Official Title: An Open-Label Evaluation of the Safety and Tolerability of SAGE-718 in Participants with Parkinson's Disease Mild Cognitive Impairment

NCT Number: NCT04476017

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9. DOCUMENTATION OF STATISTICAL METHODS

Statistical Analysis Plan (SAP) v1.0 Version Date: 05 May 2022

Statistical Analysis Plan (SAP)

Protocol Title:	An Open-Label Evaluation of the Safety and Tolerability of SAGE-718 in Participants with Parkinson's Disease Mild Cognitive Impairment
Protocol Version No./Date:	5.0/28-Apr-2021
CRF Version No./Date:	Part A - V2.0 16-Oct-2020 and Part B - V4.0 / 09-Aug-2021
SAP Version No./Date:	1.0/ 05-May-2022

1.0 Approvals

Sponsor	
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(NOTE: Electronic Signatures should only be used if all parties have the ability to eSign.)

2.0 Change History

Version/Date	Change Log
0.6/13Aug2020	Stable version
0.7/04Nov2020	Updates on distinguishing all efficacy endpoints key measures (for analysis) vs. Others (descriptive); Reclassified a few cognitive measures in consultation with the experts; Analysis window updates; Added supplemental analyses for a few efficacy outcomes to facilitate the residual trend plots.
0.8/08Sep2021	Changes due to Protocol version 5 with the inclusion of Part B study
0.9/15Nov2021	Stable version with the inclusion of Part B study
1.0/05May2022	Final Signed version

3.0 Table of Contents

4.0 Purpose

The Statistical Analysis Plan (SAP) describes the statistical methods to be used during the reporting and analyses of data collected under Sage Therapeutics Protocol 718-CNP-201: An Open-Label Evaluation of the Safety and Tolerability of SAGE-718 in Participants with Parkinson's Disease Mild Cognitive Impairment 718-CNP-201.

5.0 Scope

This SAP describes the statistical methods to be used during the reporting and analyses of data collected from Sage Therapeutics Protocol 718-CNP-201, titled "An Open-Label Evaluation of the Safety and Tolerability of Sage-718-201 in Participants with Parkinson's Disease Mild Cognitive Impairment".

The Statistical Analysis Plan outlines the following:

- Study Objectives
- Study Design
- Study Endpoints
- The Analysis sets
- Applicable Study Definitions
- Statistical Methods

6.0 Introduction

This is an open-label study evaluating the safety and tolerability of SAGE-718 and its effects on [redacted] in participants with PD-MCI. Eligible participants with a confirmed diagnosis of idiopathic PD by 2015 Movement Disorder Society (MDS) criteria at Screening and who meets MDS Task Force Criteria for MCI in PD (excluding the requirement for UK PD Brain Bank diagnostic criteria) will receive a 3.0 mg dose of SAGE-718 daily for 14 days (Part A) or 28 days (Part B).

This SAP should be read in conjunction with the study protocol and case report form (CRF). This version of the plan has been developed using the protocol version 5 dated 28-Apr-2021 and CRF dated 16-Oct-2020 for Part A and CRF dated 09-Aug-2021 for Part B.

Changes to the protocol will require an SAP amendment ONLY if the changes are to a principal feature of the protocol.

Final approval of the SAP by the Sponsor and PRA statistician will occur prior to database lock. Any changes made to the SAP after the clinical database lock, along with the justification for the changes, will be described in the CSR.

6.1 Changes from the Protocol

Protocol section 13.6.6 mentions that the prior and concomitant medications will only be listed. Along with the listing, a summary table will also be provided.

7.0 Protocol Modifications

7.1 Modifications to the Approved Clinical Study Protocol

Protocol versions 2 and 3 are updated to align procedures across protocols in the program and provide clarification on the procedures.

Version 4.0 is updated to broaden the range of eligible participants by revising the participant eligibility criteria.

The primary purpose of version 5.0 is to add a Part B study to explore the safety and efficacy of longer duration dosing for 28 days instead of 14 days in Part A. Associated changes to the planned number of participants, planned study duration and duration of treatment, schedule of assessments, and sample size and power based on the Part B study have been incorporated.

7.2 Modifications to the Approved Statistical Analysis Plan

None.

7.3 Modifications to the Approved DMC Charter

Not applicable

8.0 Study Objectives

8.1 Primary Objective

- Evaluate the safety and tolerability of orally administered SAGE-718 in participants with Parkinson's disease mild cognitive impairment (PD-MCI).

[redacted]

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

9.0 Study Endpoints

9.1 Primary Endpoint

- Incidence of treatment-emergent adverse events (TEAEs)

9.2 Secondary Endpoints

- Change from baseline in vital signs, clinical laboratory analytes, and electrocardiograms (ECGs).
- Responses on the Columbia–Suicide Severity Rating Scale (C-SSRS).

[redacted]

[redacted]

10.0 Study Design

10.1 Overall Design

This study will enroll up to 33 (11 in Part A and 22 in Part B) participants. Part A participants complete 14 days of dosing and Part B participants complete 28 days of dosing in the study. A total of 30 participants are expected to complete dosing in the study. Additional participants may be dosed if the early discontinuation rate is >10%.

This is an open-label study evaluating the safety and tolerability of SAGE-718 and its effects on [redacted] in participants with PD-MCI. Eligible participants with a confirmed diagnosis of idiopathic PD by 2015 Movement Disorder Society (MDS) criteria at Screening and who meet MDS Task Force Criteria for MCI in PD (excluding the requirement for UK PD Brain Bank diagnostic criteria) will receive a 3.0 mg dose of SAGE-718 daily for 14 days (Part A) or 28 days for (Part B) within 1 hour of 30g fat meal.

The study consists of a Screening Period, a Baseline Period, a Treatment Period, and a Follow-Up Period. The Screening Period begins with the informed consent process for prospective participants, including caregivers. Subsequent screening assessments will be performed between Day -21 and Day -8 to determine eligibility, including assessments of [redacted].

The Baseline Period will occur from Day -7 through Day -1. During this period, each participant will receive dietary counseling to aid in choosing a morning meal containing approximately 30 g of fat for dosing. On Day -7 (±1 day), participants will visit the clinic for confirmation of continued eligibility and collection of baseline [redacted] and safety data.

The Treatment Period will begin on Day 1 and continue through Day 14 in Part A and Day 28 in Part B. During this time, participants will self-administer 3.0 mg SAGE-718 (as six 0.5-mg oral tablets), once per

day in the morning within 1 hour after initiating a meal containing approximately 30 g of fat. Participants will continue to complete daily assessments of [redacted] via a mobile device either remotely (at home), or in the clinic at scheduled visits and will track IP dosing and predose food intake in a participant diary. Participants will complete daily remote assessments of [redacted]. For Part A the treatment period clinic visits will occur on Day 1, Day 7 (±1 day), and Day 14, and for Part B it will be on Day 1, Day 7 (±1 day), Day 14 (±1 day), Day 21(±1 day) and Day 28. Following pre-dose procedures, participants will eat a morning meal and take the IP under staff supervision within 1 hour after initiating the meal. At scheduled clinic visits during the treatment period, safety, efficacy, and [redacted] will be performed, and study staff will dispense a sufficient amount of SAGE-718 for daily administration until the next scheduled study visit. In addition to weekly clinic visits, study staff will contact participants by telephone on Day 4 in both Part A and Part B to document any TEAEs and/or changes in concomitant medications

The Follow-Up Period, study staff will contact participants by telephone on Day 21(±1 day) for Part A to document any AEs and/or changes in concomitant medications. Participants will then return to the clinic on Day 28 (±2 days) for a follow-up visit. In Part B, participants will return to the clinic for follow-up visits on Day 35(±1 day) and Day 42(±2 days). No formal interim analysis or DSMB review is planned for this study.

10.2 Sample Size Considerations

No formal sample size calculation was made for this study. Up to 10 participants completing 14 days of dosing in Part A and 20 participants completing 28 days of dosing in Part B are considered sufficient to assess preliminary safety and tolerability and for signal-finding of [redacted] after repeated daily dosing with SAGE-718. Assuming a 10% dropout rate, approximately 33 total participants will be required to obtain 30 completers. Additional participants may be dosed if the early discontinuation rate is >10%.

10.3 Randomization

This study does not involve any randomization of participants.

11.0 Analysis Sets

11.1 Safety Set

The Safety Set will include all participants who were administered at least one dose of an investigational product (IP). Safety set will be used to describe the safety data.

11.2 Full Analysis Set

The Full Analysis Set will include all participants in the Safety Set with baseline and at least one postbaseline efficacy evaluation.

[redacted]

12.0 Interim Analyses

There are no planned interim analyses for this study.

13.0 Statistical Methods

13.1 General Statistical Methodology

All analyses will use SAS version 9.4 or higher.

Unless otherwise noted, continuous variables will be summarized using the number of observations (n), mean, standard deviation (std), median, first quartile (Q1), third quartile (Q3), minimum, and maximum values. The minimum and maximum values will be displayed to the same level of precision as the raw data; the mean, median, Q1, and Q3 values to one additional decimal place and the std to two additional decimal places.

Categorical variables will be summarized using counts and percentages. Percentages will be rounded to one decimal place, except 100% will be displayed without any decimal places, and percentages will not be displayed for zero counts.

Any data points that are not within the expected range due to subjects not following task instructions to complete the tasks will be flagged as invalid by CANTAB EDC. These data points will be excluded from the analyses and reports.

All participants will be used in the analyses as per the analysis populations, using all non-missing data available. No imputation process will be used to estimate missing data.

For all safety, efficacy, and other analyses, where applicable, the baseline is defined as the last assessment prior to the first dose of study IP.

All summary tables will be reported separately for Part A and Part B studies.

For [redacted], the baseline is defined as the average assessments over 7 days immediately preceding Day 1.

Prior and concomitant medication start/stop date imputation and adverse event start/stop date imputation are described in Appendix 2 and Appendix 3, respectively.

AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 23.0u. All TEAEs are defined as an AE with onset after the first dose of IP or any worsening of a preexisting medical condition/AE with onset after the start of IP and throughout the study.

13.2 Participant Analysis Sets

The number and percentage of participants in the FAS, Safety, and [redacted] will be provided.

13.3 Participant Disposition

The number and percentage of participants screened, screen failed, enrolled in the study will be presented, together with the number and percentage of participants who discontinued from the study prematurely and a breakdown of the corresponding reasons for discontinuation as well as the number and percentage of participants who discontinued early from treatment and corresponding reasons.

Participant disposition will be summarized overall for the Safety analysis set, including the following:

- Number and percent of participants who completed the study (or treatment)
- Number and percent of participants who did not complete the study (or treatment) and reasons for early discontinuation of study (or treatment)

The denominator of the percentages will be based on the Safety analysis set. A by-participant disposition listing will be provided. In addition, a separate listing of screening failures with the primary reason for screen failures will be provided.

13.4 Eligibility Criteria Violations and Protocol Deviations

Protocol deviations identified during the study will be captured and categorized by the study team review as major and minor deviations on an ongoing basis. In addition, COVID-19 related protocol deviations such as remote telephone/video visit/assessment, home healthcare visit, missed visit/assessment, out of window visit/assessment, safety reporting, investigational product administration, and others will be documented and analyzed as appropriate.

All major protocol deviations will be summarized by using the FAS.

A by-participant listing of all protocol deviations will be provided with columns identifying the following: date of the deviation, type of deviation (Major/Minor), deviation category, and verbatim description.

13.5 Demographic and Baseline Characteristics

Demographic and baseline characteristics, such as sex, race, age, height (cm), baseline weight (kg), body mass index (BMI) (kg/m^2), years since the first diagnosis of Parkinson's disease, and Hoehn and Yahr stage will be summarized using the Safety analysis set. Data will be summarized using descriptive statistics including sample size (n), mean, std, median, Q1, Q3, minimum, and maximum for continuous variables and numbers and percentages of participants for categorical variables.

The baseline for weight, height and BMI is defined as the last non-missing value prior to the first dose of the investigational product.

13.6 Medical and Surgical History

Medical/surgical procedure history collected at screening will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), Version 23.0u. Medical/surgical procedures history data will be summarized by system organ class (SOC) and preferred term (PT) using the Safety analysis set. A summary of medical/surgical history that is ongoing at the time of screening will be provided separately. Medical/surgical procedures history will also be listed.

13.7 Physical/Neurological Examinations

The physical examination will be conducted at Screening (Day -21 to Day -8) and baseline (Day -7 and Day -1), as well as the end of the scheduled dose day or ET.

A full physical examination will occur at Screening and will include an assessment of body systems (eg, head, eye, ear, nose and throat; heart; lungs; abdomen; and extremities) as well as neurological examination. Thereafter abbreviated physical examinations will include an assessment of general appearance, cardiovascular, respiratory, gastrointestinal, and neurological systems, followed by a targeted physical examination as needed.

Clinically significant abnormalities found during Screening or clinic visits will be reported on the medical history CRF; clinically significant abnormalities or worsening conditions will be reported on the adverse event CRF, hence will be captured in AE displays. Therefore, no summaries will be done for physical and neurological examinations.

13.8 Prior and Concomitant Medications

The following analyses will use the Safety Set.

All medications taken and procedures undergone during the study will be recorded.

Medications will be presented according to whether they are being taken prior to and/or during the study (concomitant). Prior medications are defined as those taken prior to the initiation of the start of the investigational product, and that ended prior to the IP. Concomitant medications are defined as those with a start date on or after the first dose of investigational product or those with a start date before the first dose of investigational product that is ongoing or with a stop date on or after the first dose of investigational product.

13.9 Treatments

13.9.1 Extent of Investigational Product Exposure and Treatment Adherence

The following analyses will use the Safety Set.

Total drug exposure (in mg) is defined as the total investigational product in mg for SAGE-718 that was taken during the study.

Total exposure duration to investigational product (in days) is defined as the date of last dose – date of first dose + 1. Note that this does not exclude days when the dose has been missed

The percentage of the planned exposure received is defined as the total drug exposure, divided by planned exposure, times 100. For participants who complete the treatment period, planned drug exposure is the number of days of treatment planned times 3 mg. For participants who discontinued the treatment early, the planned drug exposure is the number of days (last dose date – first dose date + 1), times 3 mg.

Investigational product adherence (%) is defined as the number of tablets taken, divided by the number of tablets planned to be taken, times 100. The schedule of investigational product is six tablets per day.

The number of tablets planned to be taken is defined as follows:

- If the participant discontinues treatment within Day 2 and Day 14 (both inclusive), the number of tablets planned to be taken is the last dose day of investigational product × 6.
- If the Part A participant does not discontinue treatment, the number of tablets planned to be taken is 84 (6x14) whereas for Part B it is 168(6x28).

Investigational product exposure and adherence will be summarized descriptively and listed. The number and percentage of participants with investigational product adherence in categories(<80%, 80-100%, >100%) will be provided. Investigational product accountability will be listed.

All investigational product exposure data will be in by-participant listings, as well as a summary of treatment adherence.

13.10 Visit Windows

The scheduled visits will not be windowed and will be used at nominal visit value for analysis purposes. The unscheduled and early termination (ET) visit will be mapped to a scheduled visit for analysis. In order to accommodate as much data as possible for analysis, the windows in the table below have been widened compared to protocol-specified operational windows, to have no gap between them; these windows are used for analysis purposes only. Once analysis visit windows are assigned, all visits, including scheduled visits, unscheduled visits, and ET visits will be eligible for being flagged as the “analyzed record” within the analysis window; a participant’s individual analysis visit window could potentially contain more than 1

visit. In the event of multiple visits falling within an analysis window or in case of a tie, the following rules will be used in sequence to determine the "analyzed record" for the analysis visit window:

- If the data from the scheduled visit is available, then the scheduled visit data will be used.
- If there is no data from the scheduled visit is available, the data closest to the scheduled study day for that window will be used.
- If there is a tie between the data in the number of days before and after the scheduled day, the later data will be used.

Table 1A: Visit Windows for Analysis – Part A

Scheduled Visit (+/1 window days) in protocol	Target Study Day	Study Day Window for Visit in Analysis
Day 1	Day 1 (predose)	Day 1 (predose) or last non-missing assessment before pre-dose.
Day 7	Day 7	Day 2 - Day 10
Day 14	Day 14	Day 11 - Day 17
Day 28	Day 28	>= Day 18

Table 1B: Visit Windows for Analysis – Part B

Scheduled Visit (+/1 window days) in protocol	Target Study Day	Study Day Window for Visit in Analysis
Day 1	Day 1 (predose)	Day 1 (predose) or last non-missing assessment before predose.
Day 7	Day 7	Day 2 - Day 10
Day 14	Day 14	Day 11 - Day 17
Day 21	Day 21	Day 18 - Day 24
Day 28	Day 28	Day 25 - Day 31
Day 35	Day 35	Day 32 - Day 38
Day 42	Day 42	>= Day 39

The summary by visit will use the "analyzed records" only – at most one per participant. The data not flagged as the "analyzed record" will be included in listings. An unscheduled visit that does not fall under any analysis window will remain in the database and will be included in the listings.

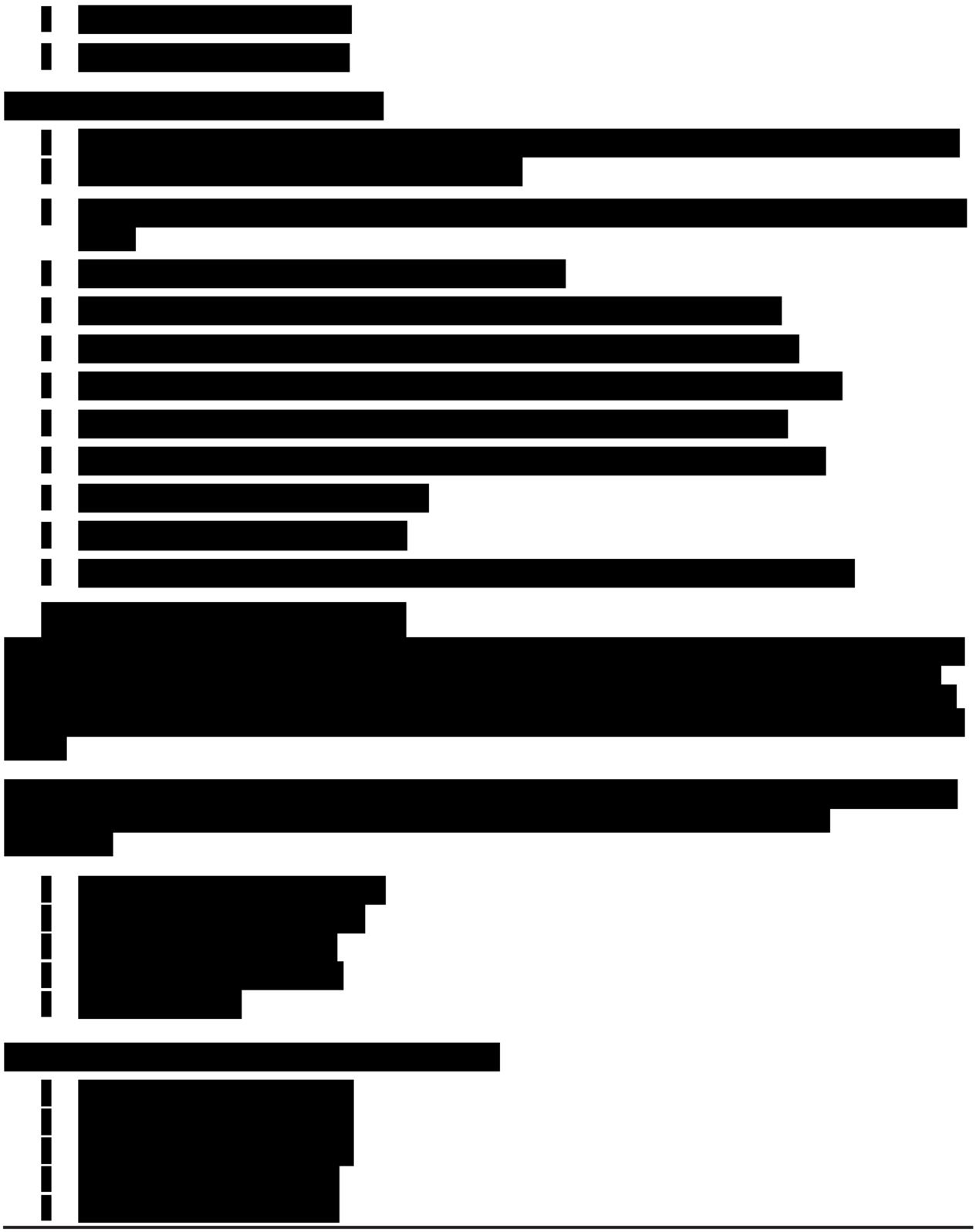
14.0 Efficacy Analysis

14.1 Definition of Efficacy Variables

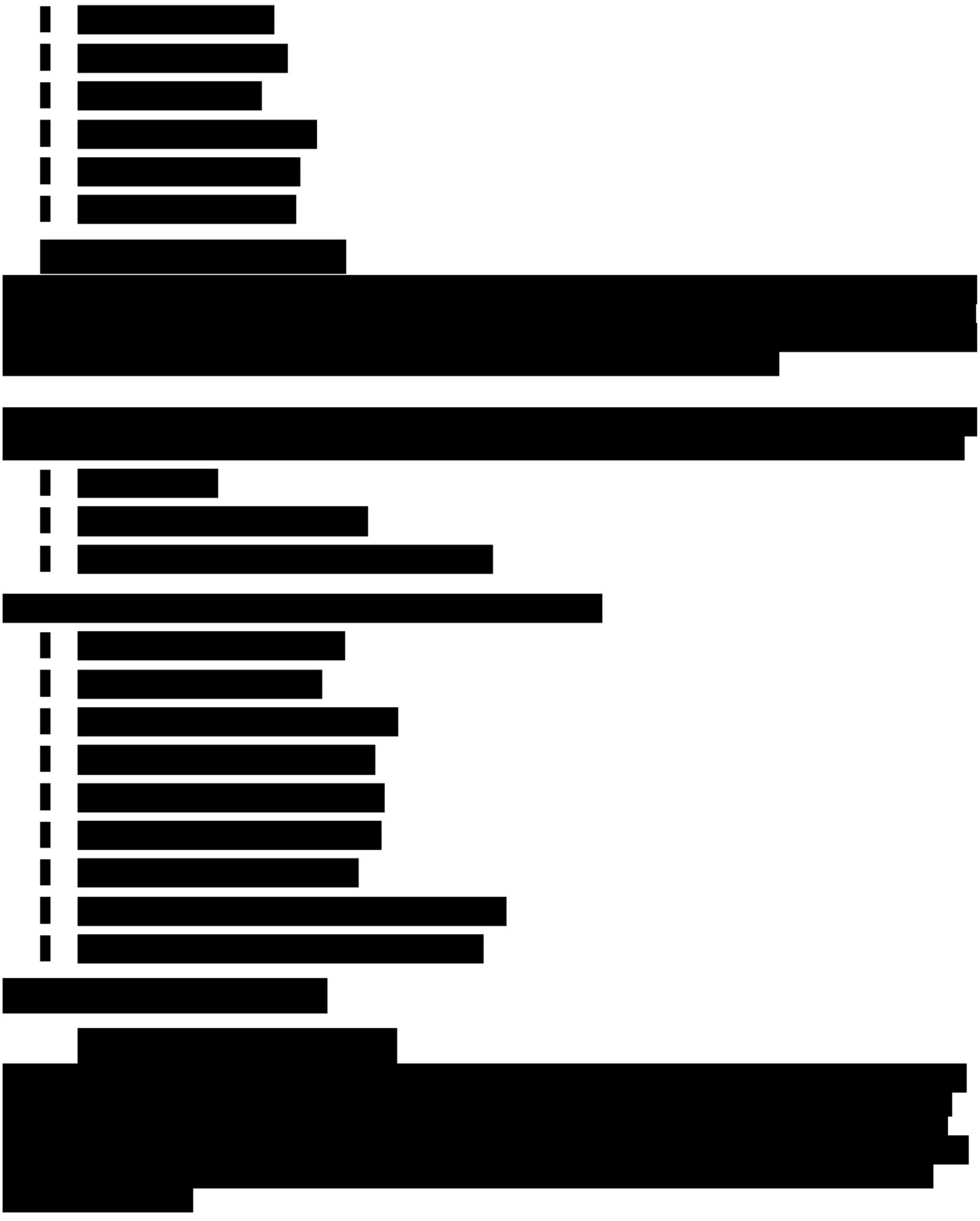
[redacted] capture participant responses on questionnaire measures, and record data for transfer to the sponsor.

[redacted]

[redacted]



[redacted]



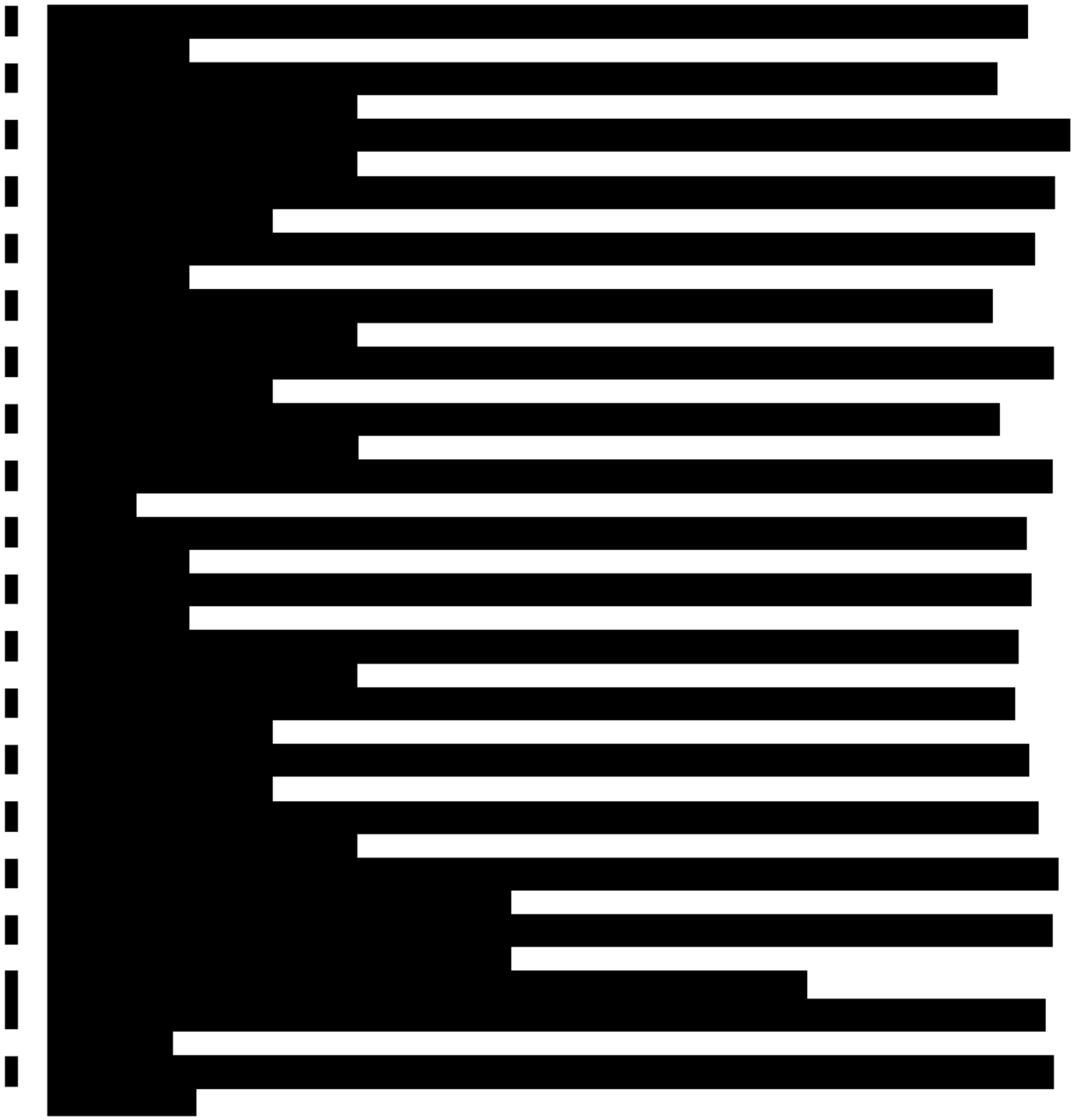
[redacted]

[redacted]

[redacted]

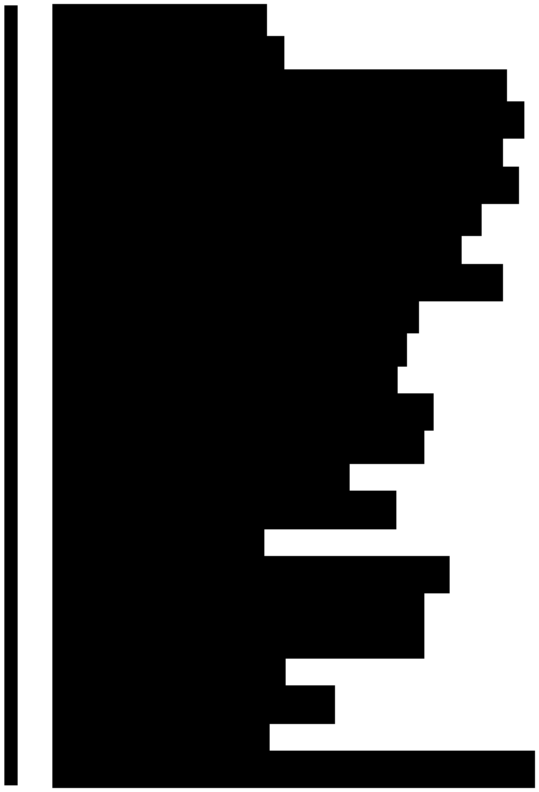
14.2.1 Descriptive Analysis

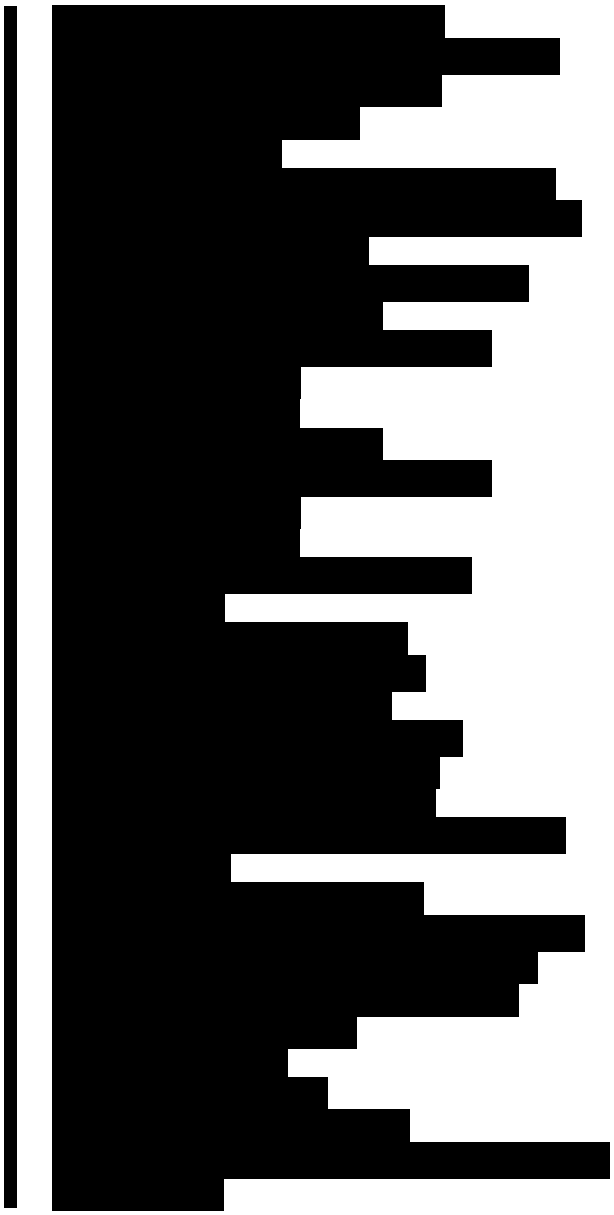
The following efficacy endpoints will be summarized descriptively (mean, standard deviation, median, Q1, Q3, minimum, and maximum for a continuous variable, number, and percent for categorical variable) by scheduled assessment time point, including mobile device delivered assessments for Part A and Part B separately:



14.2.2 Model-Based Analysis -- Mixed Effects Model for Repeated Measures (MMRM)

The following key efficacy endpoints and change from the baseline and percent change from baseline will be summarized descriptively for Part A and Part B studies. The change from baseline will be further explored using the MMRM model for Part A or Part B if 5 or more participants are dosed:





For each item above, a mixed-effects model for repeated measures will be utilized to analyze the change from baseline scores at all post-baseline assessments. The model will include visit as a fixed effect and baseline as a covariate. An unstructured covariance structure will be used to model the variance-covariance matrix of the repeated measurements. If estimation issues arise during the construction of covariance structure, Toeplitz, Autoregressive (1) [AR (1)], or Compound Symmetry (CS) covariance structure will be used, following this sequence until convergence is achieved. If the model still does not converge with the CS structure, no results will be reported. Model-based point estimates ie, least-squares [LS] means are used as the test statistic and will be reported where applicable along with 95% confidence intervals, and p-values.

Line plots of change from baseline scores will be plotted with standard error bars.

Example SAS code that will be used for this model is below:

```
proc mixed data=data1 method=rm;
class subjid Visit;
model chg = base Visit / ddfm=kr;
repeated visit / type=un subject=subjid;
lsmeans visit / cl;
run;
```

where chg is the change from baseline in the [redacted] of interest. In all statistical testing, the level of significance will be set at 5%, with no correction for multiple testing.

Additional analysis of variability in remote assessment:

For [redacted] with remote assessments, the mixed-effects model for repeated measures will be repeated with the day of remote assessment instead of the visit. Linear terms will be examined for the day of the visit. Random effects residuals derived from the model indicate the deviation of each individual from their own slope on each day, providing the difference from a statistically expected observation. These residuals will be used to investigate increased variability in response to treatment, plotting the residuals by day of remote assessment.

[redacted]

Note: The start day of IP administration is Day 1, and all sampling times are relative to this time.

[redacted]

[redacted]

[redacted]

[redacted]

Note: The start day of IP administration is Day 1, and all sampling times are relative to this time.

[redacted]

b To be collected only when participant consent is given.

[redacted]

16.0 Safety and Tolerability Analyses

All safety analyses will be performed using the safety analysis set. The baseline for safety data is defined as the last non-missing value prior to the first dose of the investigational product.

Safety and tolerability of SAGE-718 will be evaluated by treatment-emergent adverse events (TEAEs) and change from baseline vital signs, clinical laboratory analytes, electrocardiograms (ECGs), safety electroencephalogram (EEG), and responses on the Columbia–Suicide Severity Rating Scale (C-SSRS). Safety data will be listed by the participant and summarized using descriptive statistics (mean, median, range, percentages).

16.1 Adverse Events

TEAEs are defined as any AEs with an onset date on or after the date of the first dose of IP or any worsening of a preexisting medical condition/AE with onset after the start of IP and throughout the study. An AE leading to treatment discontinuation is defined as an AE with action taken of investigational product as Drug Withdrawn. AEs will be coded using the Medical Dictionary for Regulatory Activities MedDRA version 23.0u.

An overall summary of TEAEs, including the number of events, reported, the number and percentage of participants reporting at least one TEAE, the number and percentage of participants reporting at least one related TEAE, the number and percentage of participants by maximum severity, the number and percentage of participants discontinuing due to an adverse event, the number and percentage of participants with at least one serious adverse event, and the number and percentage of deaths will be presented.

A breakdown of the number and percentage of participants reporting each adverse event, categorized by System Organ Class (SOC) and preferred term (PT), will be presented. Note that counting will be by participant, not event, and participants are only counted once within each SOC and PT.

A further tabulation of these data, categorized by relationship (to SAGE-718), will be presented. Participants with multiple events within a particular body system or preferred term will be counted under the category of their drug-related event (related and not related) within SOC and PT. Relationship to SAGE-718 is categorized as related or not related.

A summary of events reported, categorized by severity, will also be provided. Participants with multiple events within a particular SOC and PT will be counted under the category of their most severe event in the following order: severe> moderate> mild within that SOC and PT.

A summary of adverse events leading to discontinuation of SAGE-718 will be provided, grouped by body system and preferred term.

All adverse events (including non-treatment-emergent events) recorded on the CRF will be listed.

Handling of missing AE start dates is defined in Appendix 3. Missing data for severity or relatedness to treatment will not be imputed.

16.1.1 Deaths and Serious Adverse Events (SAEs)

All deaths and SAEs will be listed.

16.2 Clinical Laboratory Evaluations

Laboratory assessments for biochemistry, coagulation, hematology, urinalysis, and serology, will be collected at screening, on Day -1, Day 7, Day 14, and Day 28 for Part A, whereas for Part B it is collected at screening, on Day -1, Day 14, Day 28 and Day 42. The clinical laboratory tests to be performed for monitoring safety are listed in **Table 4.** Laboratory assessments will be summarized (n, mean, std, median, Q1, Q3, minimum, and maximum) for Part A and Part B along with the change from baseline by each scheduled post-baseline visit. The International System of Unit (SI) will be used.

For the laboratory results that is "< or = *x*", where *x* is a number as collected in the data, the numeric part of the result will be used in the calculation in the summary tables. The same is true if the result is presented as below limit of quantification (BLQ) and a lower limit of quantification (LLOQ) value is provided – LLOQ value will be used for calculation in the summary tables. The actual results as collected will be displayed in the listings.

Summary tables on lab parameters will include descriptive statistics for the observed values and changes from baseline by scheduled assessment timepoint in hematology, serum chemistry, coagulation, and quantitative urinalysis test results.

Table 4 Clinical Laboratory Tests

Hematology	Serum Chemistry	Urinalysis	Coagulation
Red blood cell count Hemoglobin Hematocrit White blood cell count with differential Platelet count Red Blood Cell Indices (MCV, MCH, MCHC) Reflex to Red blood cell morphology if indices are abnormal	Alanine aminotransferase Albumin Alkaline phosphatase Aspartate aminotransferase Total bilirubin Direct bilirubin Indirect bilirubin Total protein Creatinine Blood urea nitrogen Creatine kinase Gamma-glutamyl transferase Potassium Sodium Lactate dehydrogenase Glucose Chloride Bicarbonate Calcium Phosphate Triglycerides Thyroid-stimulating hormone (TSH)	pH Protein Glucose Red blood cell Nitrite Leukocyte esterase Ketones Bilirubin Urobilinogen	Activated partial Thromboplastin time Prothrombin time International normalized ratio

If a normal range is provided for the parameter, out-of-range values will be flagged as low or high, where applicable, in the participant data listings

The number and percentage of participants with potentially clinically significant (PCS) values will be provided in separate displays in hematology, serum chemistry, and liver function tests provided for such occurrence by time point.

PCS values will be identified for specific laboratory parameters as outlined in Table 5.

Liver function tests will be monitored closely for PCS values, and will be summarized for an occurrence at any post-baseline visit for the following parameters for these PCS threshold (for conditions involving more than one parameter, the results need to be from the same timepoint):

Alanine Aminotransferase: >3xULN, >5xULN, >10xULN
Aspartate Aminotransferase: >3xULN, >5xULN, >10xULN
Alanine Aminotransferase or Aspartate Aminotransferase: >3xULN, >5xULN, >10xULN
Alkaline Phosphatase: >1.5xULN, >2xULN
Total Bilirubin: >1.5xULN, >2xULN
Total Bilirubin > 2xULN **AND** (Alanine Aminotransferase or Aspartate Aminotransferase >3xULN)
Total Bilirubin >2xULN **AND** Alkaline Phosphatase >2xULN **AND** (Alanine Aminotransferase or Aspartate Aminotransferase >3xULN)

Any lab results considered clinically significant by the investigator will be captured as adverse events, and hence will show up in AE displays.

Pregnancy test results will be listed.

Table 5 Potentially Clinically Significant Values for Specific Laboratory Parameters

Laboratory Parameter	**Gender**	**Units**	**Criteria for PCS Values (Observed values)**	
			High	**Low**
Hematology				
Hemoglobin	Male	g/L	>185	<115
	Female	g/L	>170	<100
Hematocrit	Male	Fraction of 1	>0.55	<0.385
	Female	Fraction of 1	>0.49	<0.345
Platelet count		10^9/L	>600	<125
White blood cell		10^9/L	>15	<2.5
Basophils		10^9/L	>0.5	NA
Eosinophils		10^9/L	>1.5	NA
Neutrophils		10^9/L	NA	<1.5
Lymphocytes		10^9/L	>6.0	<0.5
Monocytes		10^9/L	>1.4	NA

Laboratory Parameter	Gender	Units	Criteria for PCS Values (Observed values)	
			High	**Low**
Serum Chemistry				
Albumin		g/L	>70	<28
Blood urea nitrogen		mmol/L	>10.71	NA
Calcium		mmol/L	>2.75	<2.0
Chloride		mmol/L	>120	<90
Creatinine		mmol/L	>3xULN or >3x Baseline	
Gamma Glutamyl Transferase			>3xULN	
Glucose		mmol/L	>13.9	<2.8
Sodium		mmol/L	>150	<132
Potassium		mmol/L	>5.4	<3.3
Protein		g/L		<45
Bicarbonate		mmol/L	>34	<18
Phosphorus		mmol/L	>1.94	<0.61
Liver Function Tests (LFT)				
Bilirubin		µmol/L	>2xULN	NA
Aspartate Aminotransferase		U/L	>3xULN	NA
Alanine Aminotransferase		U/L	>3xULN	NA
Alkaline Phosphatase		U/L	>1.5xULN	NA

16.3 Physical/Neurological Examinations

The occurrence of a physical examination (yes/no) and the date performed and the neurological examination date along with the system and results will be listed by the participant.

16.4 Vital Signs

Vitals for the following parameters - respiratory rate (breaths/minute), oral temperature (degrees C), supine heart rate (beats/minute), supine systolic blood pressure (mmHg), supine diastolic blood pressure (mmHg), standing heart rate (beats/minute), standing systolic blood pressure (mmHg), standing diastolic blood pressure (mmHg), – are collected at Screening and on Days -7, -1, 1, 7, 14, and 28 for Part A, and for Part B an additional collection will be made on Days 21, 35 and 42. Descriptive summaries of observed values and changes from baseline will be provided for vital sign parameters along with body weights by scheduled assessment time points for Part A and Part B separately. Additionally, the number and percentage of participants with PCS and potentially clinically significant change (PCSC) values will be summarized for such occurrence at any post-baseline visit. Potentially clinically significant values will be identified for vital sign parameters as outlined in Table 6.

Table 6 Potentially Clinically Significant Values and Change for Vital Sign Parameters

Vital Sign	**Units**	**Criteria for PCS Values (Observed values)**		**Criteria for PCSC values (Change from Baseline values)**	
		High	Low	Increase	Decrease
Heart rate (supine and standing)	Beats/min	>120	<40	NA	NA
Systolic Blood Pressure (supine and standing)	mmHg	>180	<90	≥30	≥30
Diastolic Blood pressure (supine and standing)	mmHg	>110	<50	≥20	≥20
Supine - Standing Systolic Blood Pressure	mmHg	≥20			
Supine – Standing Diastolic Blood Pressure	mmHg	≥10			
Orthostatic hypotension: supine – standing SBP and DBP	mmHg	SBP ≥20 and DBP ≥10			
Possible Orthostatic hypotension: supine – standing SBP and DBP	mmHg	SBP ≥20 or DBP ≥10			

The orthostatic vital sign - the change from supine to standing (Supine – Standing) in heart rate, systolic and diastolic blood pressure – will be summarized by scheduled assessment timepoint, at 1 and 3 minutes.

Any vital signs result considered clinically significant by the investigator will be captured as adverse events, and hence will show up in AE displays. All vital sign assessments along with PCS will be listed.

16.5 12-Lead Electrocardiogram

Supine 12-lead ECGs will be performed in triplicate, and are collected on screening, days -1, 1, 7, 14, and 28 for Part A whereas for Part B it is performed on days -1, 14, 28, and 42. The following ECG parameters will be listed for each participant: heart rate (beats per minute), PR (msec), QRS (msec), QT (msec), and QTcF (msec).

The average of the triplicate values will be used in the summary, including baseline ECG values. The precision on averages is to keep only 2 decimal places. The observed value at each time point and change from baseline at each post-baseline scheduled time point will be summarized. Each ECG is evaluated as 'normal', 'abnormal, not clinically significant' and 'abnormal, clinically significant'; the number and percentage of participants with at least one of the triplicate values in the categories of normal, 'abnormal, clinically significant' and 'abnormal, not clinically significant' will be provided at baseline and each post-baseline scheduled assessment time point.

The number and percentage of participants with PCS and PCSC values will be summarized for such occurrence of baseline and at any post-baseline visit. Potentially clinically significant values will be identified for ECG parameters as outlined in Table 7. A listing of ECG and QTcF PCS values will be provided.

Table 7 Potentially Clinically Significant Values and Change for ECG Parameters

ECG	Units	Criteria for PCS Values (Observed values)		Criteria for PCSC values (Change from Baseline)	
		High	Low	Increase	Decrease
QTcF Interval	msec	>450 but <=480 >480 but <=500 >500	NA	>=30 to 60 >60	NA

16.6 Columbia-Suicide Severity Rating Scale (C-SSRS)

Suicidality will be monitored during the study using the C-SSRS. The C-SSRS is a questionnaire used to measure the presence and intensity of suicidal ideation and behavior. The C-SSRS will be completed at Screening, Days -7, -1, 1, 7, 14, and 28 for Part A, and additional Day 21, Day 35, and Day 42 are completed for Part B. The "Baseline/Screening" C-SSRS form will be completed at screening (lifetime history and past 24 months). The "Since Last Visit" C-SSRS form will be completed at subsequent time points.

Suicidal behavior and suicidal ideation will be summarized by visit for the Safety analysis set. The proportion of participants who meet the criterion for each of these categories at any post-baseline visit will be summarized as described in Table 8.

Table 8 C-SSRS Categories for Analysis

Category	C-SSRS Item response is "YES"
Suicidal ideation	• Wish to be dead • Non-specific active suicidal thoughts • Active suicidal ideation with any methods (not plan) without intent to act • Active suicidal ideation with some intent to act, without specific plan • Active suicidal ideation with specific plan and intent
Suicidal behavior	• Actual attempt • Interrupted attempt • Aborted attempt • Preparatory acts or behavior • Completed suicide [1]
Non-suicidal self-injurious behavior	• Non-suicidal self-injurious behavior

[1] Completed suicide is not collected at the screening visit.

16.7 Electroencephalogram (EEG)

During Screening, EEG monitoring using the 10 to 20 international system for EEG electrode placement will occur for a duration of 1 hour. The assessment may be performed on any single day during the Screening Period, at any time of day, but preferably while the participant is in a fed state. If clinical events suspicious for seizure occur after Screening (eg, episodes of altered consciousness and/or involuntary motor behaviors), an unscheduled 1-hour EEG will be performed for safety. EEG will be listed by the participant.

17.0 References

1. ICH Harmonized Tripartite Guideline. Statistical Principles for Clinical Trials E9. International conference on harmonization of technical requirements for registration of pharmaceuticals for human use. 05 February 1998. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf
2. ICH Harmonized Tripartite Guideline. Structure and Content of Clinical Study Reports E3. International conference on harmonization of technical requirements for registration of pharmaceuticals for human use. 30 November 1995. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/E3_Guideline_.pdf
3. SAS/STAT 14.2 User's Guide, The Mixed Procedure. SAS Institute, Cary NC, 2016, pp. 6138-6275.

[redacted]

18.0 Glossary of Abbreviations

Glossary of Abbreviations:	
AE	Adverse event
ATC	Anatomic Therapeutic Chemical
AUC_{0-t}	Area under the plasma concentration-time curve, from time 0 to time t
AUC_{0-last}	Area under the curve from the time of dosing to the time of the last measurable (positive) concentration
BLQ	Below the Limit of Quantification
CI	Confidence Interval
CV	Coefficient of Variation
C_{max}	Maximum observed concentration.
COVID-19	Coronavirus Disease 2019
CRF	Case Report Form
CSR	Clinical Study Report
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
FAS	Full Analysis Set
IP	Investigational Product
LLOQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
PCS	Potentially Clinically Significant
[redacted]	
PT	MedDRA Preferred Term
Q1	First Quartile
Q3	Third Quartile
SAP	Statistical Analysis Plan
SAE	Serious Treatment-emergent Adverse Event
SI	International System of Units
SOC	MedDRA System Organ Class
Std	Standard Deviation
TEAE	Treatment Emergent Adverse Event
WHO	World health Organization
WPAI:GH	Work Productivity and Activity Impairment: General Health

19.0 Appendix

19.1 Appendix-A Schedule of Study Assessments (Part A)

Study Period	Screening	Baseline		Treatment				Follow Up	
Study Day	**D -21 to D -8**	**D -7 (±1 d)**	**D -1**	**D 1**	**D 4 [a]**	**D 7 (±1 d)**	**D 14 or ET**	**D 21 [a] (±1 d)**	**D 28 (±2 d)**
Informed consent [b]	X								
Inclusion/exclusion criteria	X	X	X						
Medical history and demographics [c]	X								
Bodyweight	X			X		X	X		X
Body height	X								
Hoehn and Yahr staging	X								
Montreal Cognitive Assessment	X								
Test of Premorbid Functioning	X								
Vital signs [d]	X	X	X	X		X	X		X
Physical examination [e]	X	X	X				X		
EEG [f]	X								
12-lead ECG [g]	X		X	X		X	X		X
C-SSRS [h]	X	X	X	X		X	X		X
Clinical laboratory tests [i]	X		X			X	X		X
Alcohol test [j]	X	X							
Urine drug test	X	X	X	X		X	X		
FSH test [k]	X								
Pregnancy test [l]	X		X				X		X
Serology test [m]	X								
Participant training [o]		X	X						

Study Period	Screening	Baseline		Treatment				Follow Up	
Study Day	D -21 to D -8	D -7 (±1 d)	D -1	D 1	D 4 [a]	D 7 (±1 d)	D 14 or ET	D 21 [a] (±1 d)	D 28 (±2 d)
[redacted]									
Remote assessments [t]		X							
[redacted]									
IP self-administration [u]				X (once daily)					
IP dispensation [v]				X		X			
IP accountability [w]				X					
Safety telephone call					X			X	
TEAEs/SAEs	X								
Concomitant medications [x]	X								

Abbreviations: C-SSRS = Columbia–Suicide Severity Rating Scale; d = days; ECG = electrocardiogram; EEG = electroencephalogram; ET = early termination; FSH = follicle stimulating hormone; IP = investigational product; [redacted] SAE = serious adverse event; TEAE = treatment-emergent adverse events; [redacted]

Note: In the event of early termination, efforts should be made to collect the Day 14 visit assessments. When scheduled for the same time point, procedures should be performed in the following order: vital signs, ECG, blood draws, morning meal, IP dosing, then any scheduled postdose and/or [redacted].

In the setting of public health advisories or similar risks to patient safety, assessments scheduled to be conducted at the study site may be performed via telephone/video if feasible. For assessments that cannot be conducted by phone or video, an in-home visit may be conducted.

a Day 4 and Day 21 visits will occur via scheduled telephone calls.

b Both participants and caregivers are to be consented during the Screening Period.

c In addition to full medical history, all nonpharmacological methods (eg, psychosocial, psychotherapeutic) used to treat or prevent neuropsychiatric, functional, and cognitive manifestations of PD are to be recorded.

d Vital signs to include temperature, respiratory rate, heart rate, and blood pressure. Heart rate and blood pressure to be collected in supine position and standing position at all scheduled time points. When scheduled for the same visit, vital signs are to be assessed prior to ECG and blood collection.

e A full physical examination is to be conducted during Screening. Thereafter, physical examinations will include a brief assessment of general appearance, cardiovascular, respiratory, gastrointestinal, and

neurological systems and followed by a targeted physical assessment as needed. A symptom-directed examination may be conducted at any time at the discretion of the investigator.

f An EEG will be performed for all participants at any time of day during Screening, preferably in a fed state. Subsequently, if the investigator or study staff become aware of events suspicious for seizure, an unscheduled 1-hour EEG will be performed for that participant. A second, follow-up, 1-hour EEG may be performed at the discretion of the investigator.

g ECG will be measured after the participant has been in the supine position for at least 5 minutes.

h "Baseline/Screening" C-SSRS form at Screening and "Since Last Visit" C-SSRS form thereafter.

i Clinical laboratory assessments to include blood samples for hematology, biochemistry, coagulation, urinalysis, and serology, are to be collected ≤2 hours prior to dosing during the Treatment Period, and any time of day at other time points. Participants are to be in a fasted state for screening assessments only.

j Alcohol testing will be performed in the clinic, either by urine dipstick or breathalyzer.

k To confirm self-reported postmenopausal status in women only.

l Serum pregnancy tests for all female participants at Screening; urine pregnancy tests will be conducted for all female participants who are not postmenopausal or surgically sterile at other scheduled time points.

m To include testing for hepatitis B and C, HIV 1, and HIV 2

[redacted]

o Participants and caregivers will be trained to use all study-related software and devices. Additional guidance will be provided on choosing a meal with approximately 30 g of fat.

[redacted]

t Daily reminders will be sent to participants via a mobile device to complete assessments of [redacted] (see Section 14.1)within 1 hour following IP administration either remotely (at home) or in the clinic under observation by the study staff.

u On visit days during the Treatment Period, participants will self-administer IP in the clinic under the supervision of study staff after the predose assessments and consumption of a morning meal.

v Study staff will dispense sufficient IP for daily dosing at home until the next scheduled visit.

w On Days 7 and 14, participants will return used IP packaging and any unused IP for site staff to document.

x At Screening, to include all medications and supplements taken within 60 days and all medications used to treat PD regardless of timing. At visits subsequent to Screening, all changes to any medication should be captured

19.2 Appendix-B Schedule of Study Assessments (Part B)

Study Period	Screening	Baseline		Treatment						Follow Up	
Study Day	D -21 to D -8	D -7 (±1 d)	D -1	D 1	D 4 [a]	D 7 (±1 d)	D 14 (±1 d)	D 21 (±1 d)	D 28 or ET	D 35 (±1 d)	D 42 (±2 d)
Informed consent [b]	X										
Inclusion/exclusion criteria	X	X	X								
Medical history anddemographics [c]	X										
Bodyweight	X			X		X	X	X	X	X	X
Body height	X										
Hoehn and Yahr staging	X										
Montreal Cognitive Assessment	X										
Test of Premorbid Functioning	X										
Vital signs [d]	X	X	X	X		X	X	X	X	X	X
Physical examination [e]	X	X	X						X		
EEG [f]	X										
12-lead ECG [g]	X		X				X		X		X
C-SSRS [h]	X	X	X	X		X	X	X	X	X	X
Clinical laboratory tests [i]	X		X				X		X		X
Alcohol test [j]	X	X									
Urine drug test	X	X	X	X		X	X	X	X		
FSH test [k]	X										
Pregnancy test [l]	X		X				X		X		X
Serology test [m]	X										

Study Period	Screening	Baseline		Treatment						Follow Up	
Study Day	D -21 to D -8	D -7 (±1 d)	D -1	D 1	D 4 [a]	D 7 (±1 d)	D 14 (±1 d)	D 21 (±1 d)	D 28 or ET	D 35 (±1 d)	D 42 (±2 d)
[redacted]											
Participant training [o]		X	X								
[redacted]											
Remote assessments [t]	X										
[redacted]											
IP self-administration [u]				X	X	X	X	X	X		
IP dispensation [v]				X		X	X	X			
IP accountability [w]						X	X	X	X		
Safety telephone call					X						
TEAEs/SAEs	X										
Concomitant medications [x]	X										

Note: In the event of early termination, efforts should be made to collect the Day 28 visit assessments. When scheduled for the same time point, procedures should be performed in the following order: vital signs, ECG,
blood draws, morning meal, IP dosing, then any scheduled postdose and/or [redacted].
In the setting of public health advisories due to COVID-19 or similar risks to patient safety, assessments scheduled to be conducted at the study site may be performed via telephone/video if feasible. For assessments that cannot be conducted by phone or video, an in-home visit may be conducted.

a Day 4 visit will occur via scheduled telephone call.

b Both participants and study partners are to be consented during the Screening Period.

c In addition to full medical history, all nonpharmacological methods (eg, psychosocial, psychotherapeutic) used to treat or prevent neuropsychiatric, functional and cognitive manifestations of PD are to be recorded.

d Vital signs to include temperature, respiratory rate, heart rate, and blood pressure. Heart rate and blood pressure to be collected in supine position and standing position at all scheduled time points.

e A full physical examination is to be conducted during Screening. Thereafter, physical examinations will include a brief assessment of general appearance, cardiovascular, respiratory, gastrointestinal, and neurological systems and followed by a targeted physical assessment as needed. A symptom-directed examination may be conducted at any time at the discretion of the investigator.

f An EEG will be performed for all participants at any time of day during Screening, preferably in a fed state. Subsequently, if the investigator or study staff become aware of events suspicious for seizure, an unscheduled 1-hour EEG will be performed for that participant. A second, follow-up, 1-hour EEG may be performed at the discretion of the investigator.

g ECG will be measured after the participant has been in the supine position for at least 5 minutes.

h “Baseline/Screening” C-SSRS form at Screening and “Since Last Visit” C-SSRS form thereafter.

i Samples for clinical laboratory assessments, to include blood samples for hematology, biochemistry, coagulation, urinalysis, and serology, are to be collected ≤2 hours prior to dosing during the Treatment Period, and any time of day at other time points. Participants are to be in a fasted state for screening assessments only.

j Alcohol testing will be performed in the clinic, either by urine dipstick or breathalyzer.

k To confirm self-reported postmenopausal status in women only.

l Serum pregnancy tests for all female participants at Screening; urine pregnancy tests will be conducted for all female participants who are not postmenopausal or surgically sterile at other scheduled time points.

m To include testing for hepatitis B and C, HIV-1, and HIV-2

[redacted]

o Participants and study partners will be trained to use all study-related software and devices. Additional guidance will be provided on choosing a meal with approximately 30 g of fat.

[redacted]

t Daily reminders will be sent to participants via a mobile device to complete assessments of [redacted] (see Section 14.1) within 1 hour following IP administration either remotely (at home) or in the clinic under observation by the study staff.

[redacted]

v On visit days during the Treatment Period, participants will self-administer IP in the clinic under the supervision of study staff after the predose assessments and consumption of a morning meal.

w Study staff will dispense sufficient IP for daily dosing at home until the next scheduled visit.

y At clinic visits during the Treatment Period, participants will return used IP packaging and any unused IP for site staff to document.

x At Screening, to include all medications and supplements taken within 60 days and all medications used to treat PD regardless of timing. At visits subsequent to Screening, all changes to any medication should be captured.

19.3 Appendix-C Prior and Concomitant Medication Start/Stop Date Imputation

Imputation Rules for Partial Dates (D = day, M = month, Y = year)

Parameter	Missing	Additional Conditions	Imputation
Start date for con meds	D only	M and Y same as M and Y of investigational product administration	Date of investigational product administration
		M and/or Y not same as date investigational product administration	First day of month
	M and D	Y same as Y of investigational product administration	Date of investigational product administration
		Y not same as Y of investigational product administration	Use Jan 01 of Y
	M, D, and Y	None - date completely missing	Day prior to date investigational product administration
Stop date for con meds	D only	M and Y same as M and Y of investigational product administration	Date of investigational product administration
		M and/or Y not same as date of investigational product administration	Last day of month
	M and D	Y same as Y of investigational product administration	Date of investigational product administration
		Y not same as Y of investigational product administration	Use Dec 31
	M, D, and Y	None - date completely missing and NOT ongoing	Date of investigational product administration

19.4 Appendix-D Adverse Event Start/Stop Date Imputation

Parameter	Missing	**Additional Conditions**	**Imputation**
Start date for AEs	D	M and Y same as M and Y of investigational product administration	Date of investigational product administration
		M and/or Y not same as date investigational product administration	First day of month
	D and M	Y same as Y of investigational product administration	Date of investigational product administration
		Y prior to Y of investigational product administration but same as Y of screening date	Date of screening date
	D, M, Y	None - date completely missing	Date of investigational product administration
Stop date for AEs	D	M and Y same as M and Y of investigational product administration	Date of investigational product administration
		M and/or Y not same as date of investigational product administration	Use last day of month
	D and M	Y same as Y of investigational product administration	Date of investigational product administration
		Y not same as Y of investigational product administration	Use Dec 31
	D, M, Y	None - date completely missing	No imputation, but assume ongoing

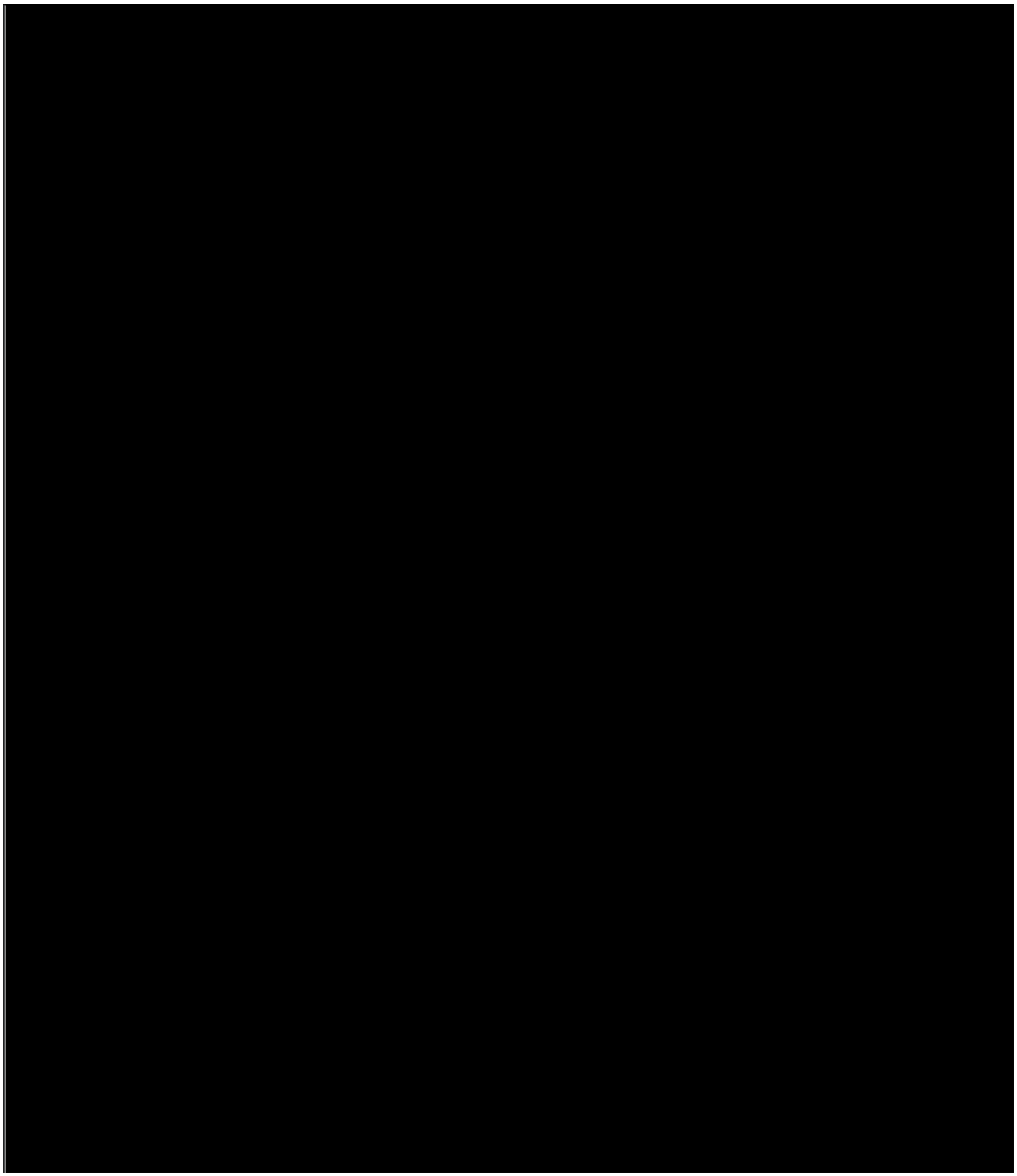
Note: In all cases, if an estimated start date is after a complete stop date, use the first day of the stop date month. Similarly, if the estimated stop date is before a complete or imputed start date, use the last day of the start day month.

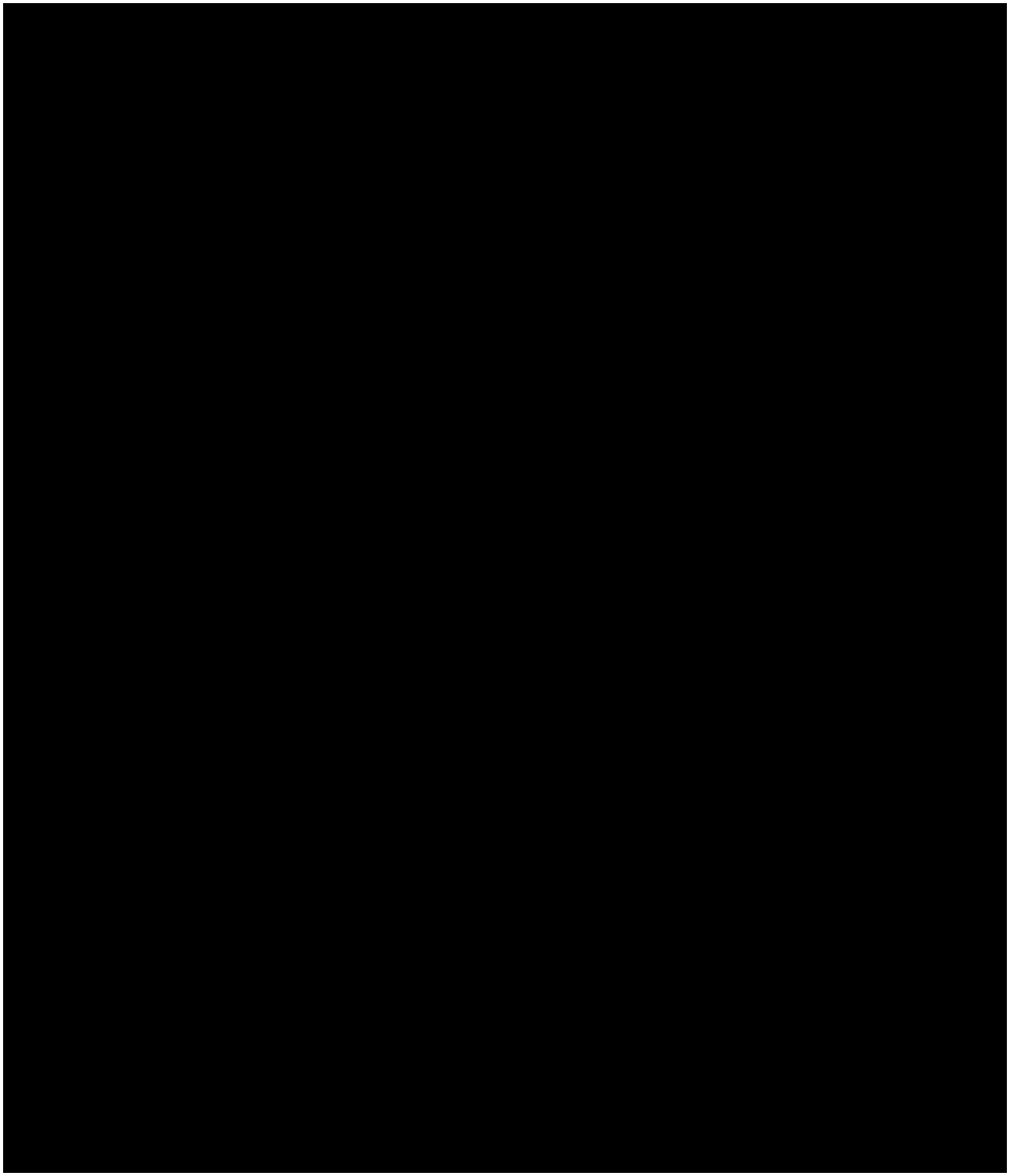
19.5 Appendix- E Calculation of years since diagnosis of Parkinson Disease

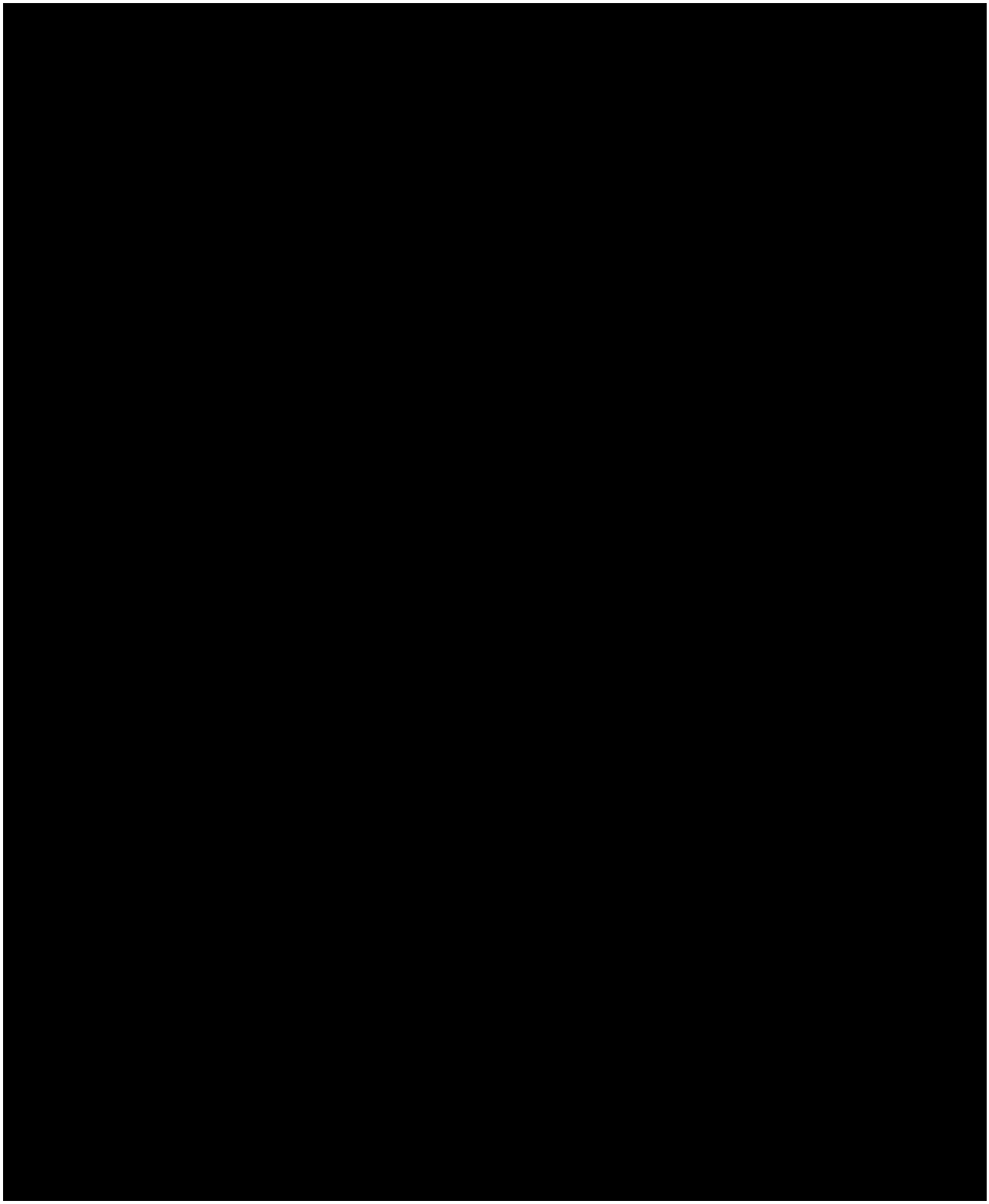
Observed	**Missing**	**Formula to Calculate Duration**
D,M,Y		(Date of Enrollment – Date of Diagnosis + 1)/365.25
M and Y	D	[Year (Date of Enrollment) – Year (Date of Diagnosis)] + [Month (Date of Enrollment) – Month (Date of Diagnosis)]/12
Y	D and M	[Year (Date of Enrollment) – Year (Date of Diagnosis)]

Note : The number of years from the date of diagnosis to the date of enrollment, which will be derived based on the table above. No imputation will be done for missing diagnosis date (Year, Month, Day).

[redacted]

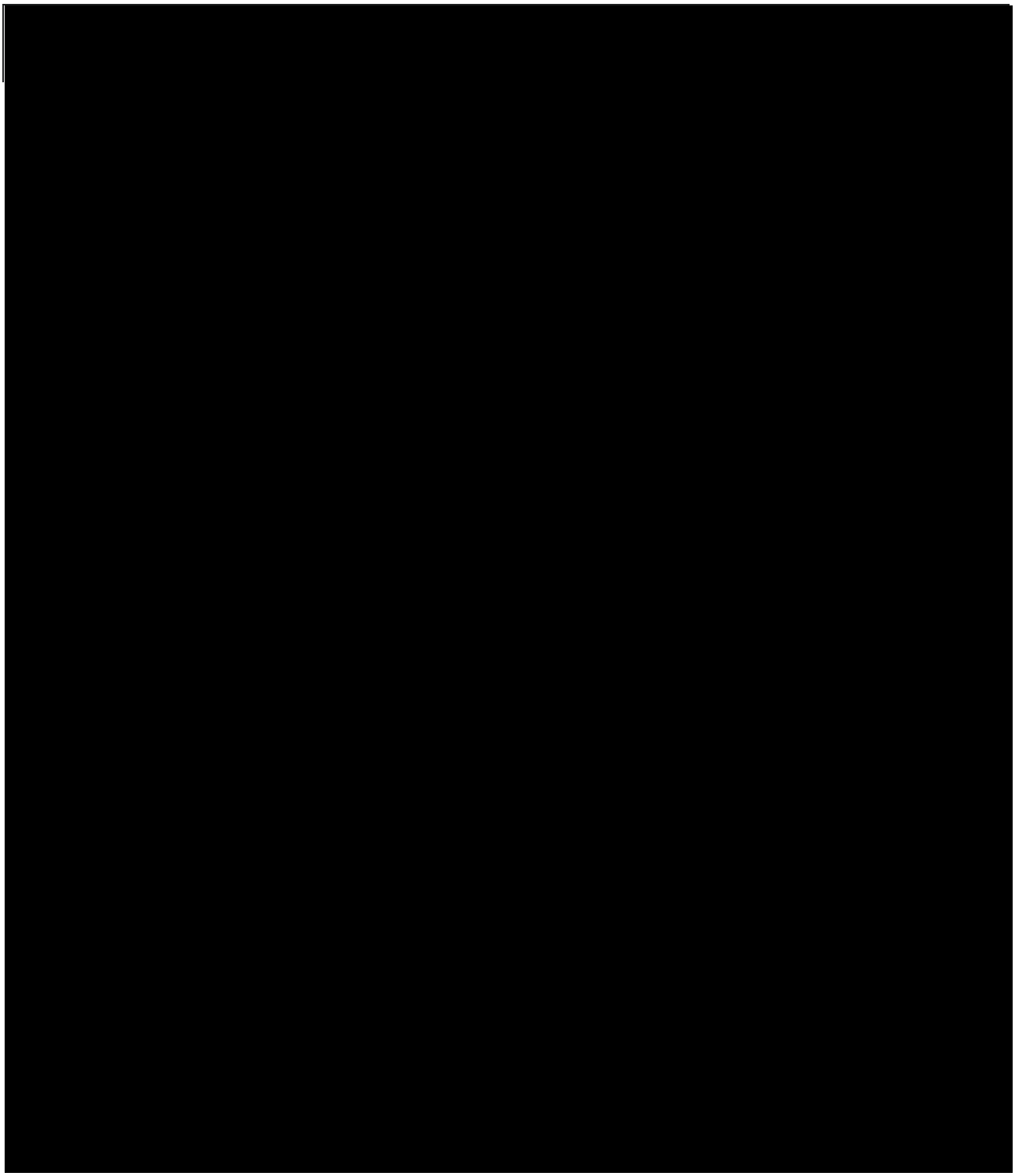






19.7 Appendix-G Tables, Figures, and Listings

Table Number	Title	Population
Table 14.1.1.1A	Subject Analysis Sets - Part A	All Screened Subjects
Table 14.1.1.1B	Subject Analysis Sets - Part B	All Screened Subjects
Table 14.1.1.2A	Subject Disposition - Part A	Safety Analysis Set
Table 14.1.1.2B	Subject Disposition - Part B	Safety Analysis Set
Table 14.1.1.3A	Major Protocol Deviations - Part A	Full Analysis Set
Table 14.1.1.3B	Major Protocol Deviations - Part B	Full Analysis Set
Table 14.1.2.1A	Demographic Characteristics - Part A	Safety Analysis Set
Table 14.1.2.1B	Demographic Characteristics - Part B	Safety Analysis Set
Table 14.1.3A	Prior Medications by ATC Classification and WHO Drug Dictionary Preferred Term - Part A	Safety Analysis Set
Table 14.1.3B	Prior Medications by ATC Classification and WHO Drug Dictionary Preferred Term - Part B	Safety Analysis Set
Table 14.1.4A	Concomitant Medications by ATC Classification and WHO Drug Dictionary Preferred Term - Part A	Safety Analysis Set
Table 14.1.4B	Concomitant Medications by ATC Classification and WHO Drug Dictionary Preferred Term – Part B	Safety Analysis Set
Table 14.1.5A	Medical and Procedures by System Organ Class and Preferred Term - Part A	Safety Analysis Set
Table 14.1.5B	Medical and Procedures by System Organ Class and Preferred Term - Part B	Safety Analysis Set
Table 14.1.6A	Medical and Procedures that are Ongoing at the time of Screening by WHO Drug Dictionary Preferred Term - Part A	Safety Analysis Set
Table 14.1.6B	Medical and Procedures that are Ongoing at the time of Screening by WHO Drug Dictionary Preferred Term - Part B	Safety Analysis Set
Table 14.1.7A	Summary of Exposure and Adherence - Part A	Safety Analysis Set
Table 14.1.7B	Summary of Exposure and Adherence - Part B	Safety Analysis Set
[redacted]		



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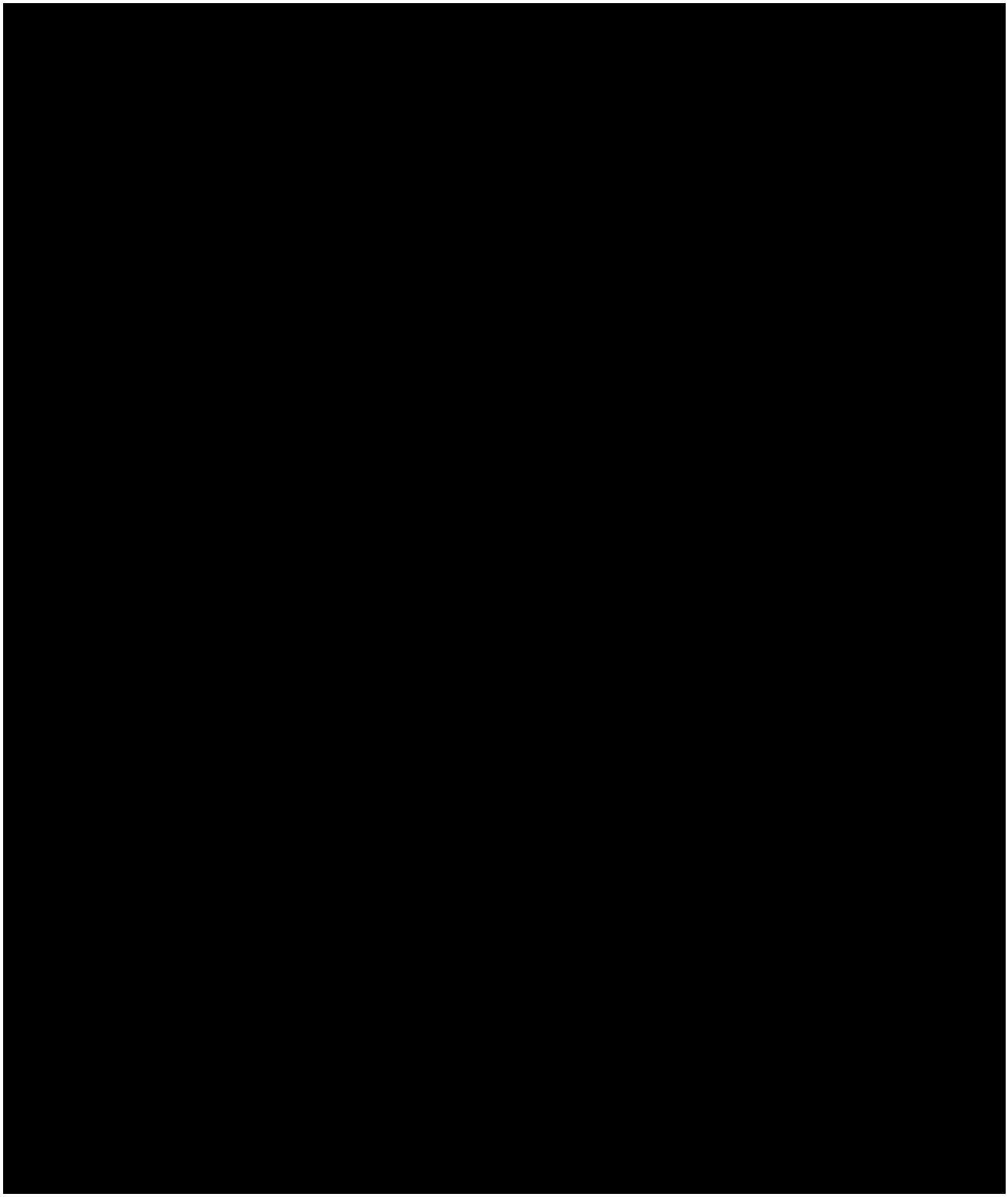
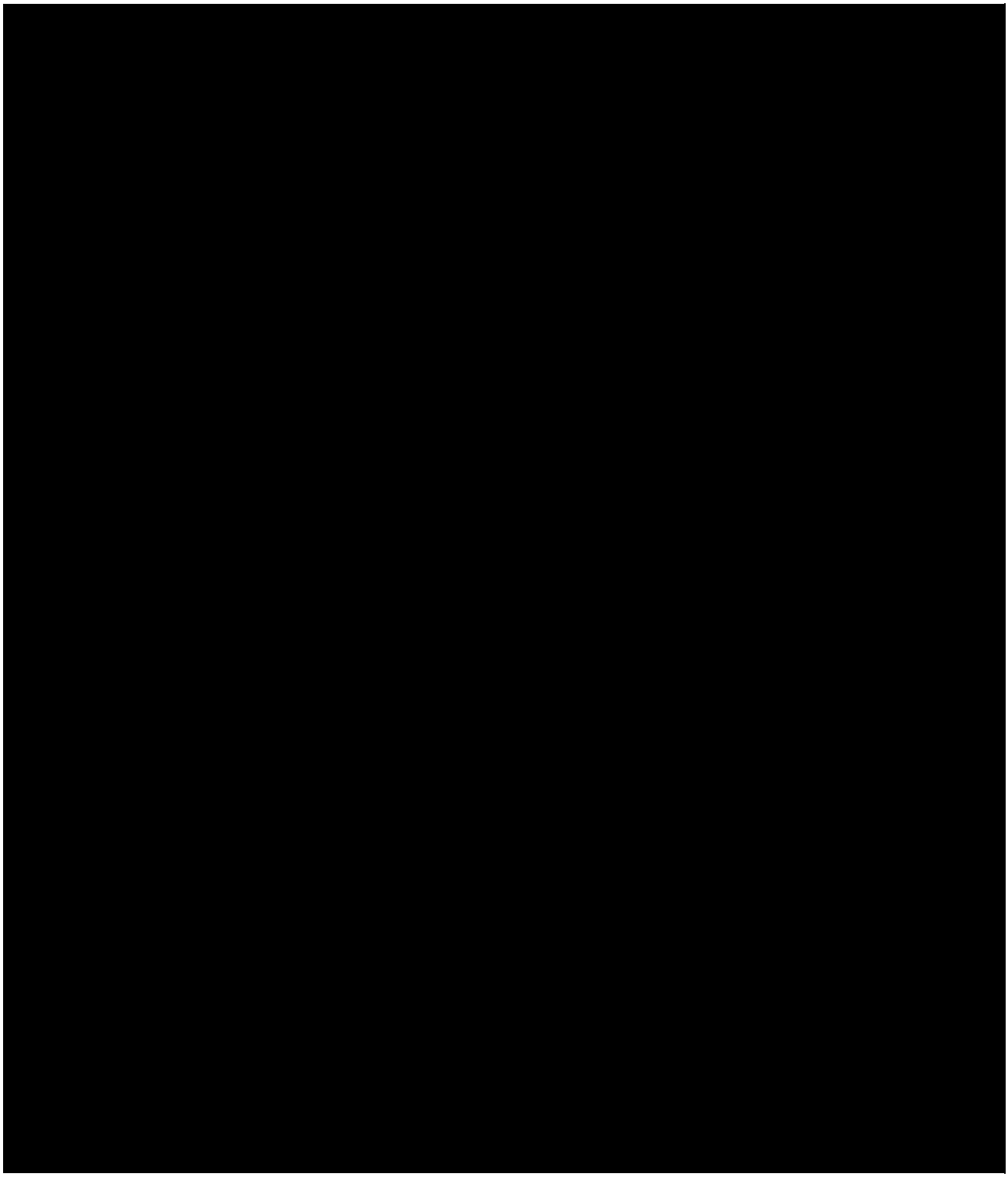




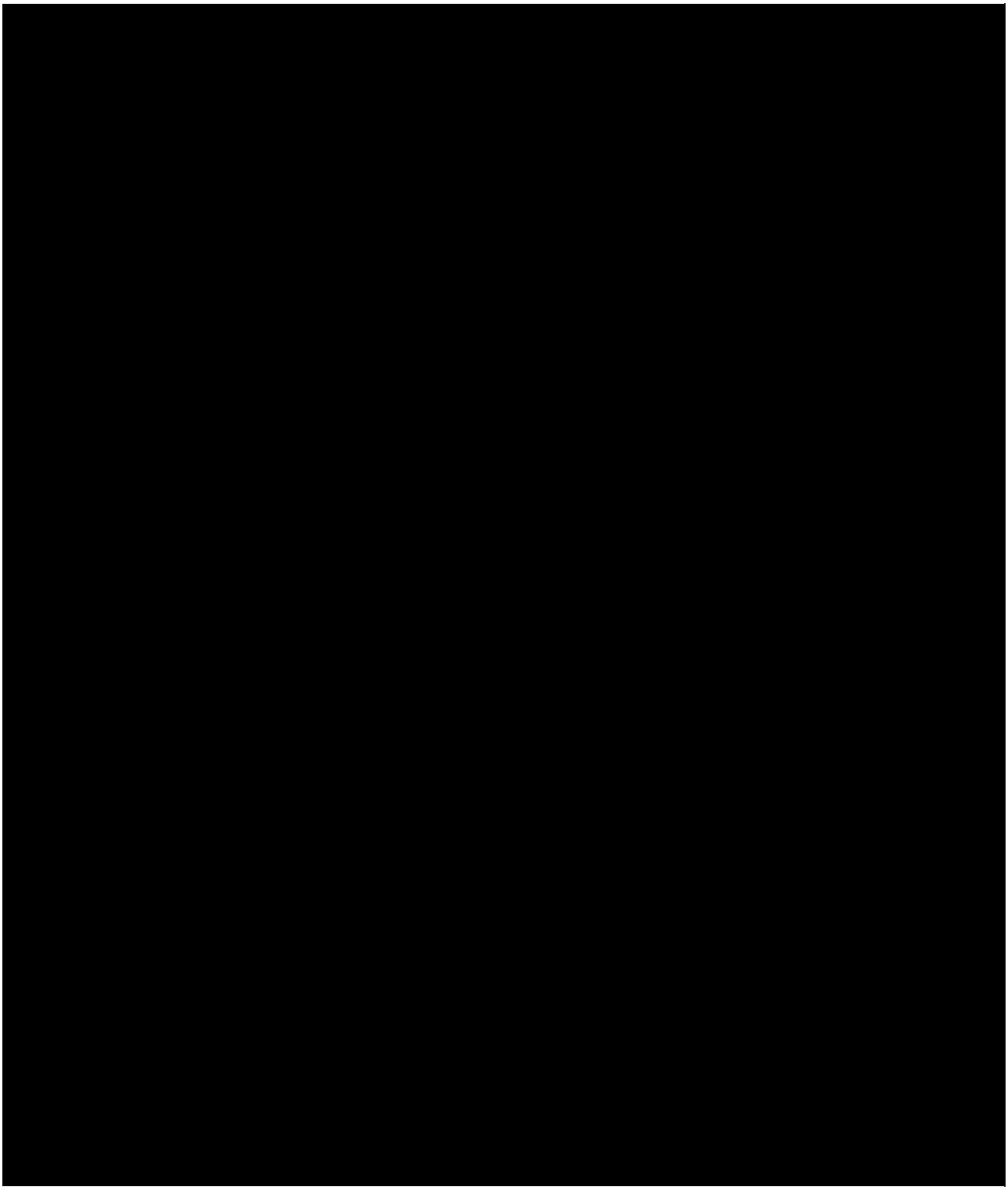
[redacted]

Table 14.3.1.1A	Overall Summary of Treatment Emergent Adverse Events - Part A	Safety Analysis Set
Table 14.3.1.1B	Overall Summary of Treatment Emergent Adverse Events - Part B	Safety Analysis Set
Table 14.3.1.2A	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Part A	Safety Analysis Set

Table 14.3.1.2B	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Part B	Safety Analysis Set
Table 14.3.1.3A	Treatment Emergent Adverse Events Leading to Discontinuation of the Study by System Organ Class and Preferred Term - Part A	Safety Analysis Set
Table 14.3.1.3B	Treatment Emergent Adverse Events Leading to Discontinuation of the Study by System Organ Class and Preferred Term - Part B	Safety Analysis Set
Table 14.3.1.4A	Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term - Part A	Safety Analysis Set
Table 14.3.1.4B	Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term - Part B	Safety Analysis Set
Table 14.3.1.5A	Treatment Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term - Part A	Safety Analysis Set
Table 14.3.1.5B	Treatment Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term - Part B	Safety Analysis Set
Table 14.3.1.6A	Treatment Emergent Adverse Events Leading to Discontinuation of Study Treatment by System Organ Class and Preferred Term - Part A	Safety Analysis Set
Table 14.3.1.6B	Treatment Emergent Adverse Events Leading to Discontinuation of Study Treatment by System Organ Class and Preferred Term - Part B	Safety Analysis Set
Table 14.3.1.7A	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to IP - Part A	Safety Analysis Set
Table 14.3.1.7B	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to IP - Part B	Safety Analysis Set
Table 14.3.1.8A	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity - Part A	Safety Analysis Set
Table 14.3.1.8B	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity - Part B	Safety Analysis Set
Table 14.3.3.1.1A	Hematology and Coagulation Results by Time Point - Part A	Safety Analysis Set
Table 14.3.3.1.1B	Hematology and Coagulation Results by Time Point - Part B	Safety Analysis Set
Table 14.3.3.1.2A	Potentially Clinically Significant Postbaseline Hematology Results by Timepoint - Part A	Safety Analysis Set
Table 14.3.3.1.2B	Potentially Clinically Significant Postbaseline Hematology Results by Timepoint - Part B	Safety Analysis Set
Table 14.3.3.2.1A	Biochemistry Results by Time Point - Part A	Safety Analysis Set
Table 14.3.3.2.1B	Biochemistry Results by Time Point - Part B	Safety Analysis Set
Table 14.3.3.2.2A	Potentially Clinically Significant Postbaseline Biochemistry Results - Part A	Safety Analysis Set
Table 14.3.3.2.2B	Potentially Clinically Significant Postbaseline Biochemistry Results - Part B	Safety Analysis Set
Table 14.3.3.3.1A	Urinalysis Results by Time Point Part 1 Continuous Variables - Part A	Safety Analysis Set
Table 14.3.3.3.1B	Urinalysis Results by Time Point Part 1 Continuous Variables - Part B	Safety Analysis Set
Table 14.3.3.3.2A	Urinalysis Results by Time Point Part 2 Categorical Variables - Part A	Safety Analysis Set

Table 14.3.3.3.2B	Urinalysis Results by Time Point Part 2 Categorical Variables - Part B	Safety Analysis Set
Table 14.3.4.1A	Vital Sign Results by Time Point - Part A	Safety Analysis Set
Table 14.3.4.1B	Vital Sign Results by Time Point - Part B	Safety Analysis Set
Table 14.3.4.2A	Potentially Clinically Significant Vital Sign Results - Part A	Safety Analysis Set
Table 14.3.4.2B	Potentially Clinically Significant Vital Sign Results - Part B	Safety Analysis Set
Table 14.3.5.1A	Electrocardiogram Results - Part A	Safety Analysis Set
Table 14.3.5.1B	Electrocardiogram Results - Part B	Safety Analysis Set
Table 14.3.5.2A	Overall Electrocardiogram Interpretations by Investigator over Time Point - Part A	Safety Analysis Set
Table 14.3.5.2B	Overall Electrocardiogram Interpretations by Investigator over Time Point - Part B	Safety Analysis Set
Table 14.3.5.3A	Potentially Clinically Significant Electrocardiogram Results - Part A	Safety Analysis Set
Table 14.3.5.3B	Potentially Clinically Significant Electrocardiogram Results - Part B	Safety Analysis Set
Table 14.3.6A	Summary of Columbia–Suicide Severity Rating Scale (C-SSRS) Suicidal Ideation and Suicidal Behavior - Part A	Safety Analysis Set
Table 14.3.6B	Summary of Columbia–Suicide Severity Rating Scale (C-SSRS) Suicidal Ideation and Suicidal Behavior - Part B	Safety Analysis Set

[redacted]



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Listing 16.1.7	Subject Enrollment	All Screened subjects
Listing 16.2.1.1	Completion/Discontinued Subjects from Study	Safety Analysis Set
Listing 16.2.1.2	Completion / Discontinuation of Investigational Product (IP)	Safety Analysis Set
Listing 16.2.2	Protocol Deviations	Safety Analysis Set
Listing 16.2.3.1	Subject Analysis Sets	All Enrolled Subjects
Listing 16.2.4.1	Demographic and Baseline Data	Safety Analysis Set
Listing 16.2.4.2	General Medical History	Safety Analysis Set
Listing 16.2.4.3	Prior and Concomitant Medications	Safety Analysis Set
Listing 16.2.4.4	Prior and Concomitant Procedures	Safety Analysis Set
Listing 16.2.5.1	Administration of Investigational Product (Oral)	Safety Analysis Set
Listing 16.2.5.2	Drug Accountability	Safety Analysis Set
Listing 16.2.5.3	Treatment Adherence	Safety Analysis Set

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Listing 16.2.7.1	Adverse Events	Safety Analysis Set
Listing 16.2.7.2	Subjects with Adverse Events with Outcome of Death	Safety Analysis Set
Listing 16.2.8.1	Hematology and Coagulation Results and Change from Baseline	Safety Analysis Set
Listing 16.2.8.2	Biochemistry Results and Change from Baseline	Safety Analysis Set
Listing 16.2.8.3	Urinalysis Results and Change from Baseline	Safety Analysis Set
Listing 16.2.8.4	Pregnancy Test Results (Females of Childbearing Potential only)	Safety Analysis Set
Listing 16.8.5	Urine Drug Screen	Safety Analysis Set
Listing 16.2.9	Vital Signs	Safety Analysis Set
Listing 16.2.10.1	Electrocardiogram Results - Part 1	Safety Analysis Set
Listing 16.2.10.2	Electrocardiogram Results - Part 2	Safety Analysis Set
Listing 16.2.11.1	Physical Examinations	Safety Analysis Set
Listing 16.2.11.2	Neurological Examination	Safety Analysis Set
Listing 16.2.12	Columbia–Suicide Severity Rating Scale (C-SSRS)	Safety Analysis Set
Listing 16.2.13	Electroencephalogram (EEG) Monitoring Test	Safety Analysis Set