Top-Line CSF Biomarker Outcomes From The Phase 2 Clinical Trial SHINE In Alzheimer's Patients

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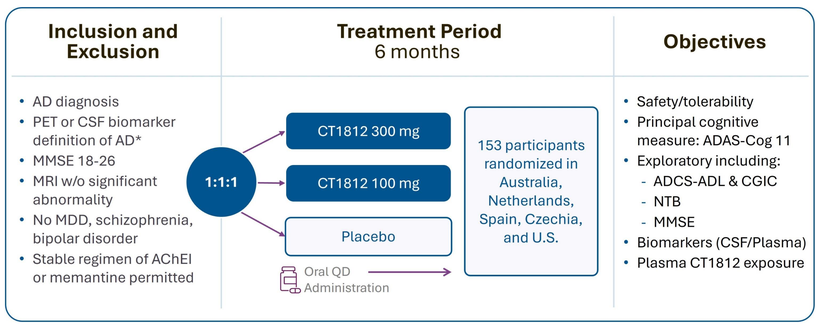
Treatment with CT1812 resulted in reductions in CSF neurofilament light chain (NfL) consistent with slowing neurodegeneration in mild-to-moderate AD

Background

- CT1812 is an experimental, oral, small molecule, allosteric Aβ oligomer antagonist in clinical development for Alzheimer's disease (AD) and dementia with Lewy bodies (DLB)
- CT1812 is a sigma-2 receptor ligand that modulates the binding of toxic amyloid beta oligomers to their targets on neurons[1,2]
- CSF biomarkers of synapse biology, tau, neurodegeneration and amyloid biology were assessed to determine treatment effects with CT1812



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

Biomarker Measurement

- The levels of CSF biomarkers Aβ40, Aβ42, pTau181, tTau, Nfl were measured by Lumipulse, neurogranin, GFAP and α-synuclein by ELISA, SNAP-25 and synaptotagmin by IP-LC-MS assay, and Aβ42/40 ratio calculated.
- An ANCOVA model was used to assess treatment effects comparing change from baseline values of CT1812 vs placebo, with treatment as the main effect, baseline value and APOE ε4 (+ or -) status as covariates.
- CSF biospecimens for 66 patients were available at baseline and following six-months treatment. Actual sample sizes varied by assay according to biospecimen availability.

Demographics & Baseline Characteristics (mITT*)

	CT1812		Placebo	Total
	100mg (N=51)	300 mg (N=50)	(N=49)	(N=150)
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
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%)

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

Acknowledgements

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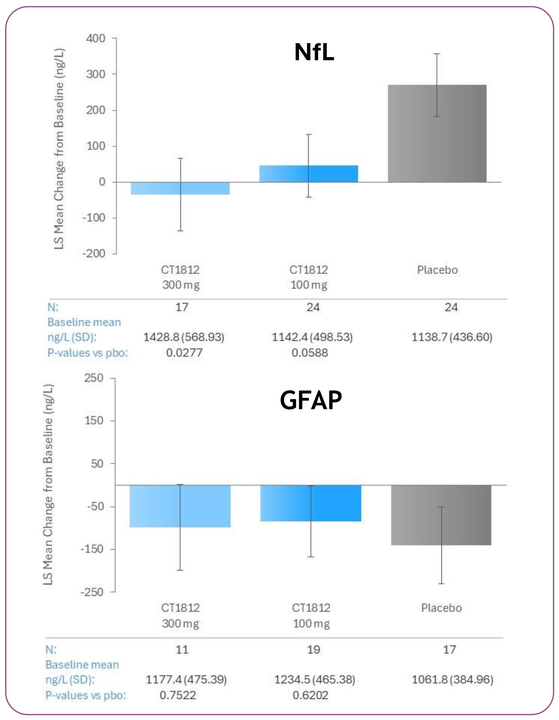
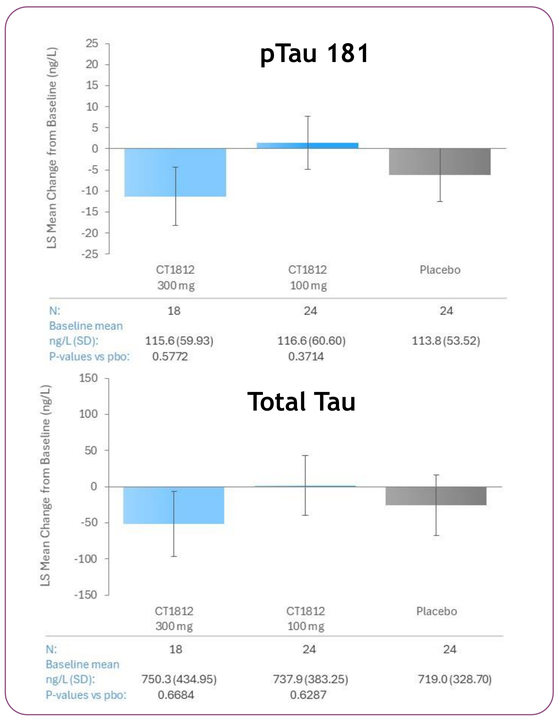
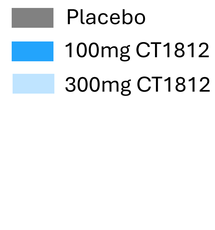
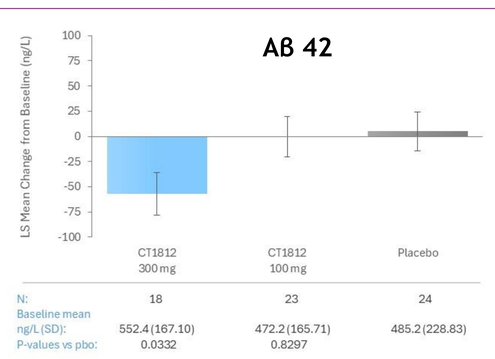
QR Code to view Cognition Therapeutics posters

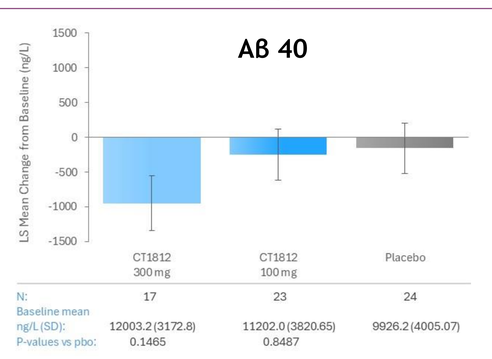
Results

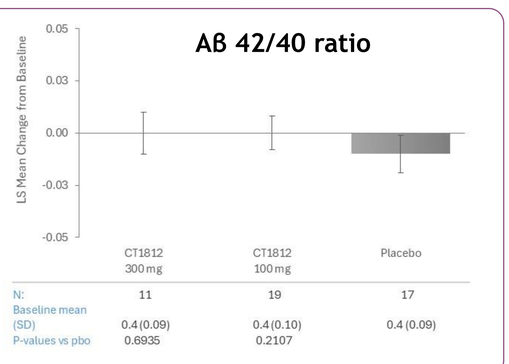


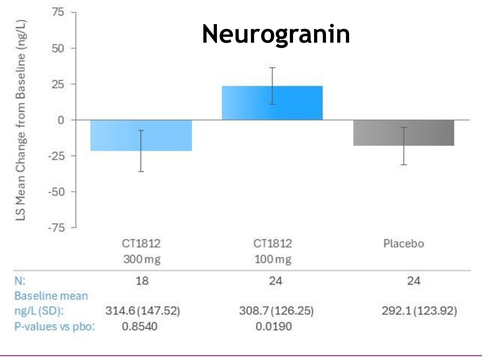


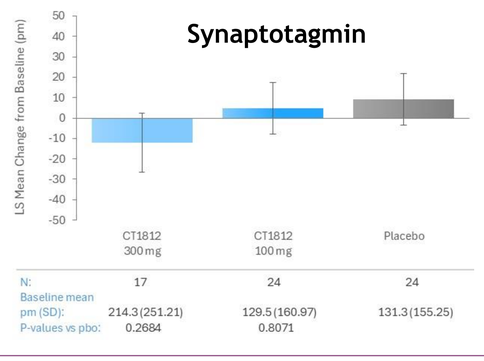


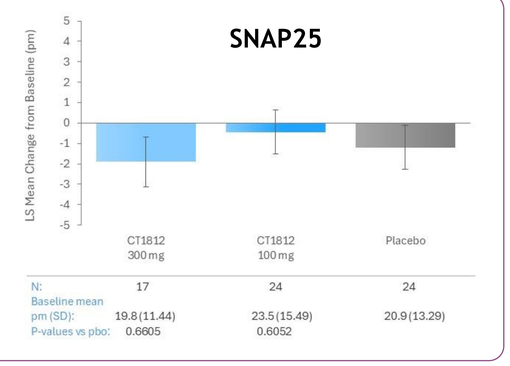












Conclusions

- CT1812 treatment was associated with lower CSF neurofilament light chain (NfL) levels for both the 300 mg (p=0.0277) and 100 mg (p=0.0588) doses compared to placebo
- CT1812 - 300 mg dose resulted in reductions in both CSF Aβ40 and Aβ42 monomer levels without changing the Aβ40/42 ratio
  - CT1812 – 100mg dose did not meaningfully alter CSF Aβ40 or Aβ42 monomer levels
- Exploratory biomarkers of synaptic function did not show a consistent pattern in this six-month trial
- Proteomic (Abstract 95770) and phosphoproteomic (Abstract 95147) analyses demonstrating the effects of CT1812 on AD-relevant proteins and pathways are presented in posters at AAIC
- Plasma biomarker analyses of the full SHINE data set to be presented at a future medical meeting
- Comprehensive biomarker program including both fluid and imaging are ongoing in the 18 month START trial in Early AD

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CT1812 is an investigational therapeutic that has not been approved for any use by the US Food and Drug Administration

References:
1. Izzo NJ, Yuede CM, LaBarbera KM, et al. *Alzheimer's Dement*. 2021 Aug; 17(8):1365-1382
2. LaBarbera, K.M., Sheline, Y.I., Izzo, N.J. et al. *Transl Neurodegener* 2023, 12(24)
3. Cut-offs from Clinical Neurochemistry Lab at Sahlgrenska University Hospital in Gothenburg, Sweden or study protocol