UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **March 15, 2022**

Cognition Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-40886**	**13-4365359**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

2500 Westchester Ave. **Purchase, NY**	**10577**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(412) 481-2210**

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol**	**Name of Exchange on Which Registered**
Common Stock, par value $0.001 per share	CGTX	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Attached as Exhibits 99.1 and 99.2 and furnished for purposes of Regulation FD are poster presentations that Cognition Therapeutics, Inc. may use from time to time in presentations or discussions with investors, analysts, and other parties.

The information in this Item 7.01 (including Exhibits 99.1 and 99.2) is being furnished solely to satisfy the requirements of Regulation FD and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, nor shall it be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The following exhibits are being furnished herewith:

Exhibit No.	Document
99.1	Poster titled "Experimental Therapeutic CT1812 Demonstrates Target Engagement in a Phase 1b Clinical Trial in Alzheimer's Patients to Measure Displacement of Abeta Oligomers into CSF," dated March 15, 2022
99.2	Poster titled "Proteomic Analysis of CSF in a Phase 2 Clinical Trial in Alzheimer's Patients to Identify Pharmacodynamic Biomarkers of the S2R Modulator, CT1812," dated March 15, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

COGNITION THERAPEUTICS, INC.

Date: March 15, 2022

By: */s/ Lisa Ricciardi*
Name: Lisa Ricciardi
Title: President and Chief Executive Officer

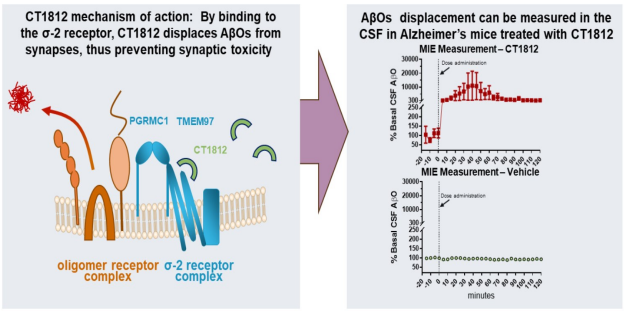
EXPERIMENTAL THERAPEUTIC CT1812 DEMONSTRATES TARGET ENGAGEMENT IN A PHASE 1b CLINICAL TRIAL TO MEASURE DISPLACEMENT OF Aβ OLIGOMERS INTO CSF

NJ Izzo PhD[1], KM LaBarbera BS[1], CM Yuede PhD[2], L Waybright BS[1], R Yurko MS[1], YI Sheline MD[3], HM Edwards BS[2], WD Gardiner BS[2], K Blennow MD[4], H Zetterberg MD[4], AB Hanson MD[5], CS Davis PhD[1], RJ Guttendorf PhD[6], LS Schneider MD[7], S DeKosky MD[8], AO Caggiano MD[1], M Grundman MD, SM[9]. Catalano PhD[1], JR Cirrito PhD[2], ME Hamby PhD[1]

1.Cognition Therapeutics, Inc, Pittsburgh, PA, USA, 2.Washington University, St Louis, USA, 3.University of Pennsylvania, Philadelphia, USA, 4. University of Gothenburg, Mölndal, Sweden, 5.Karolinska University Hospital, Stockholm, Sweden, 6.Aclairo, Vienna, USA, 7.Keck School of Medicine of USC, Los Angeles, USA, 8.University of Florida, Gainesville, USA, 9.Global R&D Partners, San Diego, USA

AIMS: A Ph1b clinical trial was conducted to verify target engagement of the sigma-2 receptor (S2R) modulator CT1812 in Alzheimer's disease (AD) patients by measuring drug related increases in Aβ oligomers (AβOs) in CSF.

BACKGROUND: CT1812 is a selective S2R modulator. In preclinical studies it has been shown to displace AβOs from cultured neurons and from cortical tissue slices from postmortem AD patients. In transgenic hAPP/PS1 mice, CT1812 displaces AβOs into the interstitial fluid in the brain and into CSF in the lateral ventricle.



(Izzo, et al, Alz & Dementia 2021)

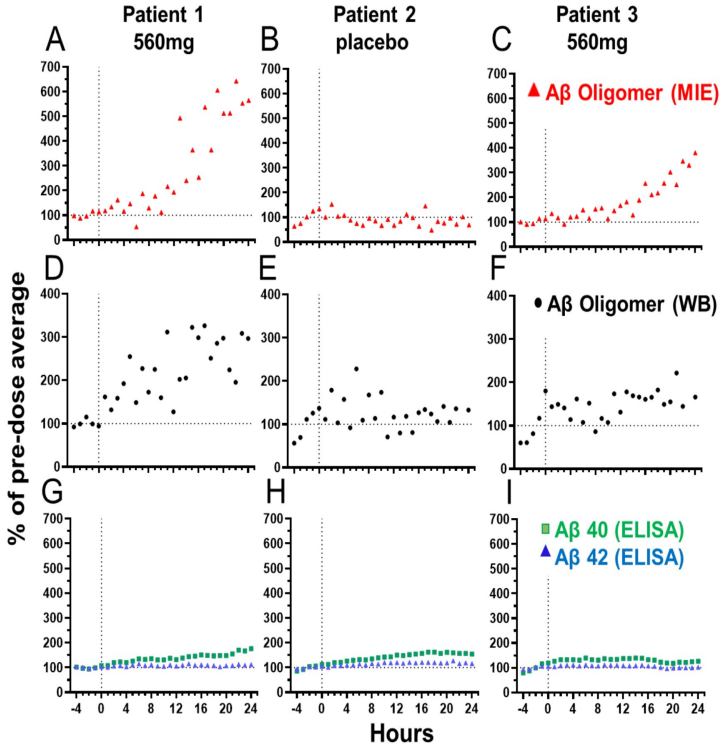
METHODS: A randomized, double-blind, placebo-controlled trial in mild to moderate AD patients (MMSE 18-26, biomarker positive). CSF was drawn from a lumbar catheter hourly over 28 hours, before and after a single p.o. dose of CT1812 (560 mg, two patients) or placebo (one patient).

AβO levels were measured via microimmunoelectrode (MIE) with oligomeric Aβ selective antibody (A11) and by native western blots (WB), Aβ40 & Aβ42 monomer levels were measured via ELISA. All Aβ measurements were normalized to the average of pre-dose levels. CT1812 concentrations were measured by LC/MSMS.

Subject	Treatment	Age Yrs	Sex	MMSE baseline	APOE
Patient 1	560 mg	67	F	18	E3/4
Patient 2	placebo	54	M	22	E3/3
Patient 3	560 mg	52	M	20	E2/3

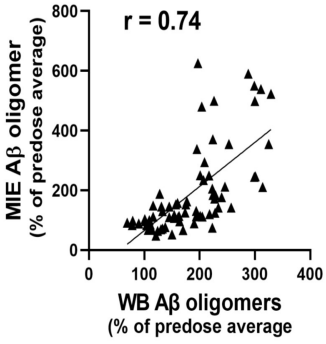
SAFETY: No subjects were withdrawn from the study due to treatment-emergent adverse events. The only serious adverse events were deemed unlikely to be related to study medication but instead due to the lumbar puncture procedure.

CT1812 treatment increases CSF AβOs, but not monomers

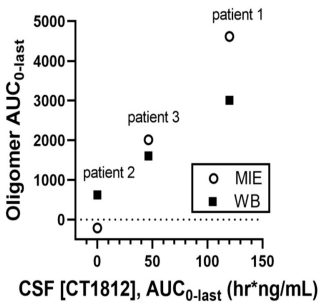


- Patients were dosed at hour 0 (dotted vertical lines).
- CSF concentrations of AβOs (A, B, C) measured by MIE increased >5 fold (Patient 1) and >2.5 fold (Patient 3) with respect to baseline with no apparent change with placebo (Patient 2).
- Similar changes in AβOs (D, E, F) in treated patients were observed on WB
- Aβ40 and Aβ42 (D,E,F) monomers increased <0.5 fold above baseline.

High correlation between AβO assays



AβO in the CSF is related to CT1812 concentration



Left: AβO concentration relative to pre-dose baseline measurements by MIE and by WB were highly correlated (Spearman r = 0.74).
Right: Higher CSF concentration of CT1812 was associated with higher CSF concentration of AβOs as measured by MIE (open circles) or Western blot (closed squares) in the same patients.

CONCLUSION: The results demonstrate the first clinical evidence of target engagement of CT1812 and support that CT1812 can engage S2Rs in brain and selectively mobilize and clear toxic AβOs from AD patient brains.

Support by National Institute on Aging AG057780

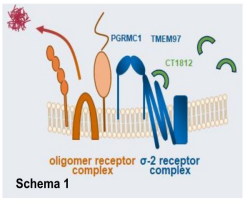
PROTEOMIC ANALYSIS OF CSF IN A PHASE 2 CLINICAL TRIAL FOR AD TO IDENTIFY PHARMACODYNAMIC BIOMARKERS OF THE S2R MODULATOR CT1812

N. Seyfried[1] , L. Waybright[2] , D. Duong[1] , E. Malagise[2] , K. Pandey[3] , C. Williams[2] , E. Dammer[1] , L. Ping[4] , K. Blennow[5] , H. Zetterberg[6] , J. Lah[4] , A. Levey[7] , L. Ricciardi[2] , A.O. Caggiano[2] , Mary E Hamby[2]

Affiliations: [1]Emory University School of Medicine, Biochemistry, Atlanta, GA, United States of America, [2]Cognition Therapeutics, Research, Pittsburgh, PA, United States of America, [3]Emtherapro Inc, Systems Biology, Atlanta, GA, United States of America, [4]Emory School of Medicine, Neurology, Atlanta, GA, United States of America, [5] Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Department of Psychiatry and Neurochemistry, Göteborg, Sweden

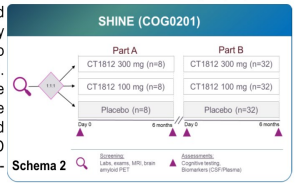
INTRODUCTION

The sigma-2 receptor (S2R) is encoded by TMEM97, a four-domain transmembrane protein that forms a complex with progesterone receptor membrane component 1 (PGRMC1). CT1812 is a highly brain-penetrant small molecule modulator of S2R, that displaces Aβ oligomers bound to neuronal synapses[1] (**Schema 1**). In preclinical studies, CT1812 protects synapses, facilitates their restoration and improves cognitive performance in transgenic Alzheimer's disease (AD) mice[1]. CT1812 is in clinical development for AD.



Schema 1

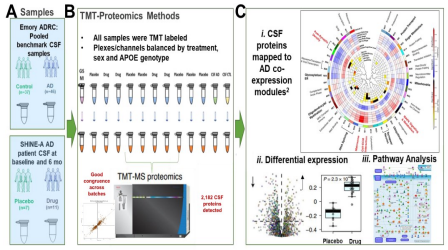
COG0201, the SHINE study, is a randomized, double-blind, placebo-controlled Phase 2 clinical trial designed to enroll ~120 patients with mild-to-moderate AD to evaluate the safety and efficacy of CT1812. Participants are divided equally in two CT1812 dose groups (100 mg, 300 mg) and placebo for once daily oral dosing for 6 mo (Schema 2). Endpoints include safety, cognitive function, as measured by the AD Assessment Scale-Cognitive Subscale 11-item version (ADAS-Cog-11), and biomarker evidence of disease modification. An interim analysis of the first 24 patients was conducted. No subjects were withdrawn from the study due to treatment-emergent adverse events and there were no SAEs attributed to study.



Schema 2

METHODS

Tandem-mass tag mass spectrometry (TMT-MS) followed by unbiased quantification of CSF proteomes was conducted on all treatment-compliant patients for which CSF at baseline and end of study CSF was collected (N=18; **Schema 3A, B**). CSF proteomes were compared to within-study pooled AD and age-matched non-demented control CSF reference standards from the Emory Alzheimer's Disease Research Center (ADRC) to compare protein levels in the SHINE-A cohort with well-characterized AD CSF and to assess treatment effects through differential expression and pathway analyses (**Schema 3C**).



Schema 3. Following sample **(A)** analysis via TMT-proteomics **(B),** differentially expressed proteins **(C*i*)** were mapped to a previously generated protein co-expression networks **(C*i*)** built from 516 brain samples with healthy individuals, asymptomatic and symptomatic AD patients (Johnson et al. 2022 *Nat Neuro*) NCT03507790. **C*iii)*** Pathway analysis was also performed on DE proteins using Metacore, STRING, and GO terms.

Proteomics Method Shows High Congruence with Clinically Validated Assays & Allows Benchmarking of SHINE-A Cohort

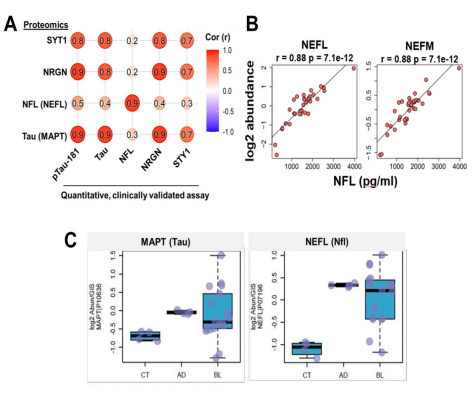


Fig 1. A) Pearson correlation analysis of AD core biomarkers from clinically validated assays[3] to that in the TMT proteomics dataset. **B)** Top two most highly correlated proteins with NFL quantitative assay (Uman Diagnostics; pg/ml). **C)** AD core biomarkers[3] from CSF proteomes from SHINE-A at baseline (BL) were compared to pooled AD and non-demented control (CT) CSF reference standards (Emory ADRC).

Pharmacodynamic (PD) Biomarkers of CT1812 (126) Identified, & Mapping to the Brain Network Supports Role at Synapses

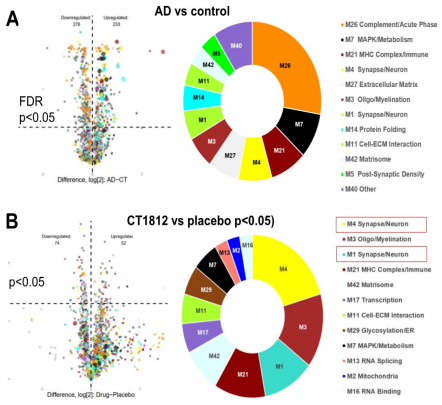
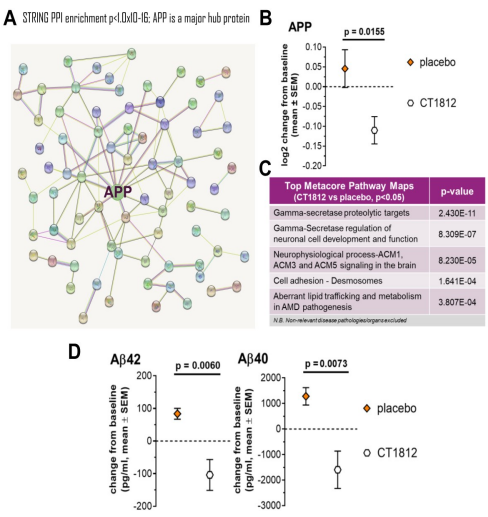


Fig 2. Differential expression analysis of CSF from AD vs control (**A, left**) and AD patients given CT1812 vs placebo (**B, left**). Differentially expressed proteins for each comparison were mapped to the AD co-expression modules[2] (Schema 3C, top panel; top 12 shown here (**A,B right**)).

Unbiased Pathway Analysis of Differentially Abundant Proteins Implicates CT1812 in Regulating Amyloid Biology

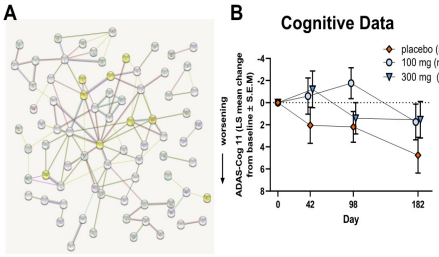


Top Metacore Pathway Maps (CT1812 vs placebo, p<0.05)	p-value
Gamma-secretase proteolytic targets	2.430E-11
Gamma-Secretase regulation of neuronal cell development and function	8.309E-07
Neurophysiological process-ACM1, ACM3 and ACM5 signaling in the brain	8.230E-05
Cell adhesion - Desmosomes	1.641E-04
Aberrant lipid trafficking and metabolism in AMD pathogenesis	3.807E-04

N.B. Non-relevant disease pathologies/organs excluded

Fig 3. A) Differentially abundant proteins in CSF from CT1812 vs placebo treated AD patients are highly interconnected (STRING analysis) and APP is a hub gene that is significantly lower in CT1812 vs placebo patients **(B)**. **C)** Metacore pathway mapping shows amyloid pathways as the top most significantly associated with CT1812 treatment vs placebo (p<0.05). **D)** Statistically significant lowering of Aβ40 and Aβ42, as assessed via Lumipulse, by CT1812 vs placebo.

Candidate PD Biomarkers Linked to Changes in Cognition Identified from SHINE-A CSF Proteomics Analyses



GO term ID	GO Biological Process	strength	FDR p-value
GO:0045055	Regulated exocytosis	0.67	1.88E-12
GO:0016192	Vesicle-mediated transport	0.46	5.81E-12
GO:0032940	Secretion by cell	0.58	9.68E-12
GO:0046903	Secretion	0.55	9.68E-12
GO:0002444	Myeloid leukocyte mediated immunity	0.71	2.41E-11
GO:0002376	Immune system process	0.39	3.73E-11

Fig 4. A) Several PD biomarkers (CT1812 vs placebo; p<0.05) are associated with GO term "cognition" (in yellow; GO:0050890; STRING). **B)** SHINE-A ADAS-Cog-11 cognitive score data which showed a non-significant but clinically meaningful (3-point difference) from placebo. **C)** Top biological processes from gene ontology of protein log2 abundance significantly correlated (Pearson, p<0.05) with ADAS-Cog11 change from baseline scores.

Candidate Disease Modification Biomarkers Identified: Proteins Dysregulated in AD Normalized with CT1812

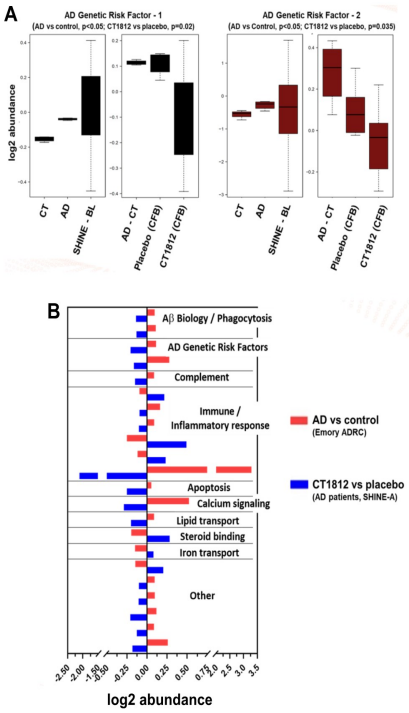


Fig 5. Within-study comparisons to CSF protein levels in reference standards (ADRC AD and control (CT)) enabled comparison of the SHINE-A AD cohort to well-characterized AD and non-demented control CSF **(A,B). A)** Box plots illustrate two proteins significantly increased in AD compared to control CSF that are significantly downregulated in CT1812 vs placebo (SHINE-A). **B)** 22 proteins are significantly (p<0.05) normalized towards control with CT1812 (log2 change in abundance in AD vs control (red) and CT1812 vs placebo (blue)).

CONCLUSIONS

- **Strong correlations with clinically validated assays for core AD biomarkers validate TMT-MS proteomics as a quantitative method**
- **Brain module association and pathway analysis corroborate the mechanism of action of CT1812 in regulating synapses and AD biology**
- **Comparisons to reference CSF standards illuminate proteins disrupted in, or genetically linked to, AD that were normalized by CT1812**
- **Pharmacodynamic biomarkers of CT1812 were identified, including that which may reflect disease modification and cognitive improvement**

Overall, data provide additional support that the S2R modulator CT1812 may be a promising therapeutic approach to AD

REFERENCES
1. Izzo et al. Preclinical and clinical biomarker studies of CT1812: A novel approach to Alzheimer's disease modification. Alz & Dementia 2021.
2. Johnson et. al. Large-scale deep multi-layer analysis of Alzheimer's disease brain reveals strong proteomic disease-related changes not observed at the RNA level. Nat Neurosci. 2022.
3. Blennow et al. Fluid biomarker-based molecular phenotyping of Alzheimer's disease patients in research and clinical settings. Prog Mol Biol Transl Sci. 2019;168:3-23.

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Corresponding author: mhamby@cogrx.com