Cognition Therapeutics, Inc.
2500 Westchester Avenue Suite 220
Purchase, NY 10577
412-481-2210

Protocol COG0108

Official Title: A Phase 1, Open-Label Study to Assess the Absorption, Metabolism, Excretion, and Mass Balance of a Single Oral Dose of [14C]-CT1812 in Healthy Adult Male Subjects

ClinicalTrials.gov ID (NCT number): NCT05225389

Document: Statistical Analysis Plan

Document Approval Date: 25January2022

ANALYTICAL PHASE PLAN

A Quantitative Determination of CT1812 and [redacted]M6 in Human Plasma (K_2EDTA) by LC-MS/MS

Version 01

PHARMARON ABS STUDY NUMBER:	**234812-21M051**
CLINICAL PROTOCOL NUMBER:	**COG0108**

TABLE OF CONTENTS

1. INTRODUCTION 4
2. MATERIALS 4
3. RECEIPT AND STORAGE OF SAMPLES AND STANDARDS 4
4. STUDY BLINDING 4
5. INCURRED SAMPLE REANALYSIS 5
6. RUN ACCEPTANCE CRITERIA 5
7. DATA TRANSFER 5
8. EXPEDITED REPORTING 5
9. REPORTING 5
10. REGULATORY COMPLIANCE 5
11. ARCHIVE 6

TABLES AND APPENDICES

Table 1: Sample Details 4
APPENDIX 1: STUDY RECORDS TO BE RETAINED 7
APPENDIX 2: ABBREVIATIONS 8
APPENDIX 3: DOCUMENT HISTORY 9

SAMPLE ANALYSIS PLAN APPROVAL PAGE

Study Title:	A Quantitative Determination of CT1812 and [redacted] M6 in Human Plasma (K_2EDTA) by LC-MS/MS
Test Site:	Pharmaron ABS Inc, 20316 Seneca Meadows Parkway, Germantown, MD 20876, United States of America
Pharmaron ABS Study Number:	[redacted]
Protocol ID:	COG0108
Approved by Pharmaron ABS Lead Scientist:	[redacted]
Acknowledged by Pharmaron ABS Management:	
Reviewed by Pharmaron ABS Manager, Quality Assurance:	
Approved by Sponsor Name:	
2500 Westchester Ave Purchase, NY 10577	

1. INTRODUCTION

A clinical study is performed at Celerion located at 621 Rose St., Lincoln, Nebraska 68052, USA (hereafter referred to as the Clinic) according to clinical protocol COG0108. The study proposed herein is a A Phase 1, Open-Label Study to Assess the Absorption, Metabolism, Excretion, and Mass Balance of a Single Oral Dose of [^{14}C]-CT1812 in Healthy Adult Male Subjects.

The proposed dose level is 300 mg CT1812 with a microtracer dose of ~1 μCi [^{14}C]-CT1812. A total of 8 healthy subjects will be enrolled in the study. Blood samples for the determination of CT1812 and [redacted]M6 and concentrations and corresponding pharmacokinetic (PK) analysis will be collected at the following time points: at 0 (predose), 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24, 36, 48, 72, 96, 120, 144, and 168 hours post dose.

CT1812 and [redacted]M6 quantification in plasma will be performed using the validated method (234M001) in study 234812-21M049. Plasma sample analysis will be performed as per Pharmaron ABS SOP SMB-003.

2. MATERIALS

The laboratory equipment, material and reagent to be used are described in the plasma analytical method 234M001 under this study.

3. RECEIPT AND STORAGE OF SAMPLES AND STANDARDS

Samples will be received frozen from the Clinic packed with dry ice. All samples will be shipped with a sample manifest (paper copy) and an electronic version will be provided in Excel format.

Sample details, including storage conditions, are outlined in Table 1. Submitted samples should be obtained from human subjects certified to be free of infective agents. The Clinic should notify Pharmaron ABS when the samples are shipped. Any special storage, handling or processing conditions should be notified to Pharmaron ABS.

Table 1: Sample Details

Part	Expected Sample Number*	Storage Conditions
1	[redacted]	-70ºC

*- Expected sample number may change and will be detailed in the final analytical report.

Reference standards were received from the Sponsor during the method development phase (Study number 234812-21M048) and are detailed in Analytical Method (234M001).

4. STUDY BLINDING

This is a non-randomized, open-label study. Randomization and blinding will not occur.

5. INCURRED SAMPLE REANALYSIS

The reproducibility of the bioanalytical method will be determined in human samples originating from clinical study by reanalysis of at least 10% of the total samples for first 1000 samples and a minimum of 5% of the remaining study samples.

Should repeat analysis be required for analytical reasons this will be documented and performed before the sample is used for the ISR assessment.

6. RUN ACCEPTANCE CRITERIA

For analytical run to be considered acceptable, calibaration curve and quality control (QC) samples should be meet the acceptanc criteria.

For calibration curve, the accuracy of at least 75% of the included non-zero calibration standards must be within 15% of nominal back-calculated concentration and 20% at LLOQ concentration.

For quality control sample acceptance criteria, the accuracy of at least 2/3rd of total QC samples should dbe within 15%. In addition, the accuracy of at least 50% of QC samples at each concentration level (LQC, MQC and hQC) should be within 15%.

7. DATA TRANSFER

Data transfer file will only be sent to the designated person identified by the Clinic if any information relating to blinding is included.

8. EXPEDITED REPORTING

If an anomalous result is obtained, that in Pharmaron ABS's best judgment may have a safety implication, Pharmaron ABS shall immediately inform the Sponsor. The Sponsor shall be responsible for deciding if there is a safety issue and whether the issue must be notified to the competent authority.

9. REPORTING

Summary data will be provided in Excel format, using 3 significant figures, concentration units of ng/mL and uploaded to the Client. The following will be reported.

- CT1812 and [redacted]M6 concentrations in plasma
- Incurred sample reanalysis of plasma samples

A detailed Analytical Report of this study will be written. The report will be provided in the Pharmaron ABS format.

10. REGULATORY COMPLIANCE

The study will be conducted according to the relevant sections of:

- GCP guidelines ICH Topic E6 (R2)
- The current guidance's of the FDA and other applicable regulatory agencies
- The compliance of all applicable federal, state and local laws, rules, regulations, guidelines and industry standards

All procedures will be performed according to Pharmaron ABS Standard Operating Procedures (SOPs) which are designed to comply with FDA Good Laboratory and ICH Good Clinical Practices. The study will be subject to Quality Assurance evaluation by Pharmaron ABS Quality Assurance Unit in accordance with SOPs. Changes to this Analytical Phase Plan will be made by means of an amendment agreed upon by the Sponsor. All deviations will be documented in the study records and, where appropriate, detailed in the Final Analytical Report.

11. ARCHIVE

All records will be retained in compliance with Pharmaron ABS procedures for five years. At the end of this retention period, the sponsor will be contacted to determine record disposition. Records include, all primary data or authenticated copies thereof, the Pharmaron ABS Analytical Phase Plan (plus amendments) and the Pharmaron ABS Final Analytical Report (plus amendments). A list of study records to be maintained is detailed in APPENDIX 1.

Primary samples (those initially supplied by the Sponsor or CRO) and reference standards will be retained until the issue of the Final Analytical Report. After this time, the Sponsor will be contacted for advice on disposal or return of samples at the Sponsor's cost.

APPENDIX 1: STUDY RECORDS TO BE RETAINED

Pharmaron ABS Analytical Plan and Amendment(s)*

Pharmaron ABS Final Analytical Report and Amendment(s)*

File Note(s)*

Primary data

Equipment and calibration records

Master Schedule

Study correspondence

Sponsor correspondence

Sample submission form

Laboratory records

Sample storage records

Records for reagents and stock solutions

Data analysis

Quality Assurance reports

*Where appropriate

APPENDIX 2: ABBREVIATIONS

DQC	Dilution quality control
EDTA	Ethylenediaminetetraacetic acid
GCP	Good clinical practice
GLP	Good laboratory practice
HQC	High quality control
HPLC	High performance liquid chromatography
INT	Intermediate
IS	Internal standard
LC-MS/MS	Liquid chromatography with tandem mass spectrometry
LLOQ	Lower limit of quantification
LQC	Low quality control
MPA	Mobile phase A
MPB	Mobile phase B
MQC	Medium quality control
MRM	Multiple reaction monitoring
N/A	Not Applicable
QC	Quality control
SOP	Standard operating procedure
STD	Standard
ULOQ	Upper limit of quantification
SS	System Suitability
S/N	Signal to Noise ratio

APPENDIX 3: DOCUMENT HISTORY

EFFECTIVE DATE	LEAD SCIENTIST	VERSION	CHANGE CONTROL LOG
Refer to the Lead Scientist's Signature	[redacted]	01	Original version