STATISTICAL ANALYSIS PLAN
FOR PROTOCOL AMP-518
Clinical Trials.gov Identifier: NCT05592418

Sponsor:

AIM ImmunoTech Inc.
2117 SW Highway 484
Ocala, FL 34473, USA

Phone: [redacted]
Fax: [redacted]

Protocol Number:	AMP-518
Protocol Title:	A Randomized, Double Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Ampligen® in Patients with Post-COVID Conditions
Protocol Version / Date:	Version 4.0/ Aug-23-2023

SAP Author: Amarex Clinical Research, LLC
20201 Century Boulevard
Germantown, MD 20874
USA

Telephone: [redacted]
Facsimile: [redacted]

Plan Version:	SAP – Final Version 1.1
Plan Date:	6-Dec-2023

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Sponsor:	AIM ImmunoTech Inc. 2117 SW Highway 484 Ocala, FL 34473, USA
Prepared by:	Amarex Clinical Research 20201 Century Boulevard Germantown, Maryland 20874
SAP Version:	SAP – Final Version 1.1
SAP Date:	6-Dec-2023

I have read and approve the Statistical Analysis Plan specified above and agree on its content:

Statistician, Amarex Clinical Research	Date
AIM ImmunoTech Inc.	Date

TABLE OF CONTENTS

ABBREVIATIONS, ACRONYMS, AND DEFINITIONS

Abbreviation/Acronym	**Definition**
ADSL	Subject-Level Analysis Dataset
ALT	Alanine Transaminase
Amarex	Amarex Clinical Research, LLC.
ANC	Absolute Neutrophil Count
ASA	American Statistical Association
AST	Aspartate Aminotransferase
BMI	Body Mass Index
COVID	Coronavirus Disease 2019
CRO	Contract Research Organization
CSR	Clinical Study Report
CTMS	Clinical Trial Management System
ECG	Electrocardiogram
EOT	End of Treatment
FDA	U.S. Food and Drug Administration
HCT	Hematocrit
ICH	International Conference on Harmonization
ITT	Intention to Treat
IWRS	Interactive Web Based Response System
IV	Intravenous
LDH	Lactate dehydrogenase
MoCA	Montreal Cognitive Assessment
MCID	Minimal Clinically Important Difference
PHQ	Patient Health Questionnaire
RBC	Red Blood Cells
SAE	Serious Adverse Event
SARS	Severe Acute Respiratory Syndrome
SAS	Statistical Analysis System
SBQ-LC	Symptom Burden Questionnaire for Long COVID
SLE	Systemic Lupus Erythematosus
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
WBC	White Blood Cells

1. INTRODUCTION

This Statistical Analysis Plan describes the planned analyses and reporting for the clinical trial protocol AMP-518, conducted by AIM ImmunoTech Inc.. The reader of this Statistical Analysis Plan (SAP) is encouraged to review the complete protocol and amendments as this plan contains only a limited overview of protocol information. The main objectives of this plan are to provide details pertaining to statistical methodology, data conventions, and processes used for the analysis of data from this trial.

The format and content of this SAP are structured to provide sufficient detail to meet the requirements specified by the International Council on Harmonization (ICH) E9: Guidance on Statistical Principles in Clinical Trials. All work planned and presented in this Statistical Analysis Plan will follow the ethical guidelines published by the American Statistical Association (ASA).

The following documents were reviewed in preparation of this Statistical Analysis Plan:

- Protocol Version 4.0/ Aug-23-2023
- ASA Ethical Guidelines for Statistical Practice (2016)
- The Royal Statistical Society: Code of Conduct (2014)
- ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3, 1996)
- ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3(R1), 2013)
- ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9, 1998)
- ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9(R1), 2017)

2. PROTOCOL DESIGN

2.1 Design Overview

2.1.1 Study Design

This is a Phase 2, two-arm, randomized, double blind, placebo controlled multicenter study to evaluate the efficacy and safety of Ampligen® in patients experiencing the Post-COVID Condition of fatigue. Patients will be randomized 1:1 to receive twice weekly IV infusions of Ampligen® or placebo.

Ampligen® and placebo will be administered via twice weekly infusions (Example:

Monday/Thursday or Tuesday/Friday schedule) for 12 weeks. [redacted]

[redacted]

Table 2-1: Study Drug Dose and Duration of Infusion

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]

2.1.1.1 Ampligen Dosing Schedule

[redacted]

[redacted]

2.1.1.2 Management of Infusion-Related Reaction

[redacted]

[redacted]

2.1.1.3 Dosage Modification

[redacted]

[redacted]

2.1.2 Study Visits

2.1.2.1 Study Schedule

The study will have three phases: Screening Phase, Treatment Phase, and Follow-Up Phase.

Screening Phase (up to 1 week):

All subjects will provide written informed consent and have a Screening visit (V1) within 7 days prior to first treatment visit (V2) to determine eligibility for subject participation.

All subjects who fail to meet eligibility criteria are considered screen failures and are exited from the study without further evaluation.

Treatment Phase (12 weeks):

Ampligen® and placebo will be administered via twice weekly infusions (Example: Monday/Thursday or Tuesday/Friday schedule) for 12 weeks. [redacted]

Follow-Up Phase (2 weeks):

Two safety follow-up visits will be performed 3 to 4 days and 2 weeks after the End of Treatment (EOT) visit (V25).

2.1.2.2 Unscheduled Visits

In the event that the subject will return to clinic at a time other than a regularly scheduled study visit, the visit will be regarded as an unscheduled visit. Assessments at unscheduled visits are at the discretion of the Investigator. All pertinent findings, including adverse events or changes in medications, will be noted in the eCRF.

2.2 Treatment Groups

The following treatment groups will be assessed in the study:

- Ampligen®
- Placebo (normal saline)

2.3 Randomization and Stratification

A total of 80 subjects (40 per group) will be randomized in a 1:1 ratio (Ampligen®: placebo). [redacted]

- [redacted]
- [redacted]

[redacted]

2.4 Blinding

This is a double-blind study. The investigator and staff, subjects and Sponsor/CRO staff directly related to study conduct will be blinded to the treatment assignment. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

2.4.1 Emergency Un-Blinding

Breaking the blind prematurely will be allowed only if the subject's well-being requires knowledge of the subject's treatment allocation. Every attempt will be made to maintain the blind throughout the study.

[redacted]

2.4.2 Final Analysis

[redacted]

2.5 Protocol Objective(s)

The purpose of this study is to assess the efficacy and safety of Ampligen® administered twice weekly by IV infusions in subjects experiencing the Post-COVID Condition of fatigue.

2.6 Efficacy Outcome Measures

2.6.1 Primary Efficacy Outcome Measure

- Change from baseline to week 13 in PROMIS® Fatigue Score (T-Score).

2.6.2 Secondary Efficacy Outcome Measures

- Change from baseline to week 6 in PROMIS® Fatigue Score (T-Score).

  Note: Additional PROMIS® Fatigue Score analysis (change from baseline) at week 6 and 13 will be performed excluding response to item, "How often did you have enough energy to exercise strenuously?"

- Change from baseline to week 6 and 13 in distance traveled during a 6-minute walk test.
- Proportion of subjects with minimal clinically important difference (MCID), defined as at least 54 m, in the Six-Minute Walk Test (6MWT) at the end of 12-week treatment phase.
- Change from baseline to week 6 and 13 in PROMIS® Cognitive Function Score (T-Score).
- Change from baseline to week 6 and 13 in PROMIS® Sleep Disturbance Score (T-Score).

2.6.3 Exploratory Outcome Measures

- Changes from baseline in COVID-19-related symptoms using Symptom Burden Questionnaire for Long COVID (SBQ-LC) during the course of the treatment phase.

  Note: A set of common COVID-19-related symptoms (see Symptom Burden Questionnaire for Long COVID (SBQ-LC)) will be evaluated at each scheduled study visit by the patient regardless of which symptoms a subject had at baseline, as new symptoms may appear following the baseline assessment.

- Change from baseline in cognitive function as measured by Montreal Cognitive Assessment (MoCA) at week 4, 8, and 13 during the treatment phase.
- Incidence of hospitalization during the treatment phase.
- Duration (days) of hospitalization during the treatment phase.
- Evaluation of lymphocyte profile by flow cytometry in patients with post-COVID-19 conditions.

- Identification and evaluation of plasma protein biomarkers in patients with post-COVID-19 conditions.

2.6.4 Safety Outcome Measures

- Incidence of treatment-related adverse events.
- Incidence and severity of treatment-emergent adverse events (TEAEs).
- Incidence of serious adverse events (SAEs).
- Incidence of TEAEs and SAEs leading to discontinuation of study medication.
- Changes in blood chemistry, hematology, and coagulation results.
- Changes in vital signs including temperature, pulse, respiratory rate, systolic and diastolic blood pressure.
- Changes in physical examination results.
- Change in electrocardiogram (ECG) results.

3. SAMPLE SIZE DETERMINATION, STATISTICAL POWER, AND SIGNIFICANCE LEVEL

The sample size of 80 subjects will be used in this study. The sample size is based on clinical judgment. No statistical power calculation is used to establish the sample size for this proof-of-concept study.

4. INTERIM ANALYSIS

There is no planned interim analysis for this early phase study.

5. PRIMARY HYPOTHESIS TO BE TESTED

There is no formal hypothesis testing for this study as the study is a Phase II evaluation and is not intended to be hypothesis generating. The study is not powered to reliably yield statistically significant conclusions.

6. ANALYSIS POPULATIONS

[redacted]

7. DATA CONVENTION AND RELATED DEFINITIONS

7.1 Baseline Definition

For all parameters, baseline will be defined as the last available value before the first randomized treatment.

7.2 Duplicate Data

[redacted]

7.3 Handling of Missing Data

7.3.1 Handling of Missing Data for Efficacy Evaluations

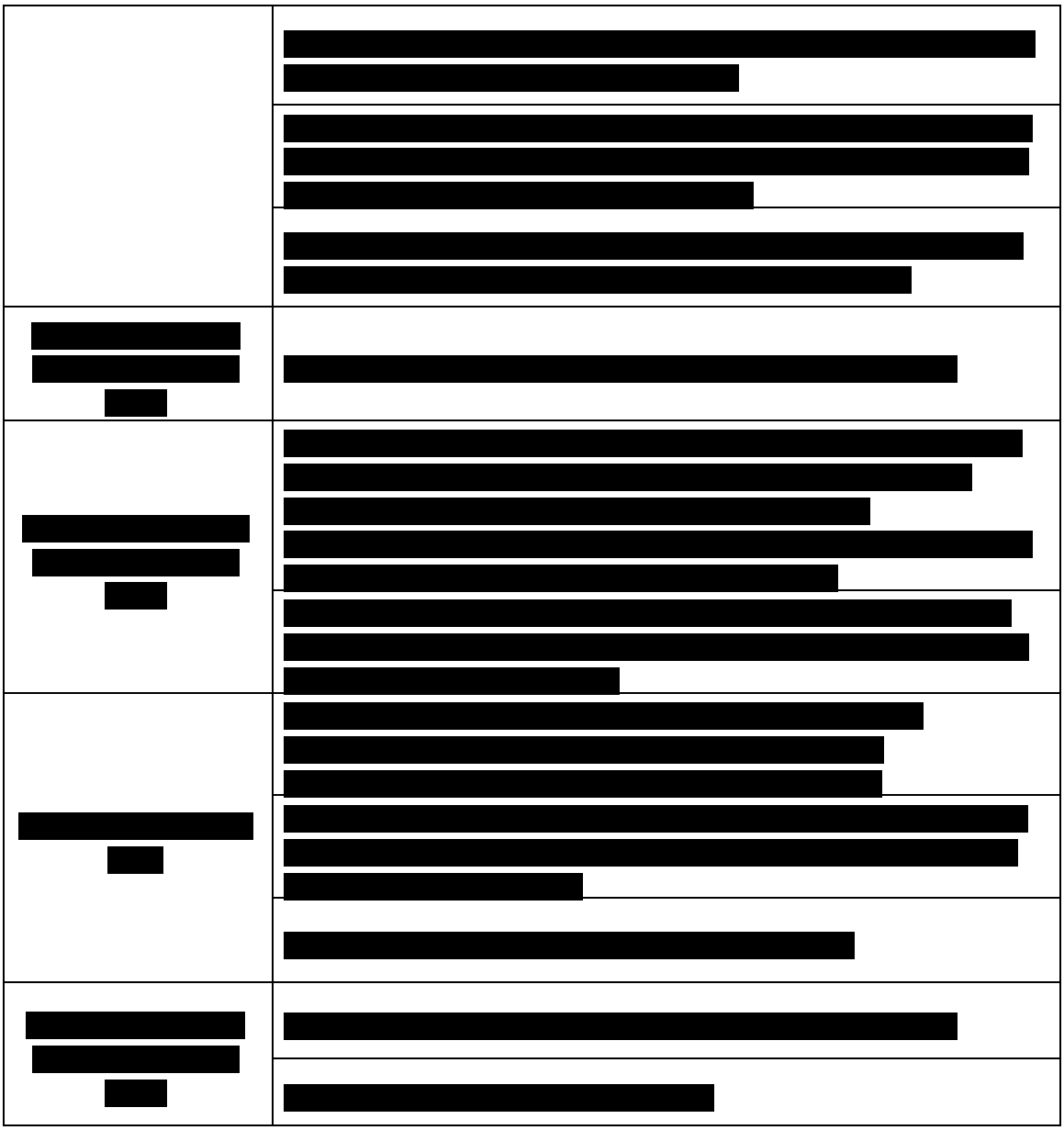
Every effort will be made to obtain required data at each scheduled evaluation from all subjects who have been randomized to minimize missing data. [redacted]

7.3.2 Handling of Missing Data for Safety Evaluations

The below imputation rules will be followed for imputation of missing dates:

[redacted]	[redacted]

[redacted]



7.4 Multicenter Clinical Trials

This is a multi-center clinical trial.

7.5 Multiple Comparisons and Multiplicity

There will be no adjustment for multiple testing or multiplicity for this phase II trial. For all effectiveness endpoints, inference will be based on type I error rate of 0.05.

7.6 Covariates and Prognostic Factors

In the efficacy analysis, the stratification factors and baseline values will be used as

covariates in the analysis of all the primary, secondary, and additional efficacy endpoints.

7.7 Subgroups

[redacted]

7.8 Standard Calculations

7.8.1 Body Mass Index (BMI)

BMI will be calculated using height (in cm) and weight (in kg) according to the formula noted below.

BMI (kg/m2) = Weight (kg)/[Height (cm)/100]^2

7.8.2 Change from baseline

Change from baseline will be calculated for each post baseline visit as follows:

Change From Baseline = Post baseline result at time - Baseline result

7.8.3 Duration (days) of hospitalization during the treatment phase

The duration (days) of hospitalization during the treatment phase will be calculated using the formula noted below.

Duration (days) = (Date of discharge – Date of hospitalization) + 1 *Duration (days) of hospitalization during the treatment phase will only be calculated for hospitalization(s) occurring after the date of first study treatment administration and prior to the date of last study treatment administration. For subject who remain hospitalized at the time of last treatment administration, the date of last treatment will be used for the calculation.* *All deaths within 91 days will be considered censored on Day 91. Conceptually, a death corresponds to an infinite length of hospitalization but censoring at any time greater than or equal to Day 91 gives the same answer as censoring at Day 91; both correspond to giving deaths the worst rank.* *In the incidence where there are multiple hospitalizations for a subject, the durations from the multiple hospitalizations will be summed to provide total duration of hospitalization for the subject.*

8. STATISTICAL METHODS

All statistical analyses will be performed using SAS® for Windows, version 9.4 or later. All data collected during this study will be presented in subject data listings.

All the efficacy analyses presented here will be conducted using mITT and PP populations. All safety analyses will be conducted using the Safety population.

[redacted]

8.1 Summarizing Disposition and Baseline Data

8.1.1 Subject Disposition and Withdrawals

There will be a detailed accounting of all subjects who sign an informed consent to participate in this trial. [redacted]

[redacted]

8.1.2 Protocol Deviations

Protocol deviations will be identified and classified as minor or major before un-blinding according to the following categories:

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

8.1.3 Demographics and Baseline Characteristics

[redacted]

8.1.4 Medical History

Medical history will be coded using the most current available version of Medical Dictionary for Regulatory Activities (MedDRA) and will be summarized by system organ class (SOC) and preferred term (PT). [redacted]

8.1.5 Prior and Concomitant Medications

Prior medication is defined as any medication with an end date prior to the first treatment date.

[redacted]

8.1.6 Extent of Exposure and Treatment Compliance

[redacted]

8.2 Analysis of Efficacy Data

The primary analysis will be conducted on the mITT population. [redacted]

The statistical tests for the primary efficacy endpoint and secondary endpoints will be two-sided with α=0.05.

8.2.1 Primary Outcome Measure and Estimand

8.2.1.1 Primary Outcome Measure

The primary efficacy outcome measure for this study is the change from baseline to week 13 in PROMIS® Fatigue Score (T-Score). [redacted]

The Fatigue - Short Form 7a includes 7 questions and each question has a 5-point severity scale (Never, Rarely, Sometimes, Often, Always). The total score (range from 7-35) will be calculated and converted to the PROMIS® Fatigue Score (T-Score) per PROMIS

Fatigue Scoring Manual as which is included here as APPENDIX 3, Section 11.1. The higher in PROMIS® Fatigue Score (T-Score) represents the worsening of fatigue.

[redacted]

8.2.1.2 Estimand

The estimand for the primary outcome measure is described by the following attributes:

Treatment: Ampligen® vs. Placebo

Study Population: Adult patients with the Post-COVID Condition of fatigue.

Primary Efficacy Variable: Change from baseline to week 13 in PROMIS® Fatigue Score (T-Score)

Primary Efficacy Analysis Population: The Modified Intent-to-Treat (mITT) population is defined as the set of subjects who have received at least one dose of study treatment (Ampligen® or placebo).

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]

8.2.2 Secondary Outcome Measures

8.2.2.1 Change from baseline to week 6 in PROMIS® Fatigue Score (T-Score)

Note: Additional PROMIS® Fatigue Score analysis (change from baseline) at week 6 and 13 will be performed excluding response to item, "How often did you have enough energy to exercise strenuously?"

[redacted] Similar analysis methods used for the primary endpoint will be applied to analyze the data from this outcome measure.

8.2.2.2 Change from baseline to week 6 and 13 in distance traveled during a 6-minute walk test

The 6-minute walk test (6MWT) will be assessed throughout the study. The 6MWT is a sub-maximal exercise test used to assess aerobic capacity and endurance. The distance covered over a time of 6 minutes is used as the outcome by which to compare changes in performance capacity.

[redacted] Similar analysis methods used for the primary endpoint will be applied to analyze the data from this outcome measure.

8.2.2.3 Proportion of subjects with minimal clinically important difference (MCID), defined as at least 54 m, in the Six-Minute Walk Test (6MWT) at the end of 12-week treatment phase

[redacted]

8.2.2.4 Change from baseline to week 6 and 13 in PROMIS® Cognitive Function Score (T-Score)

The Cognitive Function - Abilities - Short Form 8a includes 8 questions and each question has a 5-point severity scale from not at all to very much (1=Not at all, 2=A little bit, 3=Somewhat, 4=Quite a bit, and 5=Very much) ranged from 8-40. PROMIS® Cognitive Function Score (T-Score) will be converted from the total Short Form 8a score per PROMIS Fatigue Scoring Manual which is included here as APPENDIX 3, Section 11.2. The higher in PROMIS® Cognitive Function Score (T-Score) represents the better cognitive function.

[redacted] Similar analysis methods used for the primary endpoint will be applied to analyze the data from this outcome measure.

8.2.2.5 Change from baseline to week 6 and 13 in PROMIS® Sleep Disturbance Score (T-Score)

The Sleep Disturbance - Short Form 4a includes 4 questions with three 5-point severity scales from not at all to very much (1 or 5=Not at all, 2 or 4=A little bit, 3=Somewhat, 4 or 2=Quite a bit, and 5 or 1=Very much) and very poor to very good (5=Very poor, 4=Poor, 3=Fair, 2=Good, and 1=Very good) ranged from 4-20. PROMIS® Sleep Disturbance Score (T-Score) will be converted from the total Short Form 4a score per PROMIS Fatigue Scoring Manual which is included here as APPENDIX 3, Section 11.3. The higher in

PROMIS® Sleep Disturbance Score (T-Score) represents the worsening of sleep disturbance.

[redacted] Similar analysis methods used for the primary endpoint will be applied to analyze the data from this outcome measure.

8.2.3 Exploratory Outcome Measures

8.2.3.1 Change from baseline in COVID-19-related symptoms using Symptom Burden Questionnaire for Long COVID (SBQ-LC) during the course of the treatment phase

[redacted]

Similar analysis methods used for the primary endpoint will be applied to analyze the data from this outcome measure.

8.2.3.2 Change from baseline in cognitive function as measured by Montreal Cognitive Assessment (MoCA) at week 4, 8, and 13 during the treatment phase

[redacted] Similar analysis methods used for the primary endpoint will be applied to analyze the data from this outcome measure.

8.2.3.3 Incidence of hospitalization during the treatment phase

The proportion of subjects with at least one hospitalization during the treatment phase will be presented for the two treatment groups. [redacted]

8.2.3.4 Duration (days) of hospitalization during the treatment phase

The duration (days) of hospitalization during the treatment phase will be calculated using the formula stated in Section 7.8.4.

[redacted]

8.2.3.5 Evaluation of lymphocyte profile by flow cytometry in patients with post-COVID-19 conditions

[redacted] Similar analysis methods used for the primary endpoint will be applied to analyze the data from this outcome measure.

8.2.3.6 Identification and evaluation of plasma protein biomarkers in patients with post-COVID-19 conditions

[redacted]

8.3 Analysis of Safety Data

All safety analyses will be conducted using the Safety population. All data collected will be summarized according to the variable type. No inferential statistics are planned.

[redacted]

8.3.1 Adverse Events

Adverse events will be classified by system organ class (SOC) and preferred term (PT) according to the most recent version of MedDRA dictionary.

TEAE are defined as adverse events with onset date on or after the first treatment. TEAEs will be summarized by treatment group, System Organ Class, and preferred term. The following TEAE summaries will be provided:

a) Overall (*i.e.,* regardless of severity or relationship to treatment)
b) Adverse events by severity
c) Related adverse events by severity
d) Adverse events leading to treatment discontinuation by severity
e) Adverse events leading to death by severity

[redacted]

8.3.2 Clinical Laboratory Evaluations

[redacted]

8.3.2.1 Laboratory Values over Time

[redacted] Data will be summarized as appropriate for the variable type.

8.3.2.2 Individual Patient Changes

[redacted]

8.3.2.3 Individual Abnormalities

[redacted]

8.3.3 Vital Signs

Vital sign assessments are performed in order to characterize basic body function. The parameters collected in this study are: systolic BP (mmHg), diastolic BP (mmHg), temperature (^{0}C), heart rate (bpm), respiratory rate (bpm). [redacted]

8.3.3.1 Vital Signs Values over Time

[redacted]

8.3.3.2 Individual Patient Changes on Notable Vital Sign Values

Clinically notable elevated values

- [redacted]

Clinically notable below normal values

- [redacted]

[redacted]

8.3.4 Electrocardiogram (ECGs)

The ECG parameters include ventricular rate (beats per minute), PR interval (msec), QRS interval (msec), QT interval (msec), and QTc interval (msec). [redacted]

8.3.4.1 ECG Values over Time

[redacted]

8.3.4.2 Individual Patient Changes on Notable ECG Values

[redacted]

[redacted]

8.3.4.3 Individual Patient Changes on Interpretation

[redacted]

8.3.5 Pulse Oxygen Saturation (SpO2)

[redacted]

8.3.6 Physical Examination

[redacted]

8.3.7 Urine Pregnancy Test

[redacted]

8.3.9 SARS-CoV-2 (COVID-19) Qualitative Test

[redacted]

8.3.10 COVID-19 History

[redacted]

9. APPENDIX 1

FIGURE 9-11: SCHEDULE OF ASSESSMENTS V1 TO V14

Procedure/Assessments	Screening Visit	Treatment Visits												
Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14
Week	Week 0	1(Day 0)	1	2	2	3	3	4	4	5	5	6	6	7
Window Period		Within 7 days of SV												
[redacted]	X													
[redacted]	X	X												
[redacted]	X													
[redacted]	X	X												
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]	X	X										X		
[redacted]	X	X										X		
[redacted]	X	X		X		X		X		X		X		X
[redacted]		X		X		X		X		X		X		X
[redacted]		X		X		X		X		X		X		X
[redacted]		X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]		X	X		X		X		X		X		X	
[redacted]	X	X		X		X		X		X		X		X
[redacted]		X						X						
[redacted]	X					X						X		
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]		X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]		X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]														
[redacted]	X													
[redacted]	X	X										X		

Procedure/Assessments	Screening Visit	Treatment Visits												
Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14
Week	Week 0	1(Day 0)	1	2	2	3	3	4	4	5	5	6	6	7
[redacted]	X	X										X		
[redacted]	X	X						X	X					
[redacted]	X	X										X		
[redacted]		X										X		
[redacted]		X												
Intervention:														
[redacted]		X												
[redacted]		X	X	X	X	X	X	X	X	X	X	X	X	X

[redacted]

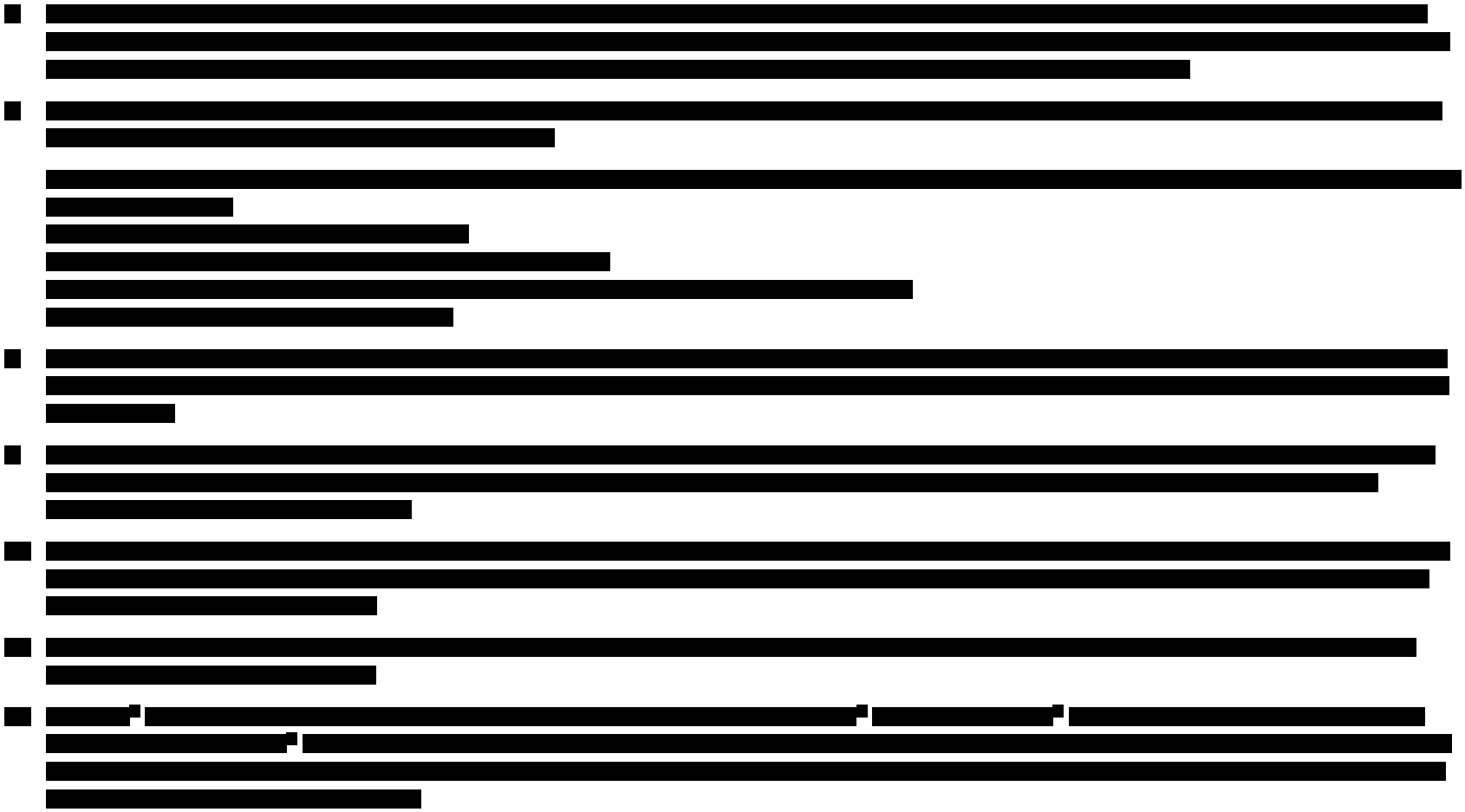
[redacted]

FIGURE 9-2: SCHEDULE OF ASSESSMENTS V15 TO V27

Procedure/Assessments	Treatment Visits											Follow-up 1	Follow-up 2
Visit	V15	V16	V17	V18	V19	V20	V21	V22	V23	V24	V25	Visit 26	Visit 27
Week	7	8	8	9	9	10	10	11	11	12	12	Week 13 (3 to 4 days after EOT)	Week 14
Window Period													± 3 days
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]										X			X
[redacted]										X			X
[redacted]		X		X		X		X		X		X	
[redacted]		X		X		X		X		X		X	
[redacted]		X		X		X		X		X		X	
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]	X		X		X		X		X		X		
[redacted]		X		X		X		X		X		X	X
[redacted]sment		X										X	
[redacted]				X								X	
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]	X	X	X	X	X	X	X	X	X	X	X		
[redacted]													
[redacted]												X	X
[redacted]												X	X
[redacted]		X	X							X			X
[redacted]												X	X

Procedure/Assessments	**Treatment Visits**											**Follow-up 1**	**Follow-up 2**
Visit	**V15**	**V16**	**V17**	**V18**	**V19**	**V20**	**V21**	**V22**	**V23**	**V24**	**V25**	**Visit 26**	**Visit 27**
Week	**7**	**8**	**8**	**9**	**9**	**10**	**10**	**11**	**11**	**12**	**12**	**Week 13 (3 to 4 days after EOT)**	**Week 14**
Window Period													± 3 days
[redacted]												X	
[redacted]												X	
[redacted]													
[redacted]	X	X	X	X	X	X	X	X	X	X	X		

[redacted]



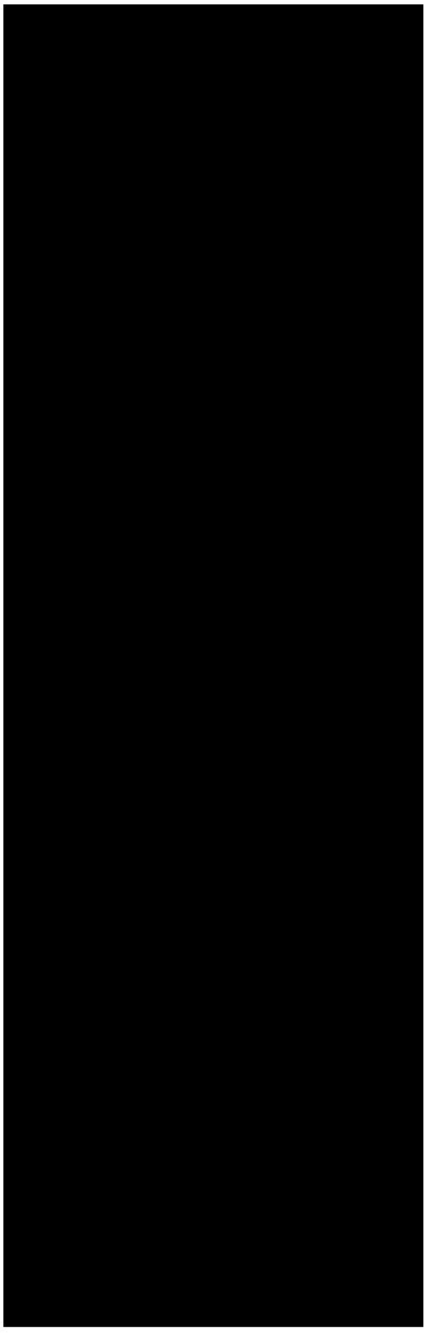
10. APPENDIX 2

10.1 Planned by-subject listings

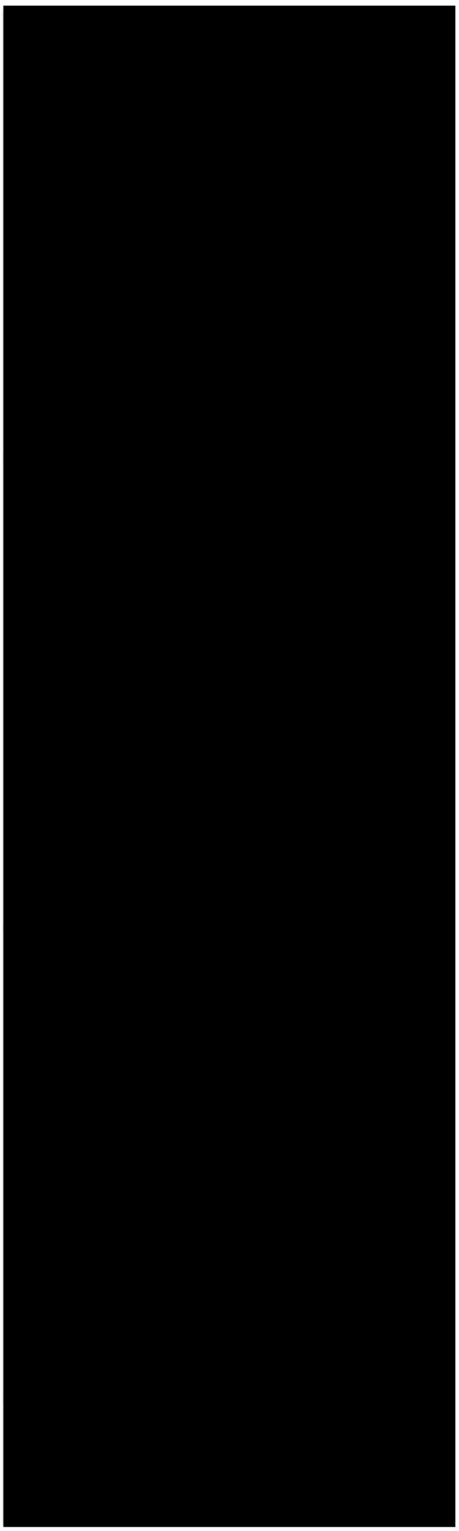
10.2 Planned Summary Tables

11. APPENDIX 3

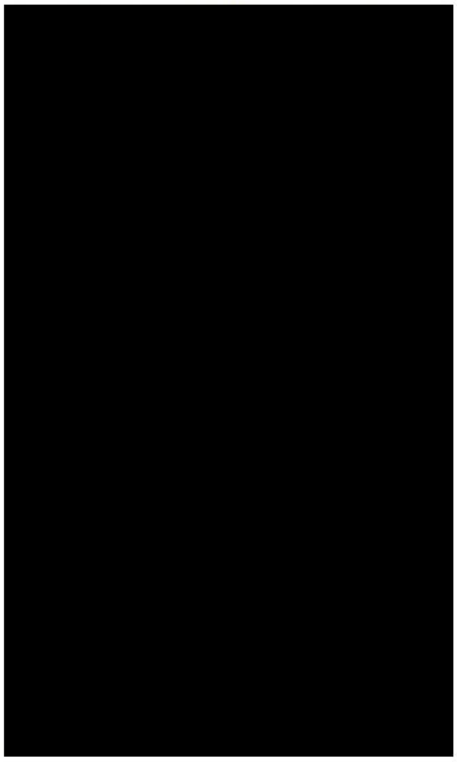
11.1 PROMIS FATIGUE SCORING TABLE



11.2 PROMIS COGNITIVE FUNCTION SCORING TABLE



11.3 PROMIS SLEEP DISTURBANCE SCORING TABLE



12. REFERENCES

1. ASA Ethical Guidelines for Statistical Practice (2016)
2. The Royal Statistical Society: Code of Conduct (2014)
3. ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3, 1996)
4. ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3(R1), 2013)
5. ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9, 1998)
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13. VERSION HISTORY

Version 1.0

This is the first final version of this document.

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