STATISTICAL ANALYSIS PLAN FOR PROTOCOL EIP19-NFD-401

VERSION: 1
DATE OF PLAN:

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STUDY DRUG:

Neflamapimod

PROTOCOL NUMBER:

EIP19-NFD-401

STUDY TITLE:

A Double-Blind, Placebo-Controlled Two-Period 10-Week Treatment Within-Subject Crossover Study Of Cognitive Effects Of Neflamapimod in Early-Stage Huntington Disease (HD)

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SIGNATURE PAGE

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TABLE OF CONTENTS

LIST OF TABLES

1. LIST OF ABBREVIATIONS

Table 1: List of Abbreviations

Abbreviation	Definition
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BID	bis in die (twice a day)
CANTAB	Cambridge Neuropsychological Test Automated Battery
CRF	Case report form
CRF	Case report form
C-SSRS	Columbia-Suicide Severity Rating Scale
ECG	Electrocardiogram
FDA	Food and Drug Administration
GGT	Gamma-Glutamyl Transferase
HD	Huntington's Disease
ICH	International Council for Harmonization
LDH	Lactate dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
MOT	Motor Screening Task

MWM	Morris Water Maze
OTS	One Touch Stockings of Cambridge
PAL	Paired Associate Learning
PCS	Potentially Clinically Significant
PRM	Pattern Recognition Memory
RTI	Reaction Time
SAE	Serious Adverse Event
SD	Standard Deviation
SRM	Spatial Recognition Memory
SS	Spatial Span
TEAE	Treatment Emergent Adverse Event
TFC	Total Functional Capacity
UHDRS	Unified Huntington's Disease Rating Scale

2. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and data displays to be included in the Clinical Study Report (CSR) for Protocol EIP19-NFD-401, Version 2.0, 20 March, 2019.

This SAP is a more detailed companion to the Statistical Methods section of the study protocol and provides a comprehensive description of the analysis data sets, efficacy endpoints, assumptions, how missing data will be handled, as well as details on statistical methods will be used to analyze the safety and efficacy data. When differences exist in descriptions or explanations provided in the protocol and this analysis plan, the SAP prevails. The document may evolve over time; for example, to reflect the requirements of protocol amendments or regulatory requests. The final SAP will be finalized, approved by the Sponsor, and placed on file before database is locked. Deviations from the final approved plan will be noted in the clinical study report.

3. STUDY OBJECTIVES

3.1. Primary Objective

To evaluate the effects of administration of neflamapimod on hippocampal function, as assessed in the virtual Morris Water Maze (MWM).

3.2. Secondary Objectives

- To evaluate the effects of neflamapimod on the Cambridge Neuropsychological Test Automated Battery (CANTAB) paired associates learning task.
- To evaluate effects of neflamapimod on a larger battery of parameters in the CANTAB.
- To evaluate tolerability and safety of neflamapimod in subjects with Huntington Disease (HD).

3.3. Exploratory Efficacy and Safety Objectives

In addition, exploratory analyses of the full set of parameters in the CANTAB will be conducted and exposure to safety relationship will be investigated if data allow.

4. STUDY DESIGN

This is a Phase 2a, single centre, randomized, double-blind, placebo- controlled, 2-period within-subject crossover proof-of-principle study of neflamapimod 40 mg or matching placebo administered twice daily (BID) for 10 weeks in subjects with Stage 1 HD.

Following completion of informed consent procedures, subjects will enter the Screening phase of the study.

One screening visit is planned within 21 days before baseline (Day 1), during which time safety screening measures and initial assessments, including CANTAB will be undertaken and subject eligibility will be confirmed.

Once eligibility is confirmed and before the first dose of study drug, subjects will be randomly assigned on a 1:1 basis to placebo or neflamapimod treatment during the first treatment period (i.e., 8 subjects will receive neflamapimod and 8 will receive placebo during the first treatment period). Investigators and subjects will be blinded to the treatment assignment.

Dosing will start on Day 1 following completion of all baseline procedures, which will include virtual Morris Water Maze (MWM) and CANTAB tests.

During the treatment period, subjects will return to the clinic every 2 weeks.

At Weeks 4 and 10 of the first treatment period, the virtual MWM and CANTAB tests will be repeated.

All subjects will return for a safety visit 2 weeks after stopping drug in the first treatment period.

After at least 8 weeks (and up to 12 weeks) after completion of the first treatment period, subjects will return to the clinic and after repeating virtual MWM and CANTAB, will resume blinded treatment; all subjects who received placebo capsules during the first treatment period will receive neflamapimod, while those who received neflamapimod will receive placebo capsules during this second treatment period.

At the end of Weeks 4 and 10 of the second treatment period, the virtual MWM and CANTAB tests will be repeated.

A Final Study Visit will be conducted 2 weeks after completion of the second treatment period.

4.1. Sample Size Justification

No formal sample size calculation was performed. A sample size of 16 subjects is considered appropriate for determination of the preliminary safety and tolerability of neflamapimod in this subject population.

4.2. Study duration and visit schedule

The study duration is 28 to 32 weeks (10 weeks of 1st treatment period + washout period (8-12 weeks) +10 weeks of 2nd treatment period). Complete descriptions of the assessments to be performed at each visit are listed in Table 2.

Table 2: Schedule of Assessments

	Screening[a]	Treatment Period 1						Washout (8 to 12 weeks)	Treatment Period 2						ET Visit[c]	Final Study Visit[d]
Evaluation	**Within 21 days of D1**	**W0[b]**	**W2 (±3)**	**W4 (±3)**	**W6 (±5)**	**W8 (±5)**	**W10 (±3)**	**2 wks (±3 d) of last dose in Period 1**	**W0[b]**	**W2 (±3)**	**W4 (±3)**	**W6 (±5)**	**W8 (±5)**	**W10 (±3)**	**Within 3 d after last dose**	**2 wks (±3 d) of last dose**
Informed Consent	X[e]															
Medical history review	X															
Pregnancy testing	X[f]	X		X		X			X		X		X			X
Physical examination[g]	X						X		X					X	X	X
C-SSRS	X						X		X					X		
Hospital Anxiety and Depression Scale	X			X			X		X		X			X		
UHDRS	X						X		X					X		
CANTAB	X	X		X			X		X		X			X	X	
MWM	X	X		X			X		X		X			X	X	
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Prior/concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events recording[h]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology and chemistry[i]	X	X		X		X		X	X		X		X			X

Evaluation	Screening[a]	Treatment Period 1						Washout (8 to 12 weeks)	Treatment Period 2						ET Visit[c]	Final Study Visit[d]
	Within 21 days of D1	W0[b]	W2 (±3)	W4 (±3)	W6 (±5)	W8 (±5)	W10 (±3)	2 wks (±3 d) of last dose in Period 1	W0[b]	W2 (±3)	W4 (±3)	W6 (±5)	W8 (±5)	W10 (±3)	Within 3 d after last dose	2 wks (±3 d) of last dose
Coagulation studies[i]	X			X				X			X					X
12-lead electrocardiogram[j]	X															
Dispense study drug[k]		X	X	X	X	X			X	X	X	X	X			
Final study drug reconciliation							X							X	X	

CANTAB= Cambridge Neuropsychological Test Automated Battery; C-SSRS: Columbia-Suicide Rating Scale; D=Day; ET = End-of-Treatment; MWM=Morris Water Maze; UHDRS= Unified Huntington's Disease Rating Scale; W=Week.

a. All screening assessments should be conducted within 21 days of Day 1.
b. At Week 0 of each treatment period, all procedures should be conducted prior to first dose of study drug.
c. Subjects who prematurely discontinue study drug for any reason will be asked to return to the clinical site for an Early Termination visit within 3 days following the last study drug dose; if it is determined that the subject will discontinue study drug while at the study center for a scheduled visit, then the Early Termination visit should be conducted at that time.
d. The Follow-up Visit should be conducted within 2 weeks (±3 days) of the last dose of study drug for subjects who complete the study or discontinueearly.
e. Informed consent procedures, including signing of informed consent, must be completed before any study-specific procedures are performed.
f. Female subjects of child-bearing potential or who have reached menopause in the previous year must have a serum or urine pregnancy test performed during Screening, Week 0, every 4 weeks during the 1st and 2nd treatment periods, and at the Follow-up Visit; subjects with positive results are not eligible for study participation.
g. Refer to Section 6.2.7 of the study protocol for details regarding physical examination.
h. Definitions and procedures for documenting and reporting AEs serious adverse events (SAEs) are provided in Section 7 of the study protocol.
i. Details of clinical laboratory sampling for chemistry, hematology, and coagulation studies are discussed in Section 6.2.9 of the study protocol.
j. Details of 12-lead ECG assessment are discussed in Section 6.2.8 of the study protocol.
k. Study drug details including packaging, storage, accountability, and dosing are presented in Section 5 of the study protocol.

5. CLINICAL ASSESSMENTS

5.1. Baseline and Disease Characteristics

Details regarding HD history will be collected during Screening, as specified in the CRF.

5.2. Efficacy Assessments

5.2.1. Morris Water Maze Test

The MWM test is used to assess hippocampal-dependent spatial learning and memory (Morris, 1984). A virtual-reality version of MWM test is to be administered at the time points specified in Table 2. This task is a human analogue of the classic MWM task commonly used in rodent studies. Patients were told to navigate through a virtual 3-dimensional pool presented on the screen using a joystick. The goal of the test is to find and remember the location of a hidden platform, using visual cues placed on the walls. Patients have a first-person view point with a field of view comparable to the human eye.

5.2.2. CANTAB

The CANTAB battery was developed for the assessment of cognitive deficits in humans with neurodegenerative diseases or brain damage. It consists of a series of interrelated computerized tests of memory, attention, and executive function, administered via a touch-sensitive screen (Fray and Robbins, 1996). Specifically, CANTAB tests include:

- Motor Screening Task: 2 minutes
- Reaction Time: 3 minutes
- Paired Associates Learning: 8 minutes
- One Touch Stockings of Cambridge: 10 minutes
- Spatial Span: 5 minutes
- Spatial Recognition Memory: 5 minutes
- Pattern Recognition Memory: 4 minutes

The CANTAB is to be administered at the time points specified in Table 2.

CANTAB Motor Screening Task (MOT):

The MOT serves as a general introduction to the CANTAB battery and provides a general assessment of whether sensorimotor deficits or lack of comprehension, will limit the collection of valid data from the participant. Coloured crosses are presented in different locations on the screen, one at a time. The participant must select the cross on the screen as quickly and accurately as possible.

CANTAB Reaction Time (RTI):

RTI provides an assessment of motor and mental response speeds, as well as measures of movement time, reaction time, response accuracy and impulsivity. The participant must select and hold a button at the bottom of the screen. Circles are presented above (one for the simple mode, and five for the five-choice mode.) In each case, a yellow dot will appear in one of the circles, and the participant must react as soon as possible, releasing the button at the bottom of the screen, and selecting the circle in which the dot appeared.

CANTAB Paired Associate Learning (PAL):

During the PAL, participants are required to remember the locations of a number of different objects which are hidden inside boxes on the computer screen. This task requires the participant to learn to pair two items in memory - in this case the type of object and the location of the object. When one of the paired features is revealed (in this case the object), the participant is asked to remember its associate (the location it is hidden in). This type of learning is essential in everyday life, for example when learning new words. When you learn a new word, not only do you learn the word itself, but you have to pair this with the meaning it represents

CANTAB Spatial Span (SS):

SS tests spatial memory span by measuring ability to memorize the order in which an increasing number of white boxes change color. The spatial span task relies on visuospatial working memory; the component of working memory that allows you to temporarily hold and manipulate information about places. Many everyday activities involve visuospatial working memory, including finding your way around your environment, judging the position of other motorists while you are driving and searching for your keys. According to one very influential cognitive model of working memory (Badderly & Hitch, 1974) visuospatial working memory depends on a specialized sub-component of the working memory system. This is referred to as the "visuospatial sketchpad" and is thought to have a visual "cache", responsible for storing visual form and color information, and an "inner scribe" which deals with spatial and movement information. This task places significant demands on the inner scribe.

CANTAB One Touch Stockings of Cambridge (OTS):

Executive functions are a set of cognitive skills that help us to regulate the other mental processes that are necessary to complete everyday activities. They allow us to produce complex goal directed thoughts and behaviors such as planning future events, carrying out tasks with multiple stages and overcoming habitual responses. Executive functions provide us with the ability to dynamically adjust and regulate behavior on the basis of internal representations and external feedback. The OTS measures the executive functions of spatial planning and working memory ability. The patient is shown two displays containing three colored balls, presented so they can be perceived as stacks of colored balls in stockings. In each trial, the patient must imagine moving the balls in the lower display to copy the pattern shown in the upper, and calculate how many 'moves' this would take. Planning ability is indexed by the number of problems solved at the first attempt at each level of difficulty. The OTS will be used in this study to determine whether performance on the sociality experiments has any relationship to deficits in executive function in HD.

CANTAB Spatial Recognition Memory (SRM)

The SRM is a test of spatial recognition memory and is linked to frontal lobe function (Owen et al, 1995). In the encoding phase, participants are shown a series of white squares which are presented at different locations on a black screen and instructed to remember where each square appears. In the recognition phase participants are shown two squares, in different locations, and ask to identify the one that is in the same place as one they have been shown previously. Spatial recognition memory is index by the percentage of placements correctly distinguished from distractor placements.

CANTAB Pattern Recognition Memory (PRM)

The PRM is a test of visual recognition memory and is linked to hippocampal function (Owen et al, 1995). In the encoding phase, participants are shown with a series of abstract line drawings presented one at a time in the centre of a blank screen. They are instructed to remember the patterns. During the recognition phase, two abstract line drawings are presented on the screen, side by side and participants are asked to identify the one they have previously been shown. Visual recognition memory is indexed by the percentage of patterns correctly distinguished from novel distractors.

5.3. Other Clinical Assessments

5.3.1. Columbia-Suicide Severity Rating Scale

T The C-SSRS is a clinician-administered instrument that assesses suicidal ideation and behavior (Posner et al, 2011). The "Baseline" version of the instrument will be administered to subjects during Screening and before beginning the second treatment period, and the "Since Last Visit" version will be used at all other time points specified in Table 2.

5.3.2. Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale is a 14-item self-assessment scale designed to determine the degree of anxiety and depression a patient is experiencing (Zigmond, Snaith, 1983). Each item on the questionnaire is scored from 0-3; thus, total scores range from 0 and 21 for either anxiety or depression. The Hospital Anxiety and Depression Scale is to be completed at the time points specified in Table 2.

5.3.3. Unified Huntington's Disease Rating Scale

The UHDRS was developed as a clinical rating scale to assess 4 domains of clinical performance and capacity in HD: motor function, cognitive function, behavioral abnormalities, and functional capacity (Huntington Study Group, 1996).

- The **motor section** of the UHDRS assesses motor features of HD with standardized ratings of oculomotor function, dysarthria, chorea, dystonia, gait, and postural stability. A demonstration of the techniques of the motor exam and examples of each grade of abnormality are provided on the accompanying videotape. The total motor impairment score is the sum of all the individual motor ratings, with higher scores indicating more severe motor impairment than lower scores.

- **Cognitive operations** are assessed by a phonetic verbal fluency test, Symbol Digit Modalities Test, and the Stroop Interference Test. The Stroop Test results are reported as the raw number of correct answers given in a 45-second period. Results for the other tests are reported as the raw number of correct responses. Higher scores indicate better cognitive performance.
- The **behavioral assessment** measures the frequency and severity of symptoms related to affect, thought content and coping styles. The total behavior score is the sum of all responses; however, this score may have less usefulness than the individual subscale scores for mood, behavior, psychosis, and obsessiveness which are created by summing the responses to the corresponding questions. The evaluator is also requested to provide a clinical impression as to whether the patient, at the time of the evaluation, has clinical evidence of confusion, dementia, or depression and whether the patient requires antidepressant therapy, according to preset definitions in the examination guidelines. Higher scores on the behavior assessments indicate more severe disturbance than lower scores.
- The **functional assessments** include the HDFCS, the Independence scale, and a checklist of common daily tasks. For the latter items, the investigator indicates if the patient could perform the task. The checklist is summed by giving a score of 1 to all "yes" replies. The HDFCS is reported as the total functional capacity (TFC) score. The independence scale is rated from 0 to 100, with higher scores on the function scales indicating better functioning than lower scores.

The UHDRS is to be administered at the time points specified in Table 2. Note that at Week 4 in each treatment period, only the motor module need be administered.

5.4. Physical Examination and Vital Signs

Physical examination will include a review of all body systems and measurement of weight, per each Investigators standard practice. Physical examination findings will be documented in the subject's source documents.

Vital signs include measurement of blood pressure, pulse, respiratory rate, and body temperature.

Any physical examination finding or vital sign measurement that represents a worsening from Baseline condition and is considered by the Investigator to be clinically significant will be recorded as an AE. The timing of assessments can be found in the schedule of assessments in Table 2.

5.5. 12-Lead Electrocardiogram

A 12-lead ECG will be performed using validated machinery available locally to each clinical site. Each report will be reviewed by the investigator for qualified sub-investigator and assessed as normal, abnormal – not clinically significant, or abnormal – clinically significant. Abnormal, clinically significant findings that represent a worsening from Baseline will be recorded as an adverse event.

5.6. Clinical Laboratory Assessment

Two blood samples will be collected at the time points specified in Table 2 for assessment of routine chemistry and hematology analytes. One additional blood sample will be collected for coagulation studies at the time points specified in Table 2. Clinical laboratory findings that represent a worsening from Baseline value and are considered by the investigator to be clinically significant will be recorded as an adverse event. Table 3 lists the analytes from routine chemistry, hematology and coagulation studies. Clinical laboratory findings that represent a worsening from Baseline value and are considered by the investigator to be clinically significant will be recorded as an adverse event.

Table 3: Clinical Laboratory Analytes

Serum Chemistry	**Hematology**
Albumin	Differential (absolute and percent):
Alkaline Phosphatase	Basophils
Alanine Aminotransferase (ALT)	Eosinophils
Aspartate Aminotransferase (AST)	Lymphocytes
Bilirubin (total and direct)	Monocytes
Glucose	Neutrophils
Blood Urea Nitrogen	Erythrocytes:
Calcium	Mean corpuscular hemoglobin (MCH)
Bicarbonate	Mean corpuscular hemoglobin concentration (MCHC)
Chloride	Mean corpuscular volume (MCV)
Total cholesterol	Hemoglobin
Triglycerides	Leukocytes
Creatinine	Platelets
Gamma-Glutamyl Transferase (GGT)	**Coagulation Studies**
Lactate dehydrogenase (LDH)	
Phosphate	Prothrombin time
Potassium	Partial thromboplastin time
Sodium	INR
Total protein	
Uric acid	

6. DEFINITIONS, CONVENTIONS AND DERIVED VARIABLES

6.1. Definitions and conventions

Age

The subject age (years) is calculated based on informed consent date and birth date.

Baseline

Baseline is defined as the measurement prior to first dose of study medication at study Day 1 of each period. If for any parameter the study Day 1 pre-dose value is not done or missing, then the value obtained at a Screening visit is used as Baseline.

Concomitant medication

Concomitant medications are defined as any medications ongoing at the start of treatment or with a start date and time on or after the date of first study medication dose at study Day 1 through the end of study. A single medication may be prior, concomitant and post-treatment. (See also prior medication and post-treatment medication in this section)

Informed consent date

Informed consent date is determined by the corresponding field in the database.

Missing Medication Dates

Medications with missing or partial start dates will be classified to any medication assignment that the available information allows. Should a stop date exist, the stop date will be taken into account. For example, if a medication has a missing start date, but the stop date is prior to first dose date, the medication will only be classified as prior. However, if a medication has a missing start date and the stop date occurs on the last day of treatment, the medication will be classified as prior and concomitant. Similarly, partial starts will use the available data to aid in the classification.

If the stop date is missing or ongoing, the medication will be classified based on the start date and then to all subsequent assignments. If there is partial stop date information, the available data will be used to aid in the classification.

Post-treatment medication

A post-treatment medication is defined as any medication ongoing or with a start date and time after the last day of treatment. A single medication may be prior, concomitant and post-treatment. (See also prior medication and concomitant medication in this section)

Prior medication

Prior medications are defined as any medications taken prior to first dose of study medication at the beginning of the study. A single medication may be prior, concomitant, and post-treatment.

6.2. Derived Variables

6.2.1. Change from Baseline at each treatment period

Change from baseline at each treatment period is defined as the post-baseline value minus the baseline value at each period.

6.2.2. Treatment Difference of Change from Baseline within Subject Between Periods

The treatment difference for a subject is change from baseline at the neflamapimod treatment period minus the change from baseline at the placebo treatment period within the same subject.

7. ANALYSIS POPULATIONS

7.1. Safety Population

The safety population is defined as all randomized subjects who receive at least 1 dose of study drug neflamapimod .

7.2. Evaluable Efficacy Population (EEP) Population

The Evaluable Efficacy Population (EEP) population will be all subjects who have both a baseline and at least one on-study assessment of the efficacy parameter (CANTAB battery and/or MWM) being evaluated.

7.3. Completer Population (CP)

The Completer Population will be subjects who have completed both periods of on-study assessment of the efficacy parameter (CANTAB battery and/or MWM) being evaluated.

8. DATA MANGEMENT, REVIEW AND PREESENTATION

8.1. Data Management and Quality Assurance Considerations

This study will employ case report forms (CRFs). The site will be trained on specific forms and procedures for source documentation and maintenance of an audit trail of the data that is entered on the CRF prior to study initiation.

Study personnel at each site will enter data from source documents corresponding to a subject's visit onto the protocol-specific CRF when the information corresponding to that visit is available.

The Investigators will prepare and maintain adequate and accurate source documents designed to record all observations and other pertinent data for each subject treated with the study drug.

The Investigator is responsible for all information collected on subjects enrolled in this study. All data collected during the course of this study must be reviewed and verified for completeness and accuracy by the Investigator.

Subjects and site personnel associated with study conduct will be blinded to treatment assignment. Treatment codes will be provided in sealed envelopes to the site and will be stored by the pharmacist or designee.

During the conduct of the study, the blind should be broken on an individual subject basis in the event of an emergency where it is necessary for the Investigator to know which treatment the subject is receiving before the subject can be treated. The code may also be broken if someone not in the study uses study drug (e.g., if a child in the participant's household takes study drug, the blind may be broken to determine treatment for the child.)

Queries will be issued for any inconsistencies, omissions, and discrepancies and will be resolved by the appropriate parties.

Database lock will occur once quality assurance procedures have been completed.

All AEs will be coded using the latest version of the Medical Dictionary for Regulated Activities (MedDRA). Concomitant medications will be coded using the latest version of the World Health Organization Drug Dictionary.

All procedures for the handling and analysis of data will be conducted using good computing practices meeting United States Food and Drug Administration (FDA), European Medicines Agency, and ICH guidelines for the handling and analysis of data for clinical studies. Data management details will be outlined in a separate data management plan.

8.2. Data Presentation

The data will be presented in standard individual subject data listings. The listings will include subject identification number, demographics, and treatment. Selected listings will be included in the Clinical Study Report. In data summaries, descriptive statistics (n, arithmetic mean, standard deviation [SD], median, lower and upper quartiles, minimum and maximum values) will be presented for continuous variables. Counts and percentages will be presented for categorical variables.

8.3. Interim Data Review

No interim analysis is planned.

9. STATISTSICAL METHODOLOGY

All statistical analyses will be performed using S-PLUS (Version 8.2) or SAS (Version 9.3 or higher). The version employed at the study start will be maintained throughout the project.

9.1. General Statistical Methodology

Data will be tabulated by treatment group by study period, with data listings provided for all data captured in the CRF including laboratory data. On-treatment data will be assessed descriptively as both observed values and as changes from baseline. When tabulated, data will be presented using descriptive statistics. Most continuous data will be summarized with the following descriptive statistics unless otherwise noted: number of observations, mean, standard deviation, median, minimum, and maximum; interquartile ranges will be provided as appropriate. Categorical data will be summarized with frequencies and percentages.

Missing data will not be imputed unless otherwise documented in this SAP. Unless stated otherwise, statistical tests conducted will be two-sided at a level of 0.05. No adjustment for multiplicity will be made.

Paired t-test will be used to test the difference between treatments if the target metric is normally distributed (symmetrical distributed at the minimal), otherwise, the nonparametric approach - Wilcoxon signed rank test will be used.

Some exploratory endpoints may also be analyzed using analysis of covariance, t-tests, Wilcoxon sign rank test or as descriptive summaries. There will be no correction to be made for multiple comparisons because of the exploratory nature of the data. Analysis of categorical exploratory endpoints may be performed using chi-square tests.

Additional exploratory analyses may be performed to further study the effects of the treatment, as data warranted. Subgroup analyses will be performed if data permit. Subgroup can be defined by disease severity (baseline TFC score, CANTAB Paired Associate Learning or Total Adjusted Error Score), sex (male/female), age (dichotomized at pretreatment median age), race (White vs. non-White, Hispanic vs. non-Hispanic), and/or other grouping covariates.

For many variables, both absolute and percent change from pre-treatment assessments might be performed if data permitted. All data collected and captured in the CRF will be included in data listings sorted by treatment, patient, study period and time point, or as appropriate.

9.2. Presentation of Efficacy Measures

Graphical presentation:

The time-course of efficacy measures will be plotted for each subject for both periods. The change from baseline of efficacy measures by period (treatment) will be plotted via boxplot. The distribution of difference of change from baseline by treatment (neflamapimod – placebo) will be plotted either via scatter plot or boxplot.

Tabular presentation:

The individual values and descriptive statistics for efficacy measures will be summarized by period/treatment and by visit.

9.3. Subject Disposition

A tabulation of subject disposition will be presented by treatment and overall, including the number in each analysis population, the number that completed the study, the number lost to follow-up, the number that withdrew prior to completing the study, and reason(s) for withdrawal.

9.4. Protocol Deviations

Protocol deviations and violations noted during clinical monitoring are entered into clinical database. Important protocol deviations that could potentially influence study outcomes will be listed. These may include deviations from inclusion and exclusion criteria, recreational drug use, prohibited concomitant medications, incorrect treatment dosing, visit windowing deviations. Specifically, windowing deviations beyond +/- 7 days from the scheduled (target) study day will be listed in the protocol deviation data listing.

9.5. Missing Values

No imputations for missing efficacy and safety are planned.

Subjects with incomplete data will be included in analyses, contributing as much as is available for any given endpoint. For AE, missing dates will not be imputed; however, if partial dates are available, they will be used to assess whether the AE occurred during the treatment period. Missing severities of AEs will be considered in any tabulations of AE severity.

9.6. Subgroups

Subgroups may be defined by baseline disease severity , gender (male/female), age (dichotomized at pre-treatment median age), and race (White vs Non-White, Hispanic versus non-Hispanic). Some exploratory outcome analyses might be assessed by post-hoc subgroups as dictated by data.

9.7. Compliance

Study drug compliance will be assessed via tablet counts. A tabulation of percent compliance will be provided, where percent compliance will be derived as:

- Total number of tablets dispensed minus total number tablets returned, divided by the EXPECTED number of tablets (based on the number of days from first dose to last dose).
- Patients who do not have the last dose date or have missing capsule counts of study medication will not be included in this calculation of compliance.
- Patients with a compliance that is calculated to be over 100% will have their compliance set to 100%.

The number (%) of patients with compliance within each of the following intervals will be derived:

- 95-100%
- 90-<95%
- 85-<90%
- 80-<85%
- 75-<80%
- 70-<75%
- <70%

9.8. Baseline Subject Data and Disease Characteristics Analyses

For those patients missing a pre-treatment value (Day 1) for a particular parameter, the screening value may be used as the baseline value for that parameter.

Screening data, demographic characteristics, and baseline TFC disease assessments will be presented using summary statistics by treatment sequence, and overall.

Baseline categorical variables will be inferentially assessed via a chi square test, while baseline continuous outcomes will be inferentially assessed via Wilcoxon rank sum test for two treatments. Since this is a crossover study design, only period 1 baseline subject data will be analyzed in the baseline analyses between treatment groups. Medical history data will be tabulated and listed.

9.9. Efficacy Analyses

9.9.1. Primary Efficacy Analysis

The primary efficacy population will be the completer population. Due to the non-symmetrical nature of the change from baseline values, the nonparametric approach -Wilcoxon signed rank test will be used. The primary efficacy analysis will be performed on the primary efficacy endpoint: change of latency during the learning phase of virtual MWM (hidden platform training) during the neflamapimod-treatment period compared to change of that during the placebo-administration period.

Let $D_{i,j}$ denote as the difference of Week 10 value minus the baseline value for ith subject at the same Period j (neflamapimod or placebo period).

Therefore, the notation and the formula for the difference of neflamapimod period compared to placebo period in terms of change from baseline of latency for ith subject is

$$\theta_{i,d,} = D_{i,neflamapimod} - D_{i,placebo}$$

The null hypothesis is that neflamapimod has no significant drug effect on the reduction of latency; and the alternative hypothesis is that neflamapimod causes a significant reduction of latency at significance level of $\alpha = 0.05$.

Wilcoxon signed rank test is expressed in terms of median for difference. Let θ_d be the population median of difference between treatments (neflamapiod period minus placebo period), the hypotheses are:

$$H_0 : \theta_d = 0$$

$$H_a : \theta_d < 0$$

9.9.2. Analysis of the Secondary Efficacy Endpoints

The secondary efficacy variables are

- Percent of time spent in the correct quadrant during MWM probe test during the neflamapimod-treatment period compared to that during the placebo-administration period.
- Number of overall errors in the CANTAB paired associates learning (PAL) task during the neflamapimod-treatment period compared to that during the placebo-administration period.

Let the derived parameter θ_d be the population mean/median of difference of secondary efficacy parameter between treatments (neflamapimod period minus placebo period) as defined in Section 9.9.1. Paired t-test will be used to test the mean difference if the target metric is symmetrical at minimal. Otherwise, the nonparametric approach -Wilcoxon signed rank test will be used to test the median difference as Stated in Section 9.9.1. The alternative hypothesis for testing the difference of (1) percent of time spent in the correct quadrant during MWM probe is $H_a : \theta_d > 0$ and (2) CANTAB PAL is $H_a : \theta_d < 0$ at significance level of $\alpha = 0.05$.

Data will be tabulated by visit and by treatment. Additional exploratory analyses, as stated in Section 9.1, may be performed to further study the effects of the treatment given data warranted.

9.9.3. Analysis of the exploratory Efficacy Endpoints

The exploratory efficacy measures are the full set of parameters in the CANTAB assessments :

Motor Screening Task (MOT)

Reaction Time (RTI)

Paired Associate Learning (PAL)

Spatial Span (SS)

One Touch Stockings of Cambridge (OTS)

Spatial Recognition Memory (SRM)

Pattern Recognition Memory (PRM)

Descriptive analyses will be performed to describe the full set of parameters in the CANTAB assessment.

Additional exploratory and subgroup analyses, as stated in Section 9.1, may be performed to further study the effects of the treatment as dictated by data.

Question: Do you want to mentioned other Virtual MWM parameters (travel path lengths, quadrant dwell times, etc.) as exploratory efficacy endpoints here?

9.9.4. Analysis of Plasma Biomarkers

There is no biomarker analysis planned.

9.9.5. Summary of Reasons for Efficacy Non-evaluability/Exclusion from Efficacy Analyses

All non-evaluable or exclusion values from efficacy analyses will be listed and tabulated by study visit and by treatment.

9.10. Pharmacokinetic Analysis

There is no pharmacokinetic analysis planned.

9.11. Safety and Tolerability Analyses

9.11.1. General Safety Analysis Methods

Safety and tolerability will be evaluated using descriptive statistics and listings of adverse events, clinical safety laboratory test values, vital signs, weight, body temperature, ECGs and other safety parameters. Safety outcomes will be presented for the safety population.

Analyses of AEs will be performed for those events that are considered treatment emergent, where treatment emergent is defined as any AE with onset (or worsening of a pre-existing condition) after the first dose of treatment. Adverse events with partial dates will be assessed using the available date information to determine treatment-emergent status. Adverse events with completely missing dates will be assumed to be treatment emergent.

Adverse events will be summarized by visit and treatment, using subject incidence rates; therefore, in any tabulation, a subject contributes only once to the count for a given AE (preferred term) per treatment. Separate tabulations will be produced for all TEAEs, treatment-related AEs (those considered by the investigator as possibly study drug related), SAEs, and discontinuations due to AEs. By subject listings will be provided for any deaths, SAEs, and AEs leading to discontinuation of treatment.

No formal hypothesis testing of AE incidence rates will be performed.

9.11.2. Routine Laboratory Data

For placebo and neflamapimod treatment groups, the actual value and change from baseline to each on-study evaluation will be summarized for each clinical laboratory parameter. Clinically significant laboratory values may be presented in a separate data listing.

9.11.3. Vital Signs and Physical Examination

Actual values and changes from baseline to each on-study evaluation will be summarized by visit and treatment for vital signs. Physical examination findings will be tabulated and summarized by visit and treatment. The number of subjects with potentially clinically significant (PCS) changes in vital signs will be tabulated. Potentially clinically significant thresholds will be defined prior to breaking the study blind.

9.11.4. Electrocardiogram Evaluations

Electrocardiogram outcomes will be summarized descriptively by visit and by treatment. Corrected QT will be calculated using Fridericia's correction. The number of subjects with PCS changes in ECG intervals will be tabulated. The PCS thresholds will be defined prior to breaking the study blind.

9.11.5. Concomitant Medications

Concomitant medications will be summarized by World Health Organization Drug Dictionary Anatomical-Therapeutic-Chemical classification and preferred term. Concomitant medications information will be tabulated and summarized by visit and by treatment.

9.11.6. Study Termination Status

Study termination status will be tabulated and summarized by visit and by treatment.

10. REFERENCE

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11. APPENDIX

11.1. Table of Contents for Data Display Specifications

The numbering of tables, data listings, and figures will be consistent with the ICH E3 guidance.

11.1.1. List of Tables

Tables are divided into 4 sections: Study characteristics, efficacy, safety, and pharmacokinetic presentations.

- Tables in the 14.1.X series are study characteristics, i.e., patient disposition and baseline characteristics tabulations.
- Tables in the 14.2.X series are efficacy-based data.
- Tables in the 14.3.X series are safety-based data.

Title		Population
14.1 Study Population Section		
14.1.1	Summary of Subject Disposition	Randomized
14.1.2	Summary of Analysis Populations	Safety; EEP
14.1.3	Demographics and Baseline Characteristics	Safety; EEP
14.1.3.1	Summary of Demographic Characteristics	Safety; EEP
14.1.3.2	Summary of Baseline/Physical Examinations Characteristics	Safety; EEP
14.1.4	Medical History and Prior Medications	Safety
14.1.5	Major Deviations	Randomized
14.2 Efficacy Section		
14.2.1 Primary Efficacy Endpoint		EEP
14.2.1.1	Summary of Latency of Virtual MWM by Visit, by Period and by Treatment	EEP
14.2.1.2	Summary of Changes of Latency of Virtual MWM by Visit, by Period and by Treatment	EEP
14.2.1.3	Summary of difference of Changes of Latency of Virtual MWM at end of period (neflamapimod period - Placebo period)	EEP
14.2.2 Secondary Efficacy Endpoints		
14.2.2.1	Summary of percent of time spent in the correct quadrant during MWM probe test by Visit by Period and by Treatment	EEP

14.2.2.2	Summary of change of percent of time spent in the correct quadrant during MWM probe test (at end of the period - at the beginning of the period) by Period and by Treatment	EEP
14.2.2.3	Summary of difference of change of percent of time spent in the correct quadrant during MWM probe test (neflamapimod period - Placebo period)	CP
14.2.2.4	Summary of number of overall error in the CANTAB paired associates leaning task by Visit by Period and by Treatment	EEP
14.2.2.5	Summary of change of number of overall error in the CANTAB paired associates leaning task (at end of the period - at the beginning of the period) by Period and by Treatment	EEP
14.2.2.6	Summary of difference of change of number of overall error in the CANTAB paired associates leaning task (neflamapimod period - Placebo period)	CP
14.2.3 Exploratory Efficacy Endpoints		
14.2.3.1	Summary of CANTAB Motor Screening Task (MOT) by visit, by Period and by Treatment	EEP
14.2.3.2	Summary of Changes of CANTAB Motor Screening Task (MOT) by visit, by Period and by Treatment	EEP
14.2.3.3	Summary of CANTAB Reaction Time (RTI) by visit, by Period and by Treatment	EEP
14.2.3.4	Summary of Changes of Reaction Time (RTI) by visit, by Period and by Treatment	EEP
14.2.3.5	Summary of CANTAB Paired Associate Learning (PAL) by visit, by Period and by Treatment	EEP
14.2.3.6	Summary of Changes of Paired Associate Learning (PAL) by visit, by Period and by Treatment	EEP
14.2.3.7	Summary of CANTAB Spatial Span (SS) by visit, by Period and by Treatment	EEP
14.2.3.8	Summary of Changes of Spatial Span (SS) by visit, by Period and by Treatment	EEP
14.2.3.9	Summary of CANTAB One Touch Stockings of Cambridge (OTS) by visit, by Period and by Treatment	EEP
14.2.3.10	Summary of Changes of One Touch Stockings of Cambridge (OTS) by visit, by Period and by Treatment	EEP
14.2.3.11	Summary of CANTAB Spatial Recognition Memory (SRM) by visit, by Period and by Treatment	EEP
14.2.3.12	Summary of Changes of Spatial Recognition Memory (SRM) by visit, by Period and by Treatment	EEP
14.2.3.13	Summary of CANTAB Pattern Recognition Memory (PRM) by visit, by Period and by Treatment	EEP
14.2.3.14	Summary of Changes of Pattern Recognition Memory (PRM) by visit, by Period and by Treatment	EEP

14.2.3.15 - 14.2.3.xx	other Virtual MWM parameters (travel path lengths, quadrant dwell times, etc.) - TBD	EEP
14.3 Safety Data		
14.3.1	Summary of Drug Count to neflamapimod by Treatment and by Visit	Safety
14.3.2.1	Summary of Adverse Events by Treatment and by Visit	Safety
14.3.2.2	Summary of Death and Serious Adverse Events by Treatment and by Visit	Safety
14.3.2.3	Summary of Drug-Related Adverse Events by Treatment Group	Safety
14.3.3	Listing of Subjects Who Became Pregnant During the Study	Safety
14.3.4	Summary of Actual Values and Changes from Baseline in Clinical Chemistry Data by Treatment Group and by Visit	Safety
14.3.5	Summary of Actual Values and Changes from Baseline in Hematology Data by Treatment Group and by Visit	Safety
14.3.6	Summary of Actual Values and Changes from Baseline in Vital Signs by Treatment Group and by Visit	Safety
14.3.7	Summary of ECG Data	Safety
14.3.8	Summary of Concomitant Medication	Safety

11.1.2. List of Figures

Title		Population
14.2 Figure for Efficacy Data		
14.2.1	**Figure Primary Efficacy Endpoint**	
14.2.1.1	Primary Efficacy Endpoint (Latency of Virtual MWM) Time Profile Plot by Individual and by Treatment	EEP
14.2.1.2	Mean Change (+ SD) of Primary Efficacy Endpoint (Latency of Virtual MWM) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.1.3	Boxplot Primary Efficacy Endpoint (Latency of Virtual MWM) Change from Baselines Values by Treatment by Visit	EEP

14.2.1.4	Boxplot Changes of Primary Efficacy Endpoint (Latency of Virtual MWM) Values from Baselines by Treatment by Visit	EEP
14.2.2	**Figure for Secondary Efficacy Endpoint**	
14.2.2.1	percent of time spent in the correct quadrant during MWM probe test - Time Profile Plot by Individual and by Treatment	EEP
14.2.2.2	Mean Change (+ SD) of percent of time spent in the correct quadrant during MWM probe test - Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.2.3	Boxplot percent of time spent in the correct quadrant during MWM probe test - Change from Baselines Values by Treatment by Visit	EEP
14.2.2.4	Boxplot Changes of percent of time spent in the correct quadrant during MWM probe test Values Baselines by Treatment by Visit	EEP
14.2.2.5	number of overall error in the CANTAB paired associates leaning task Time Profile Plot by Individual and by Treatment	EEP
14.2.2.6	Mean Change (+ SD) of number of overall error in the CANTAB paired associates leaning task Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.2.7	Boxplot number of overall error in the CANTAB paired associates leaning task Change from Baselines Values by Treatment by Visit	EEP
14.2.2.8	Boxplot Changes of number of overall error in the CANTAB paired associates leaning task from Baselines by Treatment by Visit	EEP
14.2.3	**Figure for Exploratory Efficacy Endpoint**	
14.2.3.1	CANTAB Motor Screening Task (MOT) Time Profile Plot by Individual and by Treatment	EEP
14.2.3.2	Mean Change (+ SD) of CANTAB Motor Screening Task (MOT) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.3.3	Boxplot CANTAB Motor Screening Task (MOT) Change from Baselines Values by Treatment by Visit	EEP
14.2.3.4	Boxplot CANTAB Motor Screening Task (MOT) Values Baselines by Treatment by Visit	EEP
14.2.3.5	CANTAB Reaction Time (RTI) Time Profile Plot by Individual and by Treatment	EEP

14.2.3.6	Mean Change (+ SD) of CANTAB Reaction Time (RTI) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.3.7	Boxplot CANTAB Reaction Time (RTI) Change from Baselines Values by Treatment by Visit	EEP
14.2.3.8	Boxplot CANTAB Reaction Time (RTI) Values Baselines by Treatment by Visit	EEP
14.2.3.9	CANTAB Paired Associate Learning (PAL) Time Profile Plot by Individual and by Treatment	EEP
14.2.3.10	Mean Change (+ SD) of CANTAB Paired Associate Learning (PAL) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.3.11	Boxplot CANTAB Paired Associate Learning (PAL) Change from Baselines Values by Treatment by Visit	EEP
14.2.3.12	Boxplot CANTAB Paired Associate Learning (PAL) Values Baselines by Treatment by Visit	EEP
14.2.3.13	CANTAB Spatial Span (SS) Time Profile Plot by Individual and by Treatment	EEP
14.2.3.14	Mean Change (+ SD) of CANTAB Spatial Span (SS) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.3.15	Boxplot CANTAB Spatial Span (SS) Change from Baselines Values by Treatment by Visit	EEP
14.2.3.16	Boxplot CANTAB Spatial Span (SS) Values Baselines by Treatment by Visit	EEP
14.2.3.17	CANTAB One Touch Stockings of Cambridge (OTS) Time Profile Plot by Individual and by Treatment	EEP
14.2.3.18	Mean Change (+ SD) of CANTAB One Touch Stockings of Cambridge (OTS) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.3.19	Boxplot CANTAB One Touch Stockings of Cambridge (OTS) Change from Baselines Values by Treatment by Visit	EEP
14.2.3.20	Boxplot CANTAB One Touch Stockings of Cambridge (OTS) Values Baselines by Treatment by Visit	EEP
14.2.3.21	CANTAB Spatial Recognition Memory (SRM) Time Profile Plot by Individual and by Treatment	EEP

14.2.3.22	Mean Change (+ SD) of CANTAB Spatial Recognition Memory (SRM) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.3.23	Boxplot CANTAB Spatial Recognition Memory (SRM) Change from Baselines Values by Treatment by Visit	EEP
14.2.3.24	Boxplot CANTAB Spatial Recognition Memory (SRM) Values Baselines by Treatment by Visit	EEP
14.2.3.25	CANTAB Pattern Recognition Memory (PRM) Time Profile Plot by Individual and by Treatment	EEP
14.2.3.26	Mean Change (+ SD) of CANTAB Pattern Recognition Memory (PRM) Time Profile Plot from Baselines by Treatment by Visit	EEP
14.2.3.27	Boxplot CANTAB Pattern Recognition Memory (PRM) Change from Baselines Values by Treatment by Visit	EEP
14.2.3.28	Boxplot CANTAB Pattern Recognition Memory (PRM) Values Baselines by Treatment by Visit	EEP
14.2.3.29 - 14.2.3.xx	other exploratory Virtual MWM parameters (travel path lengths, quadrant dwell times, etc.) - TBD	EEP

11.1.3. **Listings**

Title		Population	Comment
16.2.1.1	Subject Enrollment Information	Enrolled	
16.2.1.2	Subject Disposition	Safety	
16.2.2.1	Subjects who did not Satisfy Inclusion/Exclusion Criteria (if applicable)	Screening Failure	
16.2.2.2	Protocol Deviations	Safety	
16.2.4.1	Subject Demographic and Baseline Characteristics	Safety	
16.2.4.2	Listing of Medical History	Safety	
16.2.4.3	Listing of Physical Exam	Safety	
16.2.4.4	Listing of Concomitant Medications	Safety	
16.2.5.1	Listing of Drug Administration	Safety	
16.2.6.1	Listing of Relationship of Adverse Event Body Systems, Group Terms, and Verbatim Text	Safety	
16.2.6.2	Listing of All Adverse Events	Safety	
16.2.6.3	Listing of Subjects Withdrawn Due to AEs	Safety	
16.2.6.4	Listing of Deaths or SAEs (if any)	Safety	
16.2.7.1	Listing of Hematology Data	Safety	

16.2.7.2	Listing of Clinical Chemistry Data	Safety	
16.2.7.3	Listing of Urinalysis	Safety	if applicable
16.2.8.	Listing of Vital Sign Data	Safety	
16.2.9.	Listing of ECG Data	Safety	

11.2. Sample Table Template

11.2.1. Sample Template for Count Data

Table 14.x.x.x: Summary of Counts by visit and by Treatment

Population	n	Treatment	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Randomized (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
Safety (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
EEP (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
Completer (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)

Note: Percentages are based on the total number of subjects in each treatment group of the same population

Table 14.x.x.x: Summary of Efficacy/Safety/Lab Count Data by visit and by Treatment

			For Example: Difference of Efficacy Score from Baseline					
Visit	**n**	**Treatment**	**≤-2**	**-1**	**±0**	**+1**	**+2**	**≥ 3**
Visit 1 (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
Visit 2 (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
Visit 3 (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
Visit 4 (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
Follow-up (N=x)	x (x%)	Placebo	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
	x (x%)	40 mg	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)

Note: Percentages are based on the total number of subjects in each treatment group of the same visit

11.2.2. Sample Template for Continuous Data (Efficacy/Safety/Lab)

Table 14.x.x.x: Summary of Endpoint by Visit and by Treatment

Visit	Treatment	Min.	Q1	Median	Mean	Q3	Max.	N	sd
Screening	Placebo								
	40 mg								
Visit 1	Placebo								
	40 mg								
Visit 2	Placebo								
	40 mg								