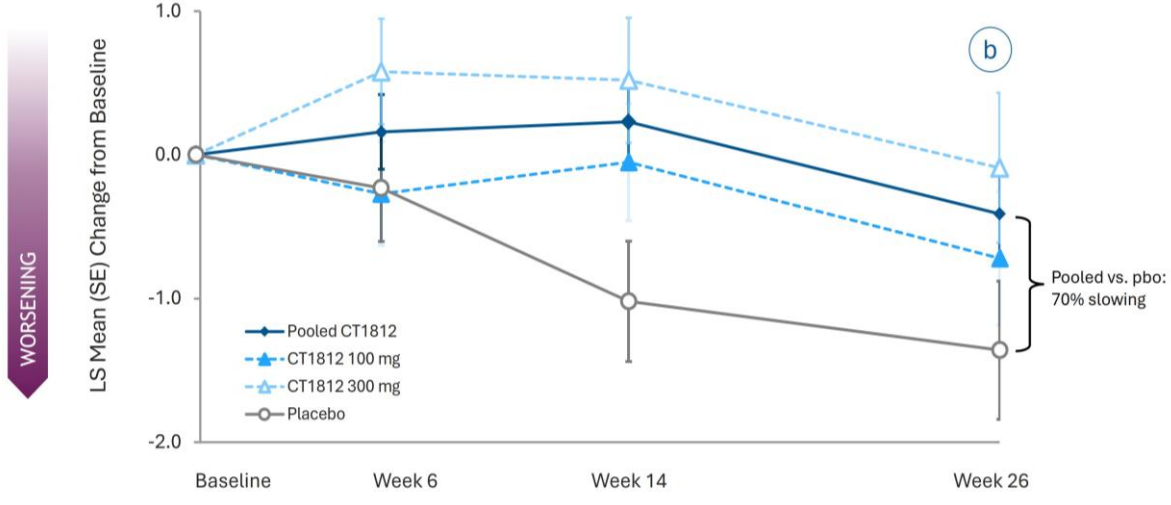
39% slowing of ADAS-Cog 11 decline at six months vs baseline compared to placebo, magnitude of effect similar to approved MAbs

ADAS-Cog 11



a) Pooled 100mg and 300mg group vs placebo p=0.3009. All other p values are nominal

MMSE



b) Pooled 100mg and 300mg group vs placebo p=0.1111.

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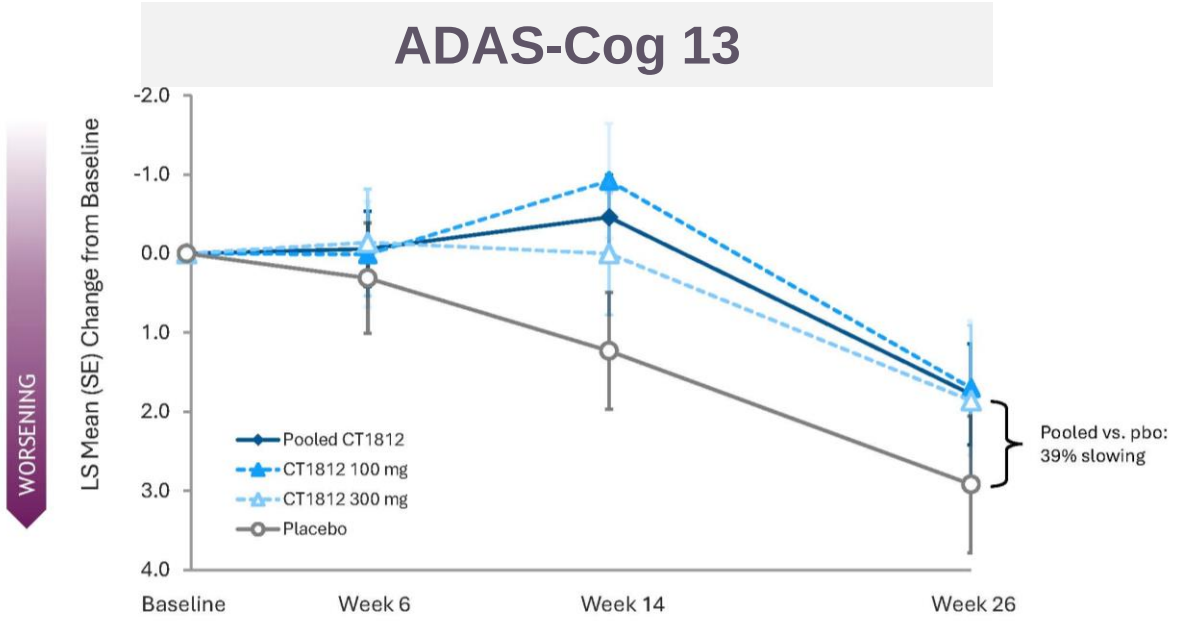
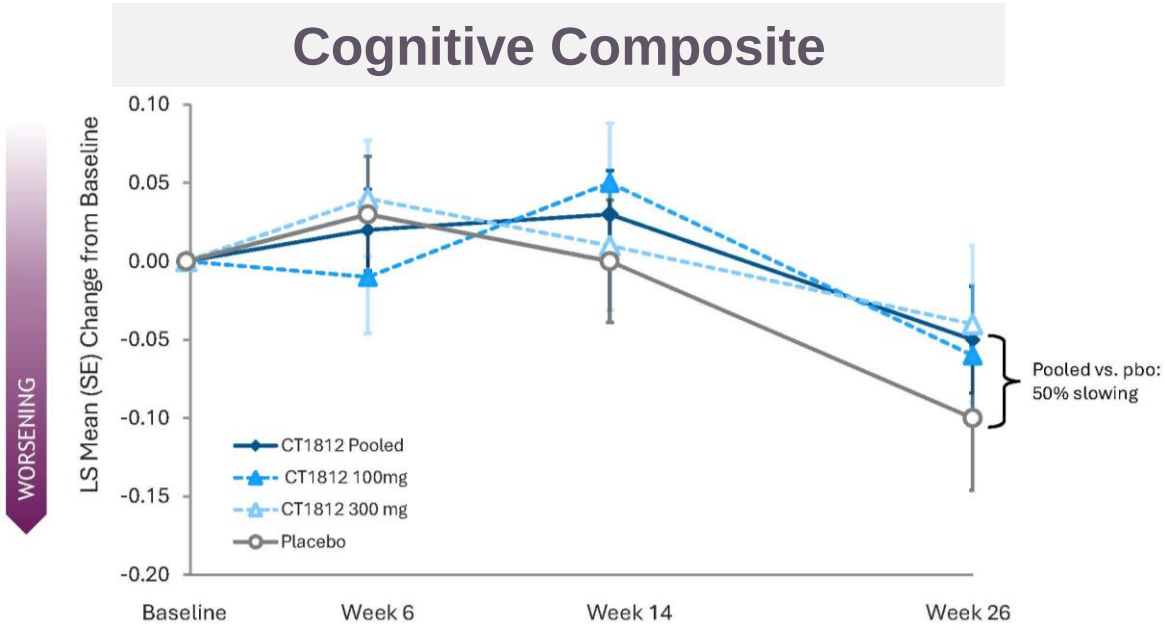
Cognitive Endpoints: ADAS-Cog 13, Cognitive Composite

Consistent results across multiple cognitive endpoints





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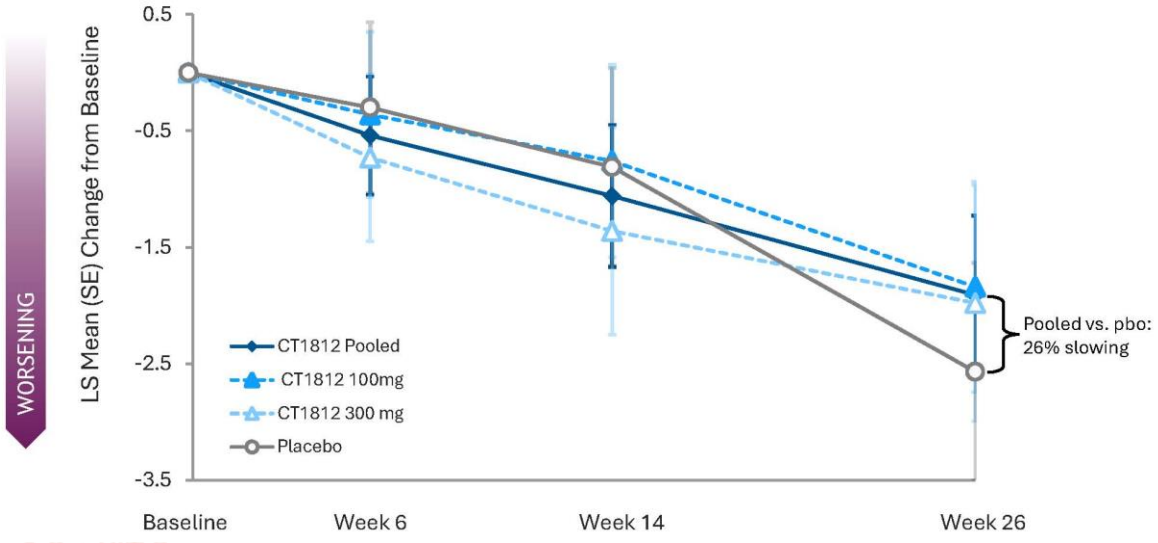
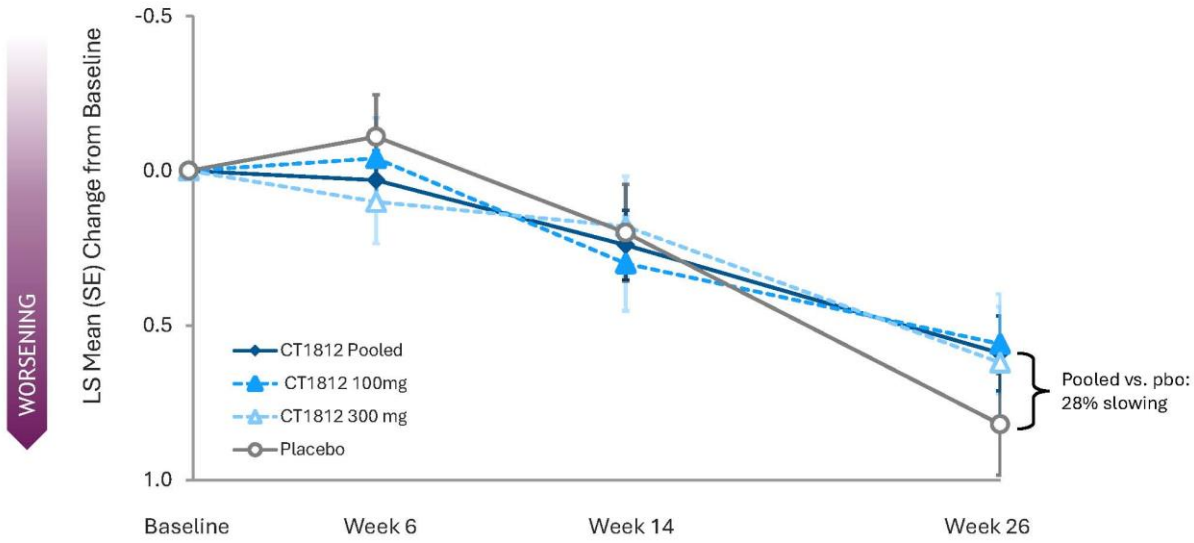
Additional Cognitive and Functional Measures

Consistent though not significant results; likely requires longer-term trial

ADCS-ADL



ADCS-CGIC



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Summary of Exploratory Outcomes

Trending positive across most cognitive and functional measures

	Time Frame	**ADAS-Cog 11**	**ADAS-Cog 13**	ADCS-CGIC	ADCS-ADL	Cognitive Composite	**MMSE**
CT1812 100mg	**Day 98**	Δ -1.79 **p = 0.0430**	Δ -2.16 **p =0.0376**	Δ 0.11 p = 0.6288	Δ 0.05 p = 0.9644	Δ 0.05 p = 0.3920	Δ 0.97 **p = 0.0972**
	Day 182	Δ -0.99 p = 0.3835	Δ -1.22 p = 0.3144	Δ -0.27 p = 0.2446	Δ 0.73 p = 0.5751	Δ 0.04 p = 0.5302	Δ 0.64 p = 0.3407
CT1812 300mg	**Day 98**	Δ -1.35 p = 0.1410	Δ -1.23 p = 0.2505	Δ -0.02 p = 0.9440	Δ -0.54 p = 0.6585	Δ 0.01 p = 0.8635	Δ 1.54 **p = 0.0118**
	Day 182	Δ -1.10 p = 0.3641	Δ -1.06 p = 0.4114	Δ -0.20 p = 0.4036	Δ 0.59 p = 0.6679	Δ 0.05 p = 0.4168	Δ 1.26 **p = 0.0766**
Pooled 100+300mg	**Day 98**	Δ -1.57 **p = 0.0441**	Δ -1.69 **p = 0.0634**	Δ 0.04 p = 0.8148	Δ -0.25 p = 0.8140	Δ 0.03 p = 0.5565	Δ 1.26 **p = 0.0155**
	Day 182	Δ -1.04 p = 0.3009	Δ -1.14 p = 0.2898	Δ -0.24 p = 0.2478	Δ 0.66 p = 0.5682	Δ 0.05 p = 0.4018	Δ 0.95 p = 0.1111

Green is directionally favorable

Trending p values < 0.1 bolded

Deltas reflect the difference in LS means vs. placebo at each timepoint.
Green highlighted cells reflect a favorable difference for CT1812 relative to placebo
Hierarchical testing strategy was pre-specified for ADAS-Cog 11 at Day 182. Order of testing: 1) Pooled 100+300mg vs. pbo, 2) 300mg vs. pbo, 3) 100mg vs. pbo.
Because p>0.05 for first test (pooled 100+300mg vs. pbo), formal testing stopped, and all p-values are considered nominal.

Summary Exploratory Outcomes - Percent Slowing Day 182

Effect as large or larger than approved MAbs and some experimental therapeutics

	ADAS-Cog 11	ADAS-Cog 13	MMSE	Cognitive Composite	ADCS-ADL	ADCS-CGIC
CT1812 100mg	36%	42%	47%	40%	28%	32%
CT1812 300mg	40%	36%	93%	60%	23%	24%
CT1812 Pooled	39%	39%	70%	50%	26%	28%

Note: above percentages reflect mean changes from baseline compared to placebo

Safety Findings

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COG0201 SHINE TEAE Summary

Adverse events are well balanced and mostly mild or moderate in nature

Subjects with:	CT 1812		Placebo (N=50)	Total (N=152)
	100mg (N=51)	300 mg (N=51)		
At least one TEAE	36 (70.6%)	42 (82.4%)	39 (78.0%)	117 (77.0%)
At least one TEAE related to treatment	11 (21.6%)	16 (31.4%)	7 (14.0%)	34 (22.4%)
At least on TEAEs leading to discontinuation	0	11 (21.6%)	3 (6.0%)	14 (9.2%)
AEs leading to death	0	0	1 (2.0%)	1 (0.7%)
At least one SAE	2 (3.9%)	3 (5.9%)	5 (10.0%)	10 (6.6%)
At least one SAE related to treatment	0	1 (2.0%)	0	1 (0.7%)
AE of Special Interest: LFT elevations ≥ 3xULN (AST or ALT)	0	9 (17.6%)	0	9 (6.0%)
At least one TEAE by maximum severity:				
Any	36 (70.6%)	42 (82.4%)	39 (78.0%)	117 (77.0%)
Mild	19 (37.3%)	22 (43.1%)	22 (44.0%)	63 (41.4%)
Moderate	16 (31.4%)	16 (31.4%)	14 (28.0%)	46 (30.3%)
Severe	1 (2.0%)	4 (7.8%)	3 (6.0%)	8 (5.3%)

Most Frequent AEs *Reported by system organ class and preferred term*

	CT 1812		Placebo	Total
	100mg (N=51)	300 mg (N=51)	(N=50)	(N=152)
Most common AE by System Organ Class and Preferred Term:				
Gastrointestinal disorders*	11 (21.6%)	7 (13.7%)	4 (8.0%)	22 (14.5%)
General disorders and administration site conditions*	2 (3.9%)	4 (7.8%)	2 (4.0%)	8 (5.3%)
Infections and infestations - Nasopharyngitis - Urinary tract infection	11 (21.6%) 0 3 (5.9%)	15 (29.4%) 3 (5.9%) 8 (15.7%)	15 (30.0%) 4 (8.0%) 5 (10.0%)	41 (27.0%) 7 (4.6%) 16 (10.5%)
Injury, poisoning and procedural complications - Fall - Post lumbar puncture syndrome - Skin laceration	14 (27.5%) 7 (13.7%) 2 (3.9%) 3 (5.9%)	4 (7.8%) 2 (3.9%) 0 0	13 (26.0%) 4 (8.0%) 4 (8.0%) 0	31 (20.4%) 13 (8.6%) 6 (3.9%) 3 (2.0%)
Investigations (see above LFT elevations)	5 (9.8%)	17 (33.3%)	7 (14.0%)	29 (19.1%)
Metabolism and nutrition disorders*	5 (9.8%)	1 (2.0%)	1 (2.0%)	7 (4.6%)
Musculoskeletal and connective tissue disorders - Arthralgia	8 (15.7%) 4 (7.8%)	4 (7.8%) 1 (2.0%)	6 (12.0%) 4 (8.0%)	18 (11.8%) 9 (5.9%)
Nervous system disorders - Headache	6 (11.8%) 4 (7.8%)	5 (9.8%) 0	12 (24.0%) 7 (14.0%)	23 (15.1%) 11 (7.2%)
Psychiatric disorders - Anxiety	2 (3.9%) 0	6 (11.8%) 3 (5.9%)	6 (12.0%) 2 (4.0%)	14 (9.2%) 5 (3.3%)
Skin and subcutaneous tissue disorders*	5 (9.8%)	3 (5.9%)	4 (8.0%)	12 (7.9%)

** no individual sub-category within this preferred term exceeded 5%*

COG0201 SHINE Safety Conclusions

Results consistent with previous clinical trials

- CT1812 demonstrated favorable safety and tolerability profile
- Most AEs were mild or moderate
- Percentage of subjects experiencing any AE was similar between the pooled CT1812 treatment group (76.5%) and the placebo group (78%)
- Serious AE rates were 4.9% among CT1812 subjects and 10% among placebo subjects
- AEs leading to discontinuation: 0% 100mg group; 6% placebo group; 21.6% 300mg
- 300mg discontinuations primarily elective discontinuations due to elevated liver enzymes
- All cases of elevated liver enzymes greater than or equal to 3X ULN occurred in the 300mg dose group

Exploratory Biomarker Findings

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Biomarker Findings

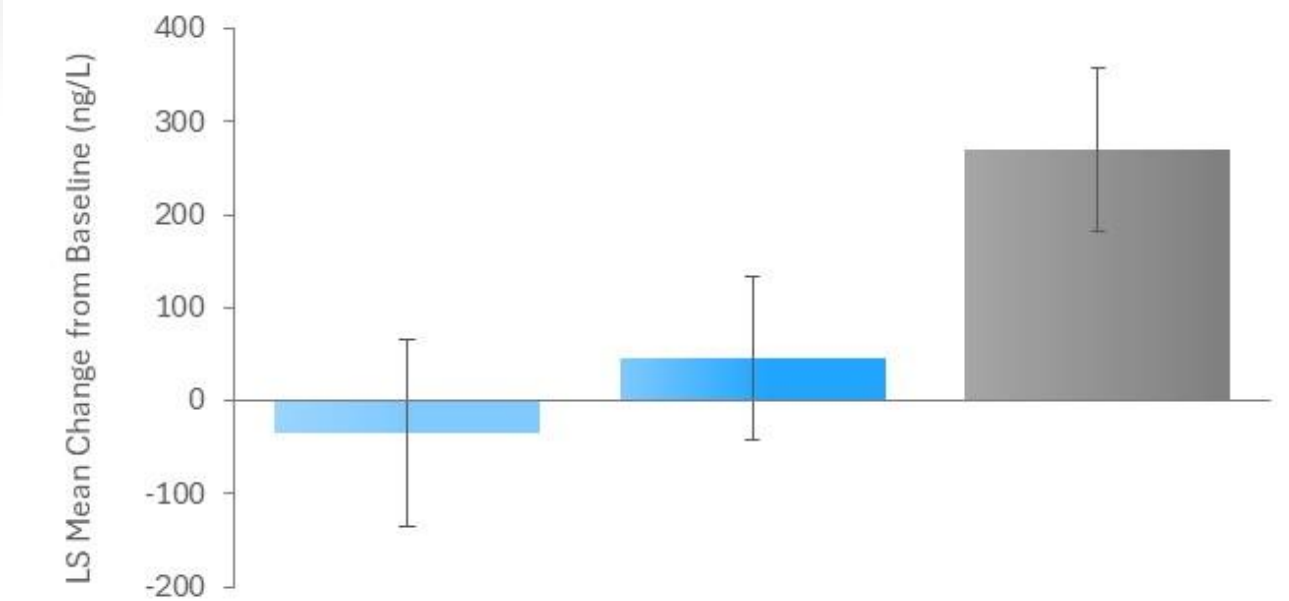
Biomarkers of Synaptic Function

- CSF samples at screening and Day 182 (optional), available in ~50% of mITT population
- Neurofilament Light Chain
  - Significant ($p<0.05$) reduction relative to placebo for 300mg dose
  - Reduction trend ($p<0.10$) for 100mg dose
  - Supports potential slowing of neurodegeneration
- No change in Aβ42/40 ratio
- CSF biomarkers p-Tau Total tau, Synaptotagmin, Neurogranin, SNAP-25, GFAP did not approach significance (Abstract #95767)
- Proteomic (Abstract #95770) and Phosphoproteomic (#95147) findings in convention hall and on CGTX website

Note: mITT included all participants receiving study drug and at least one post-baseline ADAS-Cog11 assessment

Signal of Impact on Neurodegeneration Based on NfL Change

Reductions in CSF NfL relative to placebo consistent with slowing neurodegeneration



	CT1812 300 mg	CT1812 100 mg	Placebo
N:	17	24	24
Baseline mean ng/L (SD):	1428.8 (568.93)	1142.4 (498.53)	1138.7 (436.60)
P-values vs pbo:	0.0277	0.0588	

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What we have Learned from POC SHINE Phase 2 Trial

Novel mechanism in oral, once daily form may be important for treatment options

- CT1812 showed favorable safety and tolerability profile with most AEs mild or moderate
- Results of study inform dosing for next phase of study
  - 100mg dose provided similar efficacy to 300mg dose
  - At 100mg, no discontinuations due to AEs
- Consistent efficacy signal: favorable, non-statistically significant treatment differences v. placebo with both dose groups across all key outcome measures
  - 39% slowing of prespecified clinical outcome measure (ADAS-Cog 11)
  - Comparable to the magnitude of effect of approved MAbs at six months
- Strong signal of impact on neurodegeneration based on NfL change
- No new safety signals

Science & Clinical Medicine Advance Through the Work of Many

CGTX wishes to acknowledge and thank those who made this trial possible

- Participants and their study partners
- Clinical investigators and site staff
- US and International Clinical research partners
- Cognition clinical operations team
- Funding partners including our investors, NIA/NIH and ADDF

Remarks from

Dr. Martin Sadowski, followed by Question and Answers

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Thank You

Lisa Ricciardi
President & CEO
lricciardi@cogrx.com

Tony Caggiano, MD, PhD
CMO and Head of R&D
acaggiano@cogrx.com

John Doyle
Chief Financial Officer
jdoyle@cogrx.com

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