Clinical Trial Summary Results

PROTOCOL CODE: **COG0104**

EUDRA-CT: **2018-000163-89**

A Pilot Study to Evaluate the Effect of CT1812 Treatment on Aβ Oligomer Displacement into CSF in Subjects with Mild to Moderate Alzheimer's Disease

Version 1.0

November 2nd, 2021

1 TITLE PAGE

STUDY TITLE: A Pilot Study to Evaluate the Effect of CT1812 Treatment on Aβ Oligomer Displacement into CSF in Subjects with Mild to Moderate Alzheimer's Disease.

INVESTIGATIONAL PRODUCT: CT1812 capsule (oral, in the form of a hydroxypropyl methylcellulose [HPMC] capsule).

INDICATION STUDIED: Treatment of Alzheimer's Disease (AD).

STUDY DESIGN: A randomized, double-blind, placebo-controlled, parallel-group study in patients with mild to moderate AD.

NAME OF THE SPONSOR: Cognition Therapeutics Inc., USA.

PROTOCOL IDENTIFICATION CODE: COG0104 protocol versions 2.5 (USA) and 2.8 (Sweden).

EUDRA-CT: 2018-000163-89

DEVELOPMENT PHASE OF STUDY: Phase 1b

FIRST SUBJECT IN

First Subject Screened: 19 Apr 2018

First Subject Dosed: 30 May 2018

LAST SUBJECT OUT

Last Subject Completed: 06 Feb 2019

PRINCIPAL INVESTIGATOR: Yvette Sheline, MD

Anne Börjesson-Hanson, MD, PhD

DATE OF THE VERSION REPORT: Final v1.0, 28 Oct 2021

Both the development of the study and the archiving of essential documents have been made in accordance with the guide of good clinical practice.

2 SUMMARY

<table>
<tr><td>Name of the Sponsor:
Cognition Therapeutics, Inc.</td><td rowspan="2">Individual Study Table referring to Part of the Dossier
Volume:

Page:</td><td rowspan="2">(For National Authority Use only)</td></tr>
<tr><td>Name of Active Ingredient:
CT1812</td></tr>
<tr><td colspan="3">Title of study: A Pilot Study to Evaluate the Effect of CT1812 Treatment on Aβ Oligomer Displacement into CSF in Subjects with Mild to Moderate Alzheimer's Disease.</td></tr>
<tr><td colspan="3">Investigators and Study Centres:
Yvette Sheline, MD (University of Pennsylvania, USA) – 2 subjects enrolled
Anne Börjesson-Hanson, MD, PhD (Karolinska Institute, Sweden) – 1 subject enrolled
Mardik Donikyan, DO (CliniLabs Drug Development Corporation) – no subject enrolled</td></tr>
<tr><td colspan="3">Publication (references): Not applicable</td></tr>
<tr><td colspan="2">Study Period:
First subject in:
• First Subject Screened: 19 Apr 2018
• First Subject Dosed: 30 May 2018
• Last Subject Out: 06 Feb 2019</td><td>Study development phase:
Phase 1b</td></tr>
<tr><td colspan="3">Objectives:
<u>Primary:</u>
• To evaluate target engagement of CT1812 treatment by measuring the displacement of Aβ oligomers into cerebrospinal fluid (CSF).
<u>Secondary:</u>
• To evaluate the effect of CT1812 on plasma and CSF proteomics and biomarkers known to be affected in Alzheimer's disease (AD) patients through measurement of CSF amyloid beta (Aβ)40, Aβ42, tau, phospho-tau, neurogranin, neurofilament light (NFL) and synaptosome-associated protein 25 (SNAP25).
• To evaluate the pharmacokinetics (PK) of CT1812 through measurement of plasma and CSF concentrations of CT1812 in AD patients.
• To evaluate the safety and tolerability of CT1812 in AD patients.
<u>Exploratory:</u>
To correlate cognitive measures at screening with CSF oligomer concentrations collected at baseline.</td></tr>
<tr><td colspan="3">Methodology:
This was a Phase 1b clinical trial conducted in patients with mild to moderate AD. The safety, efficacy, PK and pharmacodynamics (PD) of CT1812 delivered as an oral capsule was evaluated using a randomized, double-blind, placebo-controlled, parallel-group trial design.</td></tr>
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Name of Active Ingredient: CT1812		

Eligible patients were randomly assigned to either active or placebo treatment in a 2:1 ratio. The study drug was administered in the clinic after all baseline procedures had been conducted.

Number of subjects included:

There were 3 subjects in total enrolled in the study. The protocol allowed for up to 18 subjects. The study was prematurely ended by decision of the Sponsor due to recruitment difficulties.

Diagnosis and main criteria for inclusion:

Males and females aged ≥ 50 years to ≤ 85 years inclusive; with a diagnosis of mild to moderate AD and at least a 6 month decline in cognitive function as documented in the medical record.

Test product:

CT1812 capsules (in the form of a hydroxypropyl methylcellulose [HPMC] capsule), each containing 177.8 mg of CT1812 fumarate salt (equivalent to 140 mg of the CT1812 free base).

Administered orally at a dose level of 560 mg (4 capsules) with approximately 240 mL of water, with or without food.

Placebo capsules containing 177.8 mg of lactose monohydrate, matching the CT1812 capsules, supplied in the same packaging.

Administered orally as 4 capsules with approximately 240 mL of water, with or without food.

Duration of treatment:

Each subject and caregiver or study partner participated in a screening period of up to 42 days, followed by a confinement period of approximately 2 days (including a double-blind, placebo-controlled treatment period of 1 day) and a 24 hour follow up phone call. The total duration of subject participation in the study was up to 44 days including screening.

Criteria for evaluation:

Pharmacodynamic Endpoints:

- Effect of CT1812 on Aβ40 and Aβ42 in plasma.
- Change from baseline in CSF Aβ oligomer concentration.
- Effect of CT1812 on the following biomarkers in CSF: total-tau, phospho-tau, Aβ40, Aβ42. The following potential biomarkers were not analyzed: neurogranin, NFL and SNAP25.

Pharmacokinetic Endpoints:

- CT1812 PK parameters measured in plasma and CSF.

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Safety Endpoints:

- The incidence and severity of adverse events (AE)
- The incidence of serious adverse events (SAE)

Changes in safety assessments including vital signs, physical and neurological exam findings, electrocardiogram (ECG) findings, clinical laboratory testing (serum chemistry, hematology, urinalysis), Columbia Suicide Severity Rating Scale (C-SSRS).

Statistical Methods:

Refer to the protocol for planned statistical methods.

There were no interim analyses, since fewer than 6 subjects were enrolled.

Results:

Safety:

There were no deaths. No subjects were withdrawn from the study due to treatment-emergent AEs (TEAEs). One subject (CT1812) had SAEs of nausea/vomiting and headache, both severe and both deemed unlikely related to study medication, but related to lumbar puncture procedure.

Treatment-emergent AEs were reported for all 3 subjects (100%) following dose administration with CT1812 or placebo, with a total of 11 TEAEs.

Most TEAEs were classified as mild (9 of 11, 82% of all TEAEs) in severity, with no TEAEs classified as moderate in severity, and 2 TEAEs (18% of all TEAEs) classified as severe, as noted above. The only TEAE reported in more than 1 subject who received CT1812 was headache.

No TEAEs reported in subjects who received CT1812 were deemed to be related (possibly) to study drug, only in the 1 subject who received placebo. The 3 treatment-related TEAEs in the 1 subject who received placebo were of mild severity.

There was one AE (mild, unlikely related to study drug) of procedure related coloured CSF in one subject (placebo) on Day 2.

There were no TEAEs arising from vital signs, ECGs, physical examinations, C-SSRS, or clinical laboratory assessments of blood and urine.

PD/PK:

Evaluation of PD/PK is provided separately, attached as appendix documents to this abbreviated clinical study report.

Conclusion:

Overall, CT1812 was generally well tolerated when delivered as a single dose of 560 mg in subjects with mild to moderate Alzheimer's Disease.

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Date of version report: Final v1.0, 28 Oct 2021		

3 DISCUSSION AND OVERALL CONCLUSIONS

This study was a Phase 1b, single dose randomized, double-blind, placebo-controlled, parallel-group study of CT1812 in patients with mild to moderate AD.

There were 3 subjects in total enrolled in this study, of whom 2 received CT1812 at a dose level of 560 mg, and 1 received placebo.

No evaluations were performed of efficacy. Evaluations of PK and PD data are presented separately.

PK evaluation

As indicated in the PK report, CT1812 drug exposure levels were measured for patients given CT1812 and AUC, C_{max}, and $t_{1/2}$ were determined as appropriate. Results indicate that CT1812 drug exposure levels were detected in both plasma and CSF in all post-dose plasma and CSF draws in patients treated with CT1812. PK analysis of pre-dose CSF and plasma were below quantitation for patients given CT1812.

PD evaluation

As indicated in the PD reports in, a time-dependent increase in CSF Aβ oligomer levels, was observed in both patients given CT1812, but not placebo; a finding supported through the use of two independent methodologies (MIE and western blot). In contrast, Aβ 1-40 and 1-42 (measured via ELISA) monomer measurements showed increases in patients irrespective of treatment (drug or placebo) given. Combined with PK data, this supports that acute measurement of CSF Aβ oligomers following a single dose administration of CT1812 may be used as a PD biomarker for CT1812. Further, the fact that this treatment-related increase was selective to AβO and not observed with monomeric Aβ is supportive of CT1812's mechanism of action that has been elaborated preclinically.

Safety and Tolerability Conclusions

There were no deaths. No subjects were withdrawn from the study due to TEAEs. One subject (CT1812) had SAEs of nausea/vomiting and headache, both severe and both deemed unlikely related to study medication, but related to the lumbar puncture procedure. All other AEs were mild in severity.

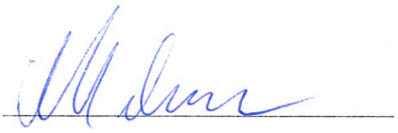
The only TEAE reported in more than 1 subject who received CT1812 was headache.

Overall, CT1812 was generally well tolerated in mild to moderate AD patients when delivered as a single dose of 560 mg.

4 Reason for premature ending of the trial

There were 3 subjects in total enrolled in the study. The protocol allowed for up to 18 subjects (3 sites opened). The study was prematurely ended by decision of the Sponsor due to recruitment difficulties.

Signature Sponsor or Sponsor's Representative:



03. Nov 2021

Name, Signature

Date

Dr. Nikola Helmberg

CEO NeuroScios GmbH