STATISTICAL ANALYSIS PLAN

SEP361-301

A RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, PLACEBO-CONTROLLED, FIXED-DOSE, MULTICENTER STUDY TO EVALUATE THE EFFICACY AND SAFETY OF SEP-363856 IN ACUTELY PSYCHOTIC SUBJECTS WITH SCHIZOPHRENIA

PHASE: PHASE III

AUTHOR: PPD PPD

VERSION NUMBER AND DATE: VERSION 2.1, 29NOV2023

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

Statistical Analysis Plan Version 2.1 (Dated 29NOV2023) for Protocol SEP361-301.

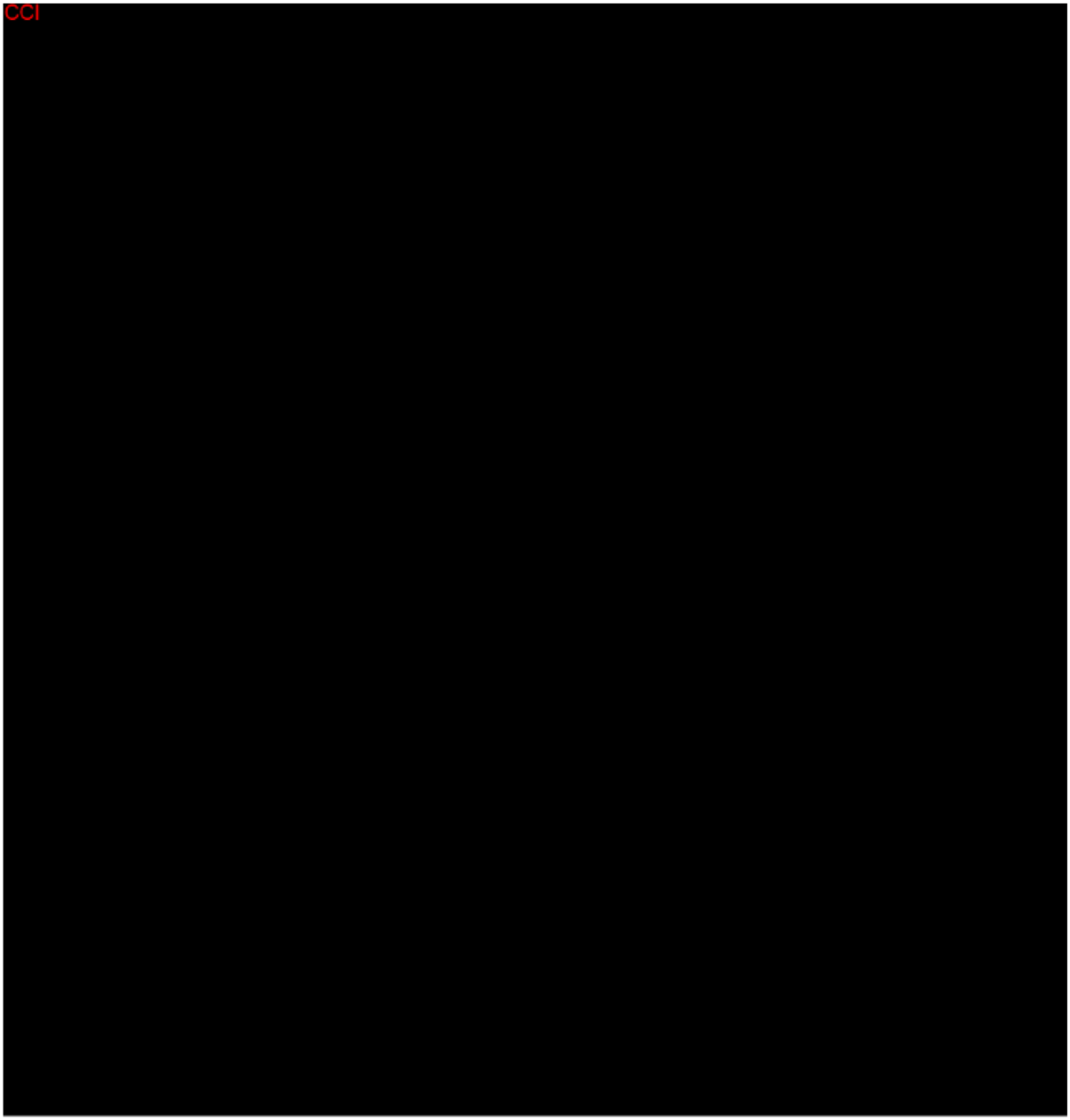
	Name	Signature	Date
Author:	PPD	DocuSigned by PPD	
Position:	PPD	PPD I approve this document November 29, 2023 | 2:00:23 PM EST	
Company:	IQVIA	PPD	

Upon review of this document, the undersigned approves this version of the Statistical Analysis Plan, authorizing that the content is acceptable for the reporting of this study.

	Name	Signature	Date
Approved By:	PPD	DocuSigned by PPD	
	PPD signed on beh of	PPD I approve this document November 30, 2023 | 3:59:02 AM JST	
Position:	PPD	PPD	
Company:	IQVIA		
Approved By:	PPD PhD, MS	DocuSigned by PPD	
Position:	PPD	PPD I approve this document November 29, 2023 | 2:19:46 PM EST	
Company:	Sumitomo Pharma America, Inc.	PPD	
Approved By:	PPD , PhD	DocuSigned by PPD PPD I approve this document November 29, 2023 | 1:57:32 PM EST	
	PPD signed on be lf of PPD	PPD	
Position:	PPD		
Company:	Sumitomo Pharma America, Inc.		

	Name	Signature	Date
Approved By:	PPD , PhD	DocuSigned by PPD PPD I approve this document November 29, 2023 | 2:29:17 PM EST	
Position:	PPD		
Company:	Sumitomo Pharma America, Inc.	PPD	
Approved By:	PPD , MD	DocuSigned by PPD PPD I approve this document November 29, 2023 | 2:25:20 PM EST	
Position:	PPD		
Company:	Sumitomo Pharma America, Inc.	PPD	
Approved By:	PPD	DocuSigned by PPD PPD I approve this document November 29, 2023 | 2:29:08 PM EST	
Position:	PPD		
Company:	Sumitomo Pharma America, Inc.	PPD	
Approved By:	PPD PhD	DocuSigned by PPD PPD I approve this document November 29, 2023 | 2:59:23 PM EST	
Position:	PPD		
Company:	Sumitomo Pharma America, Inc.	PPD	

CCI



CCI

[redacted]

TABLE OF CONTENTS

CCI

APPENDIX 15. SCHEDULE OF EVENTS 189

1. INTRODUCTION

This statistical analysis plan (SAP) Version 2.1 is modified from SAP Version 2.0 which was finalized and signed off prior to the adult subject database lock.

No analyses were changed for the adult subjects.

The modifications in SAP Version 2.1 apply to the analyses specified for the adolescent cohort only. Several adolescent cohort analyses were removed due to the fact that this cohort was terminated on October 9, 2023, prior to reaching the originally planned sample size. At the time of study termination, only 28 out of the originally planned 90 subjects had been enrolled.

The adolescent contents in SAP Version 2.1 replace the adolescent contents in SAP Version 2.0. The adolescent contents in SAP Version 2.0 are voided.

This document describes the rules and conventions to be used in the presentation and analysis of efficacy, safety and pharmacokinetic (PK) data for Protocol SEP361-301. It describes the data to be summarized and analyzed, including specifics of the statistical analyses to be performed.

This SAP is based on protocol version 5.00, dated 13OCT2022.

The Data and Safety Monitoring Board (DSMB) analysis plan will be described in a separate document. An Important Protocol Deviation (IPD) Review Plan and a Blinded Data Review (BDR) Plan will be written to describe the process and the outputs to be delivered during the IPD/BDR meetings.

The subject populations to be analyzed in this SAP separately refer to adult (aged 18 to 65 years) and adolescent (aged 13 to 17 years) subjects. Adolescent subjects are included in this study for the purpose of evaluating the consistency of treatment effects between adult and adolescent subjects and characterizing the safety profile in this age group.

In statistical analyses, a subject will be analyzed as an adult subject or an adolescent subject based on the "Is the subject adult (18-65) or adolescent (13-17)?" question on the "*Demographics*" case report form (CRF). If the calculated age does not align with the selected age group, the selected age group from CRF will be used to assign subjects into cohorts for analysis purpose.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. STUDY OBJECTIVES FOR ADULT SUBJECTS (18 TO 65 YEARS)

2.1.1. PRIMARY OBJECTIVE

The primary objective is to evaluate the efficacy of fixed doses of SEP-363856 (50 and 75 mg/day) compared with placebo in acutely psychotic adult subjects with schizophrenia as measured by the Positive and Negative Syndrome Scale (PANSS) total score.

2.1.2. Secondary Efficacy Objective

The secondary efficacy objective is to evaluate the efficacy of fixed doses of SEP-363856 (50 and 75 mg/day) compared with placebo in acutely psychotic adult subjects with schizophrenia as measured by the Clinical Global Impression-Severity (CGI-S) score.

2.1.3. Other Efficacy Objectives

- To evaluate the efficacy of fixed doses of SEP-363856 (50 and 75 mg/day) compared with placebo in acutely psychotic adult subjects with schizophrenia as measured by:
  - PANSS subscale scores (positive, negative, and general psychopathology).
  - Brief Negative Symptom Scale (BNSS).
  - Montgomery-Asberg Depression Rating Scale (MADRS).
- To assess the effects of SEP-363856 on cognition as measured by the Brief Assessment of Cognition in Schizophrenia (BACS).
- To evaluate the effects of SEP-363856 on functional impairment as measured by the Personal and Social Performance Scale (PSP).
- To evaluate the effects of SEP-363856 on health-related quality of life as measured by the EuroQol-5 Dimensions – 5 Levels (EQ-5D-5L).
- To evaluate the effects of SEP-363856 on functional outcome as measured by the University of California San Diego (UCSD) Performance-based Skills Assessments, Brief Version (UPSA-B).
- To evaluate medication satisfaction as measured by the Medication Satisfaction Questionnaire (MSQ).

2.1.4. Safety Objectives

- To evaluate the safety and tolerability of SEP-363856 (50 and 75 mg/day) using:
  - Physical examinations (PE).
  - 12-lead electrocardiograms (ECG).
  - Vital sign measurements.
  - Adverse event (AE) reports.
  - Clinical laboratory tests.
  - Columbia – Suicide Severity Rating Scale (C-SSRS).
  - Simpson-Angus Scale (SAS).
  - Barnes Akathisia Rating Scale (BARS).
  - Abnormal Involuntary Movement Scale (AIMS).

- To characterize the subjective effects of SEP-363856 on sleep as measured by the Pittsburgh Sleep Quality Index (PSQI).

CCI [redacted]

2.2. STUDY OBJECTIVES FOR ADOLESCENT SUBJECTS (13 TO 17 YEARS)

2.2.1. OTHER EFFICACY OBJECTIVES

- To evaluate the effects of fixed doses of SEP-363856 (50 and 75 mg/day) as measured by:
  - PANSS total and subscale scores (positive, negative and general psychopathology).
  - CGI-S score.
- To assess the effects of SEP-363856 on cognition as measured by the BACS.
- To evaluate the effects of SEP-363856 on functional impairment as measured by the PSP.
- To evaluate the effects of SEP-363856 on health-related quality of life as measured by the EuroQol-5 Dimensions – 5 Levels (EQ-5D-5L).
- To evaluate medication satisfaction as measured by the MSQ.

2.2.2. OTHER SAFETY OBJECTIVES

- To evaluate the safety and tolerability of SEP-363856 (50 and 75 mg/day) using:
  - Physical examinations.
  - ECGs.
  - Vital sign measurements.
  - AE reports.
  - Clinical laboratory tests.
  - C-SSRS.
  - SAS.
  - BARS.
  - AIMS.

- To evaluate the effects of SEP-363856 on sexual maturation / development as assessed by:
  - Tanner staging.
  - Menstrual cyclicity (female adolescents only).
  - Follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (female adolescents only); testosterone (male adolescents only).
- To evaluate the impact of SEP-363856 on healthcare resource utilization (HCRU).

CCI [redacted]

2.3. STUDY ENDPOINTS FOR ADULT SUBJECTS (18 TO 65 YEARS)

2.3.1. PRIMARY ENDPOINT

- Change from Baseline in PANSS total score at Endpoint (Week 6).

2.3.2. SECONDARY EFFICACY ENDPOINT

- Change from Baseline in CGI-S score at Endpoint (Week 6).

2.3.3. OTHER EFFICACY ENDPOINTS

- At each scheduled visit except Endpoint (Week 6), change from Baseline in
  - PANSS total score.
  - CGI-S score.
- At each scheduled visit, change from Baseline in
  - PANSS subscale scores.
  - BNSS total score.
  - MADRS total score.
  - BACS composite score.
  - PSP total score.
  - EQ-5D-5L: visual analog scale (VAS), index score and dimension score.

- UPSA-B total score.
- MSQ score.

- PANSS response, defined as a 20% or greater improvement from Baseline in PANSS total score, at each scheduled visit.

- Tobacco use at Baseline and Endpoint.

2.3.4. SAFETY ENDPOINTS

- The incidence of overall AEs, serious AEs (SAEs), and AEs (or SAEs) leading to discontinuation.

- Observed values and changes from Baseline at each scheduled visit in clinical laboratory tests (hematology, chemistry, and urinalysis), vital signs (including temperature, body weight, body mass index (BMI), waist circumference, blood pressure [supine and standing], pulse rate [supine and standing] and respiration rate) and 12-lead ECG parameters.

- Frequency and severity of suicidal ideation and suicidal behavior based on the C-SSRS.

- Change from Baseline in SAS, BARS and AIMS scores at each scheduled visit.

- Change from Baseline in PSQI global score at each scheduled visit.

CCI [redacted]

2.4. STUDY ENDPOINTS FOR ADOLESCENT SUBJECTS (13 TO 17 YEARS)

2.4.1. OTHER EFFICACY ENDPOINTS

- At each scheduled visit, change from Baseline in

  - PANSS total and subscale scores.
  - CGI-S score.
  - BACS composite score.
  - PSP total score.
  - EQ-5D-5L: VAS, index score and dimension score.
  - MSQ score.

- PANSS response, defined as a 20% or greater improvement from Baseline in PANSS total score, at each scheduled visit.

2.4.2. Other Safety Endpoints

- The incidence of overall AEs, serious AEs (SAEs), and AEs (or SAEs) leading to discontinuation.
- Observed values and changes from Baseline at each scheduled visit in clinical laboratory tests (hematology, chemistry, and urinalysis), vital signs (including temperature, height [as measured by a stadiometer], body weight, body mass index (BMI), waist circumference, blood pressure [supine and standing], pulse rate [supine and standing] and respiration rate) and 12-lead ECG parameters.
- Frequency and severity of suicidal ideation and suicidal behavior based on the C-SSRS.
- Change from Baseline in SAS, BARS and AIMS scores at each scheduled visit.
- Tanner stages at Baseline and each scheduled visit.
- Menstrual cyclicity (female adolescents only) at Endpoint (Week 6).
- Observed values and changes from Baseline at each scheduled visit in FSH, LH and estradiol (female adolescents only) and testosterone (male adolescents only).
- Healthcare resource utilization (HCRU) (including numbers of physician office visits, ER visits and hospitalizations, length of hospital stays, and average number of hours caregiver spend helping subjects per week).

CCI [redacted]

3. Study Design

3.1. General Description

This is a multicenter, randomized, double-blind, parallel-group, fixed-dosed study evaluating the efficacy and safety of two doses of SEP-363856 (50 and 75 mg/day) versus placebo over a 6-week Treatment Period in acutely psychotic subjects with schizophrenia. This study is projected to randomize approximately 435 adult subjects (18 to 65 years) to 3 treatment groups (SEP-363856 50 mg/day, SEP-363856 75 mg/day, or placebo) in a 1:1:1 ratio. CCI [redacted] In addition, the study will randomize approximately 90 adolescent subjects (13-17 years of age) at 1:1:1 ratio to the three treatment groups (with approximately 30

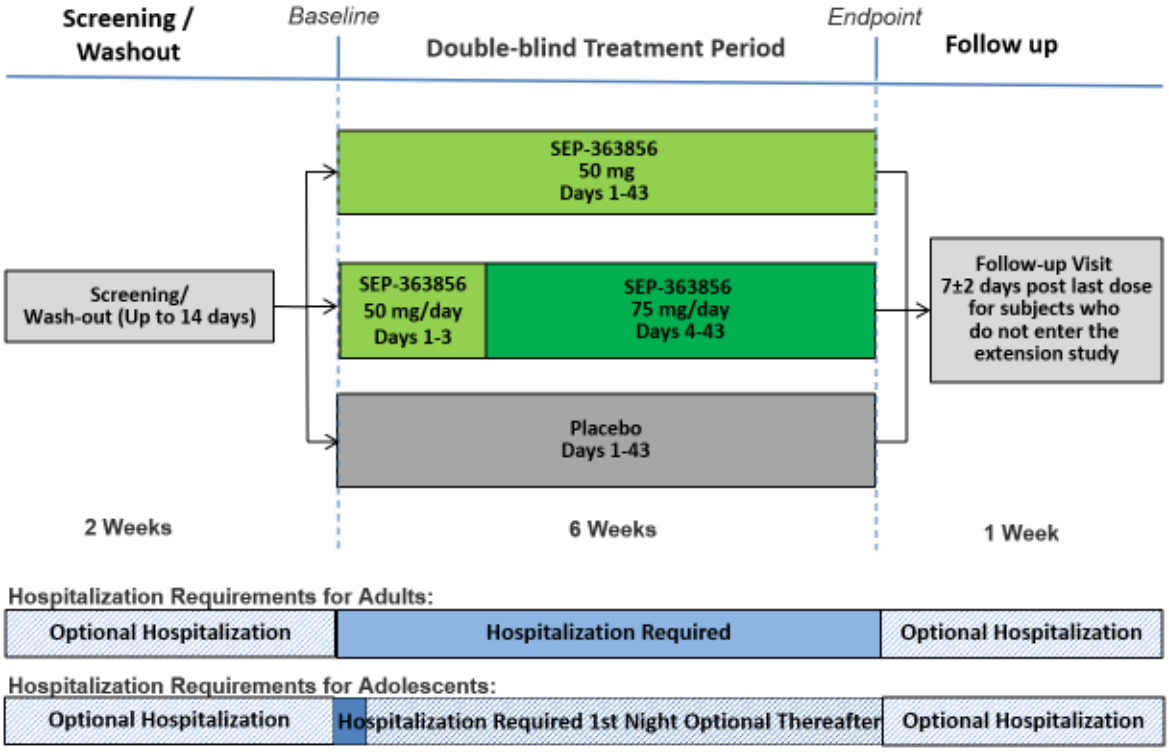
subjects per group) in a separate cohort. Treatment assignment will be stratified by country.

Study drug will be taken at the same time each evening at bedtime and may be taken with or without food.

The study will consist of 3 periods: Screening/Washout (up to 14 days), Treatment (6 weeks), and a Follow-up Visit (7 days after last study drug dose for subjects who discontinue prior to the Week 6 visit [Visit 9] or who complete the study but do not elect to enroll in the open-label extension study [SEP361-303]).

A study schematic is presented in Figure 1.

Figure 1: Study schematic – All Subjects



3.2. METHOD OF ASSIGNING SUBJECTS TO TREATMENT GROUPS

The randomization schedule is generated by a non-study biostatistician.

The adult and adolescent subjects are treated as two separate cohorts in the randomization schedule. Within each cohort, the randomization schedule is based on permuted blocks; in addition, randomization is stratified by country.

Once a subject is deemed eligible to be randomized at Day 1, an interactive web response system

(IWRS) will perform treatment assignment. Subjects will be randomized to one of the following treatment groups in a 1:1:1 ratio:

- SEP-363856 50 mg/day for 6 weeks
- SEP-363856 75 mg/day for 6 weeks
- Placebo once daily for 6 weeks

Once a randomization number has been assigned, it cannot be reused.

3.3. BLINDING

Subjects, Investigators, clinical site staff, persons performing the assessments, clinical operations personnel, data analysts, and personnel at central laboratories will remain blinded to the identity of the treatment from the time of randomization until database lock and unblinding, using the following methods:

- Randomization data are kept strictly confidential until the time of unblinding in the IWRS, and will not be accessible by anyone else involved in the study with the following exceptions: bioanalytical laboratory personnel involved in the analysis of PK samples, Data and Safety Monitoring Board (DSMB) members involved in regular review of safety data, external statistical staff involved in preparing materials for DSMB reviews, pharmacovigilance department for evaluation and reporting of SAEs, and the Sponsor's clinical trial materials management.
- Prolactin levels will be blinded except for results from Visit 1 (Screening).
- The identity of the treatments will be concealed by the use of study drugs that are all identical in packaging, labelling, schedule of administration and appearance.

CCI [redacted]

In the case of a medical emergency, where knowledge of study drug by the Investigator or an authorized delegate is essential for immediate medical management, a 24-hour code-break service will be available via the IWRS. The date and reason for unblinding are to be documented in the source documents. Any subject for whom the treatment assignment was unblinded is to be discontinued from further study participation. The subject should return for a final study assessment. The identity of those individuals at the study site who gain access to the unblinded treatment assignment must be documented. It is mandatory that all personnel who are involved in the unblinding, and who have access to the unblinded treatment assignment, maintain the confidentiality of the information and do not divulge the treatment assignment.

3.4. DETERMINATION OF SAMPLE SIZE

A total of 369 adult subjects (123 per treatment group: SEP-363856 50 mg/day, SEP-363856 75 mg/day, and placebo) with a global 2-sided alpha of 0.05 will provide 90% power to reject the null hypothesis of no difference in the mean primary efficacy endpoint against placebo for at least one SEP-363856 dose level and 75% power to reject the null hypothesis for both SEP-363856 dose levels using a truncated Hochberg ($\gamma = 0.9$) procedure, assuming a treatment effect size of 0.385 for both dose levels. A clinically meaningful effect size of 0.385 was estimated based on results from Study SEP361-201 and review of published studies of other antipsychotics for the short-term treatment of schizophrenia. The observed effect size in Study SEP361-201 was 0.45 after four weeks of flexible dosing with SEP-363856 at 50 or 75 mg/day. An upward adjustment of approximately 18% is used to compensate for information lost due to subjects who are randomized but drop out and are without complete efficacy data at all scheduled visits. The total sample size for the adult subjects will be 435 subjects randomized in 1:1:1 allocation ratio (or 145 subjects per treatment group). CCI [redacted]

In addition, 90 adolescent subjects (13-17 years) are planned to be randomized at 1:1:1 ratio to three treatment groups (with approximately 30 subjects per group). This sample size was not determined statistically, but rather based on clinical and practical considerations. This cohort of adolescents is considered sufficient for the evaluation of consistency of treatment effects with adult subjects and for the characterization of safety profile in this age group.

3.5. CHANGES IN THE CONDUCT OF THE STUDY

The first adult subject was screened on 17SEP2019 under protocol Version 1.00 (dated 24APR2019) and randomized on 24SEP2019 under the same protocol version. Additional protocol versions and amendments are listed below.

- Protocol version 2.00 (29JUL2019); Amendment 1.00 (29JUL2019).
- Protocol version 2.01 (18SEP2019); Non-substantial Amendment 1.00 (18SEP2019).
- Protocol version 3.00 (16SEP2020); Substantial Amendment 2.00 (16SEP2020).
- Protocol version 4.00 (26JAN2021); Substantial Amendment 3.00 (26JAN2021).
- Protocol version 5.00 (13OCT2022); Substantial Amendment 4.00 (13OCT2022).

3.6. SCHEDULE OF EVENTS

Schedule of events can be found in Section 1, Table 2 (Adult Subjects) and Table 3 (Adolescent Subjects) of the Clinical Study Protocol (CSP). These tables are also included in APPENDIX 15 of the SAP.

CCI [redacted]

4. PLANNED ANALYSES

The following analyses will be performed for this study:

- Analyses for independent DSMB meetings

CCI [redacted]

- Final Analysis

4.1. DATA AND SAFETY MONITORING BOARD

A DSMB SAP and charter, describing the methodology, meeting schedule, and presentation of results as well as access to results will be maintained by another Contract Research Organization (CRO) and Sumitomo Pharma America, Inc. (formerly Sunovion Pharmaceuticals Inc.; herein referred to as SMPA) as separate documents. All DSMB analyses will be performed independently by the CRO approximately three times a year after enough subjects are randomized.

CCI [redacted]

CCI [redacted]

4.3. FINAL ANALYSIS

All final, planned analyses specified in this SAP will be performed by IQVIA following SMPA authorization of this SAP, SMPA authorization of Analysis Populations, Database Lock, and Unblinding of Treatment.

If the adult portion of the study (main study) completes considerably earlier than the adolescent portion of the study, following the completion of the adult portion of the study, data from the adult subjects only will be locked, unblinded, and analyzed. The primary and secondary efficacy analyses are based on the adult subjects only. All Type I error will be used during these analyses. Adolescent data will be analyzed upon completion of the adolescent portion of the study and the adolescent database lock and treatment unblinding. Furthermore, analyses combining adult and adolescent subjects will be performed on selected data upon the completion of both portions.

Some minor modifications may be necessary to the planned design of tables, figures, and listings to accommodate data collected during the actual study conduct.

4.4. COHORTS ANALYSIS

The adolescent subject data will be reported separately from the adult subject data. Analyses combining adult and adolescent subjects will only be performed on selected data as specified in the respective sections.

5. ANALYSIS POPULATIONS

Agreement and authorization of subjects included/excluded from each analysis population will be conducted prior to database lock and the unblinding of the study treatment. Analysis populations will be determined separately for adult subjects and adolescent subjects.

No analysis population definition was updated due to COVID-19 or the Russia-Ukraine geopolitical conflict.

Randomized subjects will include all subjects who were randomized into the treatment period of the study and assigned a randomization number.

5.1. MODIFIED INTENT-TO-TREAT [MITT] POPULATION

The modified intent-to-treat (mITT) population will consist of all subjects who are randomized, have received at least one dose of study drug, and have a Baseline (see Section 6.2) and at least one post-Baseline efficacy measurement in PANSS or CGI-S. Subjects will be included in the mITT population

regardless of any protocol deviation.

The mITT population will be the primary population for the efficacy analyses. Subjects will be analyzed according to the treatment to which they are randomized.

5.2. PER PROTOCOL [PP] POPULATION

The per protocol (PP) population will consist of all mITT population subjects who satisfy the following conditions:

- Have 7 days or more overall exposure to study drug
- Did not receive benzodiazepines or hypnotics within 8 hours of the Baseline or final PANSS assessment
- Have no important protocol deviations that can potentially impact the integrity of the primary and/or secondary efficacy endpoint analysis, as determined by blinded data reviews prior to database lock

Selected efficacy endpoints will be analyzed using the PP population. Subjects will be analyzed according to the treatment to which they are randomized.

The PP population is not applicable to the adolescent cohort.

5.3. SAFETY [SAF] POPULATION

The safety (SAF) population will consist of all subjects who are randomized and have received at least one dose of study drug.

Safety population will be the primary population for the safety analyses. Subjects will be analyzed according to the actual treatment received. The actual treatment group will be determined as follows:

- For subjects randomized to the Placebo group:
  - If a subject took at least one dose of placebo during the entire double-blind treatment period, then the actual treatment group = Placebo.
  - If a subject took only SEP-363856 50 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 50 mg/day.
  - If a subject took only SEP-363856 75 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 75 mg/day.
  - If a subject took a mix of SEP-363856 50 mg and 75 mg treatments during the entire double-blind treatment period, then the actual treatment group = the SEP-363856 treatment that's taken for longer cumulative days. In case of tie, the actual treatment group = SEP-363856 75 mg/day.
- For subjects randomized to the SEP-363856 50 mg/day group:
  - If a subject took at least one dose of SEP-363856 50 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 50 mg/day.

- If a subject took only placebo during the entire double-blind treatment period, then the actual treatment group = Placebo.
- If a subject took only SEP-363856 75 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 75 mg/day.
- If a subject took a mix of placebo and SEP-363856 75 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 75 mg/day.

- For subjects randomized to the SEP-363856 75 mg/day group:
  - If a subject's last study drug dose date is prior to Day 4 and the subject took at least one dose of SEP-363856 treatment (regardless of dose level) during the entire double-blind treatment period, then the actual treatment group = SEP-363856 75 mg/day.
  - If a subject's last study drug dose date is prior to Day 4 and the subject took only placebo during the entire double-blind treatment period, then the actual treatment group = Placebo.
  - If a subject's last study drug dose date is on or after Day 4 and the subject took at least one dose of SEP-363856 75 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 75 mg/day.
  - If a subject's last study drug dose date is on or after Day 4 and the subject took only placebo during the entire double-blind treatment period, then the actual treatment group = Placebo.
  - If a subject's last study drug dose date is on or after Day 4 and the subject took only SEP-363856 50 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 50 mg/day.
  - If a subject's last study drug dose date is on or after Day 4 and the subject took a mix of placebo and SEP-363856 50 mg treatment during the entire double-blind treatment period, then the actual treatment group = SEP-363856 50 mg/day.

6. General Considerations

6.1. Reference Start Date and Study Day

Study Day will be calculated from the reference start date and will be used to show the start/stop day of assessments and events.

Reference start date is defined as the date of the first dose of study medication (Day 1 is the Study Day of the first dose of study medication).

- If the date of assessment or event is prior to the reference start date, then:

  Study Day = (date of assessment or event - reference start date).

- If the date of assessment or event is on or after the reference start date, then:

  Study Day = (date of assessment or event - reference start date) + 1.

In the situation where the assessment or event date is partial or missing, Study Day and any corresponding durations will appear missing in the listings. Partial assessment or event dates will however be presented as is in the listings.

6.2. BASELINE

Unless otherwise specified, Baseline is defined as the last non-missing measurement taken prior to the first dose of study medication (including unscheduled assessments).

Whenever available, the time information should be accounted for in the derivation of Baseline values. In the case where time is not available and the date of the last non-missing measurement and the date of the first dose of study medication coincide, that measurement will be considered the Baseline.

Baseline will be derived for the following outcome measures:

- PANSS: total score, subscale scores, Marder factor scores, uncorrelated PANSS score matrix (UPSM) factor scores and total factor score, and individual item scores. For a given subject, the Baseline values for all PANSS summary and individual item scores should come from the same assessment (i.e., have the same visit number and assessment start date/time) and it should be the last assessment prior to first dose where PANSS total score is available (i.e., not set to missing). In the rare event where no PANSS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most PANSS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- CGI-S score.

- BNSS (adult subjects only): total score, subscale scores, and individual item scores. For a given subject, the Baseline values for all BNSS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where BNSS total score is available. In the rare event where no BNSS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most BNSS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- MADRS (adult subjects only): total score and individual item scores. For a given subject, the Baseline values for all MADRS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where MADRS total score is available. In the rare event where no MADRS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most MADRS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- BACS: composite T score, component test T scores, and component test raw scores. For a given subject, the Baseline values for all BACS derived and raw scores should come from the same assessment and it should be the last assessment prior to first dose where BACS composite T score is available. In the rare event where no BACS composite T score is available before first dose due to partially completed assessments, the assessment prior to first dose with most BACS component test T scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- PSP: total score, individual domain scores, and the derived binary variables. For a given subject, the Baseline values for all PSP data should come from the same assessment and it should be the last assessment prior to first dose where PSP total score is available. In the rare event where no PSP total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most PSP individual domain scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- EQ-5D-5L: visual analog scale (VAS), index value, and dimension scores. For a given subject, the Baseline value for EQ-5D-5L VAS should come from the last assessment prior to first dose where the VAS value is available; the Baseline values for the index value and dimension scores should come from the same assessment and it should be the last assessment prior to first dose where the index value is available. In the rare event where no index value is available before first dose due to partially completed assessments, the assessment prior to first dose with most dimension scores available should be taken as the Baseline assessment for the dimension scores.

- UPSA-B (adult subjects only): total score, subscale scores, and individual item scores. For a given subject, the Baseline values for all UPSA-B summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where UPSA-B total score is available. In the rare event where no UPSA-B total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most UPSA-B item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- MSQ score.

- C-SSRS: Suicidal ideation categories 1-5 (yes/no) and suicidal behavior categories 6-10 (yes/no); C-SSRS composite endpoints: any suicidal ideation (yes/no), any suicidal behavior (yes/no), any suicidality (yes/no); the suicidal ideation score (0-5). See Section 17.6.1 for the definition of a C-SSRS Baseline.

- SAS: mean score and individual item scores. For a given subject, the Baseline values for all SAS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where SAS mean score is available. In the rare event where no SAS mean score is available before first dose due to partially completed assessments, the assessment prior to first dose with most SAS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- BARS: total score and individual item scores. For a given subject, the Baseline values for all BARS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where BARS total score is available. In the rare event where no BARS total score is available before first dose due to partially completed assessments, the assessment prior to first dose with most BARS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- AIMS: total score and individual item scores. For a given subject, the Baseline values for all AIMS summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where AIMS total score is available. In the rare event where no AIMS total score is

available before first dose due to partially completed assessments, the assessment prior to first dose with most AIMS item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- PSQI (adult subjects only): global score, component scores, and individual item scores. For a given subject, the Baseline values for all PSQI summary and individual item scores should come from the same assessment and it should be the last assessment prior to first dose where PSQI global score is available. In the rare event where no PSQI global score is available before first dose due to partially completed assessments, the assessment prior to first dose with most PSQI item scores available should be taken as the Baseline assessment for all raw and derived scores as applicable.

- Clinical laboratory parameters (blood chemistry, hematology, urinalysis, HOMA-IR, and adolescent specific hormonal parameters [FSH, LH, estradiol, testosterone]). For a given subject, the Baseline values for the clinical laboratory parameters do not have to all come from the same assessment; the only exception is: the Baseline flag for the counts of leukocytes and its differential should be applied to records from the same assessment and it should be the last assessment prior to first dose where counts of leukocytes and its differential are reported. Baseline flag does not need to be derived for RBC morphology findings, WBC morphology findings, and urinalysis microscopic examination findings (excluding urine erythrocytes and leukocytes).

- Urine drug screening: For a given subject, the Baseline values for all urine drug screening parameters should come from the same assessment and it should be the last assessment prior to first dose where a urine drug screening test was administered.

- Vital sign parameters (supine and standing systolic blood pressure [SBP], supine and standing diastolic blood pressure [DBP], supine and standing pulse rate, respiratory rate, oral temperature), height, weight, BMI, and waist circumference. For a given subject, the Baseline values for all vital sign parameters, height, weight, BMI, and waist circumference do not have to come from the same assessment; the only exceptions are: (1) the Baseline flag for weight and BMI should be applied to records from the same assessment and it should be the last assessment prior to first dose where weight is available (see note at the end of this bullet point about a situation where this rule may not hold), (2) the Baseline flag for supine SBP and DBP, standing SBP and DBP, and the derived corresponding orthostatic endpoints (i.e., standing SBP – supine SBP; standing DBP – supine DBP) should be applied to records from the same assessment and it should be the last assessment prior to first dose where all four BP measures are available, and (3) the Baseline flag for supine and standing pulse rate and the derived corresponding orthostatic endpoint (i.e., standing pulse rate – supine pulse rate) should be applied to records from the same assessment and it should be the last assessment prior to first dose where both pulse rate measures are available. [Note: If an adolescent subject only has height data available at the Screening visit, then their Baseline weight and Baseline BMI may come from different assessments.]

- ECG parameters: For a given subject, the Baseline values for all ECG parameters do not have to come from the same assessment. Baseline flag does not need to be derived for ECG parameters in the category of "FINDINGS".

- Tobacco use data (adult subjects only): Baseline of this outcome measure should be taken strictly from the assessment given at Visit 1 without regard to its temporal relationship to the first dose of study medication.

- Healthcare resource utilization data: Baseline of this outcome measure should be taken strictly from the assessment given at Visit 2 without regard to its temporal relationship to the first dose of study medication.

- Tanner staging data (adolescent subjects only): Baseline of this outcome measure should be taken strictly from the assessment given at Visit 2 without regard to its temporal relationship to the first dose of study medication.

- Menstrual cyclicity data (adolescent subjects only): Baseline of this outcome measure should be taken strictly from the assessment given at Visit 2 without regard to its temporal relationship to the first dose of study medication.

The Baseline flag may be derived for additional outcome measures based on the needs during analyses.

6.3. DERIVED TIMEPOINTS

The last non-missing post-Baseline (i.e., post-first dose) measurement collected during the study up to and including the Visit 9 (EOT/ET) measurement will be carried forward and defined as the last observation carried forward (LOCF) endpoint. Both scheduled and unscheduled assessments as well as the early termination assessments that are collected during this period will contribute to the derivation of the LOCF endpoint. However, unscheduled measurements taken after the Visit 9 (EOT/ET) measurement will not be used in the derivation.

The LOCF endpoint will be derived for the following outcome measures:

- PANSS: total score, subscale scores, Marder factor scores, UPSM factor scores and total factor score, individual item scores, and derived binary variables for PANSS response. For a given subject, the LOCF values for all PANSS summary and individual item scores and derived binary variables should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where PANSS total score is available. In the rare event where no PANSS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- CGI-S score.

- BNSS (adult subjects only): total score, subscale scores, and individual item scores. For a given subject, the LOCF values for all BNSS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where BNSS total score is available. In the rare event where no BNSS total score is available after first dose due to partially

completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- MADRS (adult subjects only): total score and individual item scores. For a given subject, the LOCF values for all MADRS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where MADRS total score is available. In the rare event where no MADRS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- BACS: composite T score, component test T scores, and component test raw scores. For a given subject, the LOCF values for all BACS derived and raw scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where BACS composite T score is available. In the rare event where no BACS composite T score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- PSP: total score, individual domain scores, and the derived binary variables. For a given subject, the LOCF values for all PSP data should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where PSP total score is available. In the rare event where no PSP total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- EQ-5D-5L: visual analog scale (VAS), index value, and dimension scores. For a given subject, the LOCF value for EQ-5D-5L VAS should come from the last post-Baseline assessment up to and including Visit 9 where the VAS value is available; the LOCF values for the index value and dimension scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where the index value is available. In the rare event where no index value is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for the dimension scores.

- UPSA-B (adult subjects only): total score, subscale scores, and individual item scores. For a given subject, the LOCF values for all UPSA-B summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where UPSA-B total score is available. In the rare event where no UPSA-B total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- MSQ score.

- C-SSRS suicidal ideation score (0-5).

- SAS: mean score and individual item scores. For a given subject, the LOCF values for all SAS summary and individual item scores should come from the same assessment and it should be the last post-Baseline

assessment up to and including Visit 9 where SAS mean score is available. In the rare event where no SAS mean score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- BARS: total score and individual item scores. For a given subject, the LOCF values for all BARS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where BARS total score is available. In the rare event where no BARS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- AIMS: total score and individual item scores. For a given subject, the LOCF values for all AIMS summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where AIMS total score is available. In the rare event where no AIMS total score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- PSQI (adult subjects only): global score, component scores, and individual item scores. For a given subject, the LOCF values for all PSQI summary and individual item scores should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where PSQI global score is available. In the rare event where no PSQI global score is available after first dose due to partially completed assessments, the last post-Baseline assessment up to and including Visit 9 should be taken as the LOCF assessment for all raw and derived scores as applicable.

- Clinical laboratory parameters (blood chemistry, hematology, urinalysis, HOMA-IR, and adolescent specific hormonal parameters [FSH, LH, estradiol, testosterone]). For a given subject, the LOCF values for the clinical laboratory parameters do not have to all come from the same assessment; the only exception is: the LOCF flag for the counts of leukocytes and its differential should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where counts of leukocytes and its differential are reported. LOCF endpoint does not need to be derived for RBC morphology findings, WBC morphology findings, and urinalysis microscopic examination findings (excluding urine erythrocytes and leukocytes).

- Urine drug screening: For a given subject, the LOCF values for all urine drug screening parameters should come from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where a urine drug screening test was administered.

- Vital sign parameters (supine and standing SBP, supine and standing DBP, supine and standing pulse rate, respiratory rate, oral temperature), height (adolescent only), weight, BMI, and waist circumference. For a given subject, the LOCF values for all vital sign parameters, height, weight, BMI, and waist circumference do not have to come from the same assessment; the only exceptions are: (1) the LOCF flag for weight and BMI should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where weight is available (see note at the end of this bullet point

about a situation where this rule may not hold), (2) the LOCF flag for supine SBP and DBP, standing SBP and DBP, and the derived corresponding orthostatic endpoints (i.e., standing SBP – supine SBP; standing DBP – supine DBP) should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where all four BP measures are available, and (3) the LOCF flag for supine and standing pulse rate and the derived corresponding orthostatic endpoint (i.e., standing pulse rate – supine pulse rate) should be applied to records from the same assessment and it should be the last post-Baseline assessment up to and including Visit 9 where both pulse rate measures are available. [Note: If an adolescent subject only has height data available at the Screening visit, then their LOCF BMI cannot be derived even though a LOCF weight may be derived so long as weight data are available at one or more visits post Baseline.]

- ECG parameters: For a given subject, the LOCF values for all ECG parameters do not have to come from the same assessment. LOCF endpoint does not need to be derived for ECG parameters in the category of "FINDING".

- Tobacco use data (adult subjects only): LOCF of this outcome measure should come from the same assessment and it should be the last assessment post first dose up to and including Visit 9 where any data are reported.

- Healthcare resource utilization data (adolescent subjects only): LOCF of this outcome measure should come from the same assessment and it should be the last assessment post first dose up to and including Visit 9 where any data are reported.

- Tanner staging data (adolescent subjects only): LOCF of this outcome measure should come from the same assessment and it should be the last assessment post first dose up to and including Visit 9 where any data are reported.

- Menstrual cyclicity data (adolescent subjects only): LOCF of this outcome measure should come from the same assessment and it should be the last assessment post first dose up to and including Visit 9 where any data are reported.

The study visits will be mapped to analysis visits for table summaries and statistical analyses where applicable (Table 1). No follow-up visit (i.e., Visit 10) data will be included in any MMRM/ANCOVA analyses.

Table 1: Mapping of study visits to analysis visits.

Study Visit	Analysis Visit Number	Analysis Visit
Visit 1	1	Screening/Visit 1
Visit 2	2	Randomization/Visit 2
Visit 3	3	Day 4/Visit 3
Visit 4	4	Week 1/Visit 4

Study Visit	Analysis Visit Number	Analysis Visit
Visit 5	5	Week 2/Visit 5
Visit 6	6	Week 3/Visit 6
Visit 7	7	Week 4/Visit 7
Visit 8	8	Week 5/Visit 8
Visit 9 (if representing true EOT visit). For ET visit mapping see Section 6.4.	9	Week 6/Visit 9
Visit 10	10	Week 7/Follow-up/Visit 10

Original study visit collected on the case report forms (CRFs) will be displayed in the listings.

6.4. Retests, Unscheduled Visits, and Early Termination Data

In general, for by-visit summaries, data recorded at the planned visits where assessment is intended to be given will be presented, as well as the derived Baseline value and the LOCF value.

Unscheduled measurements will not be included in by-visit summaries as a separate time point. Unscheduled measurements collected prior to the first dose of study medication will contribute to the derivation of the Baseline value. Unscheduled measurements collected post Baseline will contribute to the derivation of the LOCF value, the potential clinically significant (PCS) value, and the best/worst case value where required (e.g., shift table).

In the case of a retest, the assessment recorded under the planned visit will be used for by-visit summaries, and the assessment(s) recorded under unscheduled visit(s) will be presented in listings only.

As per protocol, study Visit 9 can be a Week 6/End of Treatment (EOT) visit or an Early Termination (ET) visit. If a subject terminates early, his/her measurements taken at the ET visit will be mapped to the next planned visit (after the last scheduled visit the subject attended) during which that assessment was expected to be performed as specified by the Schedule of Assessments table in the protocol. This applies to both efficacy and safety data.

Listings will include scheduled, unscheduled, retest and early discontinuation data with original dates and visits displayed.

6.5. Windowing Conventions

No visit windowing will be performed during the analysis for this study. Data will be analyzed according to the schedule outlined in the CSP.

6.6. Statistical Tests

The default significance level will be 5%; confidence intervals (CIs) will be 95%. All p-values and CIs will be two-sided, unless otherwise specified in the description of the analyses or the outputs.

6.7. Common Calculations

For quantitative measurements, change from Baseline will be calculated as:

- Test Value at Visit X - Baseline Value

For PANSS total score, percentage change from Baseline will be calculated as:

- (Test Value at Visit X - Baseline Value) × 100 / (Baseline Value - 30)

For other quantitative measurements, percentage change from Baseline will be calculated as:

- (Test Value at Visit X - Baseline Value) × 100 / Baseline Value

6.8. Software Version

All analyses will be conducted using SAS version 9.4 or later.

7. Statistical Considerations

7.1. Adjustments for Covariates and Factors to be Included in Analyses

The following covariates and factors are used in the analyses. For details of their inclusion in the models, see the specific analysis sections.

- Baseline value of the variable to be analyzed
- Country (adult subjects)
  - United States
  - Bulgaria
  - Russia
  - Serbia
  - Ukraine

- Country (adolescent subjects)
  - United States
  - Serbia
- Region
  - US
  - Non-US

7.2. MULTICENTER STUDIES

This study will be conducted by multiple investigators at multiple centers in the US and non-US countries, including Bulgaria, Russia, Serbia, and Ukraine. Randomization is stratified by country.

When specified, statistical analysis will be adjusted for country.

A term for treatment-by-country interaction will not be included in the primary analysis model, but the presence of such an interaction at Week 6/Visit 9 will be explored as part of the subgroup analysis (see Section 16.1.6 and Section 16.2.6). A significant interaction effect is defined as having a nominal p-value ≤ 0.10. Additionally, graphical methods (i.e., Forest plots) will be used to present the analysis results separately for each country and to assess whether the interaction, if there is one, is quantitative (i.e., the treatment effect is consistent in direction but not in size) or qualitative (i.e., the treatment is beneficial for some but not for other countries). Countries that do not have at least 2 mITT population subjects with change from Baseline data relevant to the given by-country subgroup analysis at Week 6/Visit 9 in each of the three treatment groups will be excluded from the analysis.

Center pooling will not be implemented in analyses for this study.

7.3. MISSING DATA

For the MMRM models on observed data, missing observations are treated as missing at random (MAR) and no imputation for missing data will be applied.

With the exception of one supplementary analysis on PANSS total score (see Section 16.1.5.4), BNSS total score (see Section 16.3.3.9), and MADRS total score (see Section 16.3.3.10), individual missing items in any scale will not be imputed in any analysis. When calculating a total score, subscale score, or any summary scores based on more than one item, if one or more items are missing at a visit, then the associated summary score will be set to missing. For additional details, see the individual scale description sections.

- Handling of missing efficacy data, if any, is described in Sections 16.1.2, 16.2.2 and 16.3.2.
- Handling of missing safety data, if any, is described in Sections 0 and 17.6.
- See APPENDIX 2 for details of handling incomplete/missing dates.

- Handling of missing data due to COVID-19-related early discontinuation in sensitivity analyses are detailed in Section 16.1.4.2, Section 16.1.4.3, and Section 16.1.4.4.

7.4. MULTIPLE COMPARISONS/ MULTIPLICITY

Type I error control will only be performed for the primary analysis of the primary and secondary efficacy endpoints in the adult mITT population. Nominal p-values (i.e., without multiplicity adjustment) will be reported for all other statistical tests.

Multiplicity adjustment will be applied to address the following three sources of multiplicity:

1) Analysis of the primary endpoint and the secondary efficacy endpoint
2) Analysis of two SEP-363856 dose-placebo comparisons

CCI

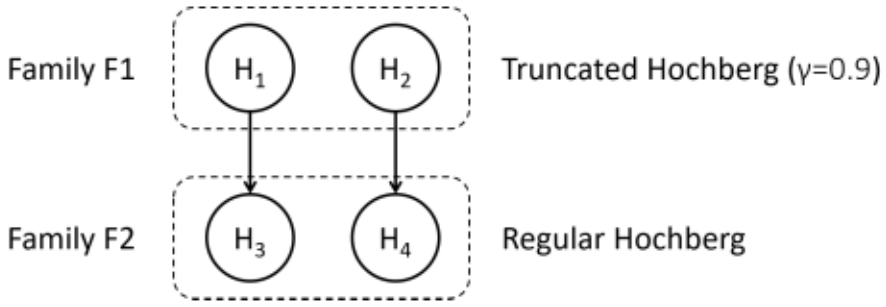
The first two sources of multiplicity will be addressed through a Hochberg-based gatekeeping procedure derived using the enhanced mixture method. This gatekeeping procedure is derived using the mixture methodology that was originally proposed in (Dmitrienko & Tamhane, 2011) (Dmitrienko & Tamhane, 2013) and later enhanced in (Kordzakhia, et al., 2018).

The null hypotheses of no difference in treatment effect between each of the SEP-363856 dose levels and placebo associated with the primary and the secondary efficacy endpoint are grouped into two hierarchical families:

- Family F1: SEP-363856 50 mg/day vs placebo (H_1), and SEP-363856 75 mg/day vs placebo (H_2), based on change from Baseline in PANSS total score at Week 6 (E_1)
- Family F2: SEP-363856 50 mg/day vs placebo (H_3), and SEP-363856 75 mg/day vs placebo (H_4), based on change from Baseline in CGI-S score at Week 6 (E_2)

In this Hochberg-based gatekeeping procedure, the truncated Hochberg ($\gamma = 0.9$) procedure will be applied to the hypotheses in Family F1 (H_1 and H_2) and the regular Hochberg procedure will be applied to the hypotheses in Family F2 (H_3 and H_4). There is a serial logical restriction among the hypotheses, that is, H_3 is testable only if H_1 is rejected and H_4 is testable only if H_2 is rejected (Figure 2).

Figure 2: Gatekeeping procedure for multiplicity problem with a serial logical restriction



CCI [redacted]

Let p_1 through p_4 denote the one-sided treatment effect p-values of the 4 null hypotheses (H_1 through H_4) computed from the Stage 1 data using the MMRM models described in Section 16.1.3.3 and Section 16.2.3.3 for the primary endpoint and the secondary efficacy endpoint respectively. Similarly, let q_1 through q_4 denote the one-sided treatment effect p-values of the 4 null hypotheses computed from the Stage 2 data. These two sets of raw p-values will be combined using a pre-defined weighted inverse normal combination function to obtain the combined one-sided p-values (r_1 through r_4) for the four null hypotheses:

$$r_i = c(p_i, q_i) = 1 - \Phi\left(\sqrt{w}\Phi^{-1}(1-p_i) + \sqrt{1-w}\Phi^{-1}(1-q_i)\right), \quad i = 1,2,3,4$$

where $\Phi(x)$ denotes the cumulative distribution function of the standard normal distribution, and w and $1-w$ are the pre-defined weights assigned to Stage 1 and Stage 2 respectively. The Stage 1 weight w will be set to 0.6 CCI [redacted]

These combined one-sided p-values are then passed to the Hochberg-based gatekeeping procedure which is defined using the closed testing principle. The closed family associated with these four null hypotheses contains 15 intersection hypotheses. For an arbitrary index set I, let $H(I)$ denote the intersection hypothesis and let $r(I)$ denote the local p-value for $H(I)$ which will be calculated using the enhanced mixture method (Kordzakhia, et al., 2018) (APPENDIX 4).

The resulting local p-values can be used to perform inferences for the four null hypotheses at the final analysis. A given null hypothesis will be rejected if the local p-values of all intersection hypotheses containing this hypothesis are less than or equal to a one-sided α = 0.025. In other words, a given null hypothesis H_i (i = 1, 2, 3, 4) will be rejected if its adjusted p-value, defined as

$$\tilde{r}_i = max_{I:i\in I} r(I)$$

does not exceed a one-sided α = 0.025.

7.5. EXAMINATION OF SUBGROUPS

Subgroup analyses will be conducted for adult subjects as stated in Section 16.1.6 for PANSS, Section 16.2.6 for CGI-S, and Section 17.1.10 for Adverse Events. It should be noted that the study was not designed to detect treatment differences with high statistical power within subgroups.

The following subgroups will be assessed:

- Geographic region:
  - US
  - Non-US
- Country:
  - United States
  - Bulgaria
  - Russia
  - Serbia
  - Ukraine
- Sex:
  - Female
  - Male
- Age group:
  - ≤40 years
  - >40 years
- Race (in 3 categories):
  - White (White)
  - Black (Black or African American)
  - Other (All other races combined)
- Number of prior hospitalizations for treatment of schizophrenia:
  - 0
  - 1
  - 2
- Duration of schizophrenia (years):
  - <5
  - ≥5
- BMI (kg/m^2) categories:
  - Underweight: <18.5 kg/m^2
  - Normal: ≥18.5 to <25.0 kg/m^2
  - Overweight: ≥25.0 to <30.0 kg/m^2
  - Obese: ≥30.0 kg/m^2
- Baseline patient type based on UPSM factor scores at Baseline (Hopkins S. , Ogirala, Loebel, & Koblan, 2020) (only used in the subgroup analysis of the primary endpoint):

- Type 1: Prominently Disorganized
- Type 2: Prominently Negative
- Type 3: Prominently Hostile
- Type 4: Prominently Positive
- Type 5: Prominently Affective

Subjects will be classified into one of 5 patient types based on their PANSS UPSM factor scores at Baseline. See APPENDIX 13 for details of how the classification will be made.

- Baseline Marder PANSS Negative Symptoms (MPNS) enrichment based on Screening/Visit 1 and Randomization/Visit 2 PANSS item scores (only used in the subgroup analysis of the primary endpoint):

  - MPNS enriched
  - MPNS de-enriched

  See APPENDIX 14 for details of how the classification will be made.

8. Output Presentations

APPENDIX 1 shows conventions for presentation of data in outputs.

The templates provided with this SAP describe the presentations for this study and therefore the format and content of the summary tables, figures, and listings to be provided by IQVIA.

9. Disposition and Withdrawals

Disposition data will be presented both separately for adult subjects and adolescent subjects and with adult and adolescent subjects combined.

Unless otherwise specified, the disposition summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, SEP-363856 Combined, and Total.

All subjects who provide informed consent will be accounted for in this study. For adolescent subjects both informed consent and informed assent are required.

Subject disposition will be presented by the randomized treatment group (where applicable). The number and percentage of subjects who were screened, screen failed, randomized, received study drug, randomized but did not receive study drug, and completed or discontinued from the double-blind treatment period (including reasons for discontinuation) will be presented. In addition, the number and percentage of subjects who rolled over to the open-label extension study (SEP361-303) will be presented. Disposition will be presented separately for each country as well for adult subjects.

With respect to the above, the following definitions apply:

- Screened Subjects: Any subject who signed the study specific informed consent. (For adolescent subjects the study specific informed consent and informed assent are both required.)

- Screen Failures: Any subject who signed the study specific informed consent but either failed to meet study requirements during screening or met study requirements at screening but was not randomized.

Subjects who were screened more than once will be counted only once in the disposition summary based on the outcome of the last screening. If a subject failed multiple screenings, they will only be counted once as a screen failure. If a subject is randomized after multiple screenings, they will only be counted once as a randomized subject.

Discontinuation by visit will be summarized for the randomized subjects by the randomized treatment group.

Time to discontinuation of the double-blind treatment since first dose of study drug will be plotted using Kaplan-Meier curves for the safety population by the actual treatment group. Probability of remaining on treatment at Day 42, median time to discontinuation, and their 95% confidence intervals will be estimated using the Kaplan-Meier method for the safety population by the actual treatment group. For adult subjects, the log rank testing method will be used to test for differences among the treatment groups for time to discontinuation. The time to discontinuation table will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, and Total.

The number and percentage of randomized subjects will also be summarized by Region, Country, and Site, by the randomized treatment group.

Lastly, the number and percentage of randomized subjects included in and excluded from each analysis population will be summarized by the randomized treatment group, along with the reason for exclusion.

COVID-19 related analysis updates:

The number of subjects who failed screening due to COVID-19 related reasons, who discontinued early due to COVID-19 related reasons, and who completed the treatment period but did not roll over to the open-label extension study due to COVID-19 related reasons will be summarized in the disposition table.

Subjects affected by COVID-19 related study disruptions will be provided in data listings. These subjects will be identified as:

- *Subjects who failed screening due to COVID-19.*
- *Subjects who were randomized but discontinued from the treatment period due to COVID-19.*
- *Subjects who completed the treatment period but did not roll over to the open-label extension study (SEP361-303) due to COVID-19.*
- *Subjects who experienced a pre-treatment event / adverse event related to COVID-19.*
- *Subjects who had any protocol deviations related to COVID-19.*
- *Subjects who had any investigator comments related to COVID-19.*

A subject may be identified in one or more categories listed above.

Russia-Ukraine geopolitical conflict related analysis updates:

The number of subjects who failed screening due to geopolitical conflict related reasons, who discontinued early due to geopolitical conflict related reasons, and who completed the treatment period but did not roll over to the open-label extension study due to geopolitical conflict related reasons will be summarized in the disposition table.

Subjects affected by geopolitical conflict related study disruptions will be provided in data listings. These subjects will be identified as:

- *Subjects who failed screening due to geopolitical conflict.*
- *Subjects who were randomized but discontinued from the treatment period due to geopolitical conflict.*
- *Subjects who completed the treatment period but did not roll over to the open-label extension study (SEP361-303) due to geopolitical conflict.*
- *Subjects who experienced a pre-treatment event / adverse event related to geopolitical conflict.*
- *Subjects who had any protocol deviations related to geopolitical conflict.*
- *Subjects who had any investigator comments related to geopolitical conflict.*

A subject may be identified in one or more categories listed above.

9.1. DERIVATIONS

- Time to discontinuation of the double-blind treatment in days

  For the purpose of this analysis, a subject's last dose date will be derived as follows:

  - If a subject's observed last dose date is before or on the date of Study Day 42, the derived last dose date will be set to the observed last dose date.
  - If a subject's observed last dose date is after the date of Study Day 42, the derived last dose date will be set to the date of Study Day 42.

  Time to discontinuation (days) = Derived last dose date – First dose date + 1.

  Subjects who complete the double-blind treatment will be censored on the derived last dose date.

10. IMPORTANT PROTOCOL DEVIATIONS

Important protocol deviations (IPDs) will be identified and documented for both adult and adolescent subjects based on blinded reviews of data listings and the protocol deviations log; the data will be presented separately.

Unless otherwise specified, the IPD summary tables will include the following columns: Placebo, SEP-

363856 50 mg/day, SEP-363856 75 mg/day, SEP-363856 Combined, and Total.

The IPD categories may include, but may not be limited to:

- Did not satisfy inclusion and/or exclusion criteria.
- Received prohibited medication.
- Overall double-blind compliance rate <75% or >125%.

IPDs will be identified for all randomized subjects and presented in a data listing. The number and percentage of subjects within each IPD category will be summarized by the randomized treatment group for the mITT population and by the actual treatment group for the SAF population.

A dedicated listing will present protocol deviations related to COVID-19 in randomized subjects. A separate dedicated listing will present protocol deviations related to the Russia-Ukraine geopolitical conflict in randomized subjects.

Two sets of clinical trial management system (CTMS) deviation categories are used in the study: former categories used for deviations reported up to 15MAY2022 and new categories for deviations reported as of 16MAY2022. These categories will be presented as is in the listings.

11. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic and other Baseline characteristics will be presented separately for adult subjects and adolescent subjects.

Unless otherwise specified, the demographic and Baseline characteristics summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, SEP-363856 Combined, and Total.

Demographic data and other Baseline characteristics will be presented for the mITT population, SAF population, and PP population (adult subjects only). In addition, for adult subjects only, demographics and other Baseline characteristics data will be summarized separately for Stage 1 and Stage 2 subjects (as defined in Section 7.4) on the mITT population. For the mITT and PP populations, the data will be presented by the randomized treatment group. For the SAF population, the data will be presented by the actual treatment group.

Basic demographic data (age, sex, race, ethnicity, country, and region) will also be summarized for all screened subjects by randomization status (i.e., randomized vs. not randomized).

No statistical testing will be carried out for demographic or other Baseline characteristics.

The following demographic and other Baseline characteristics will be reported for this study. Unless otherwise specified, the categories below apply to both adult subjects and adolescent subjects.

- Age (years) - calculated relative to date of informed consent for adult subjects, and relative to the later of (date of informed consent and date of informed assent) for adolescent subjects; as a continuous variable
- Age (years) categories for adult subjects:

- <18 years
- ≥18 to ≤40 years
- >40 to ≤65 years
- >65 years

- Age (years) categories for adolescent subjects:

  - <13 years
  - ≥13 to <16 years
  - ≥16 to <18 years
  - ≥18 years

- Age (years) categories for ClinicalTrials.gov (CTR.GOV) (to be presented for both adult subjects and adolescent subjects):

  - ≤18 years
  - >18 to <65 years
  - ≥65 years

- Age (years) categories for European Union Drug Regulating Authorities Clinical Trials Database (EudraCT) (to be presented for both adult subjects and adolescent subjects):

  - <12 years
  - ≥12 to <18 years
  - ≥18 to <65 years
  - ≥65 years

- Sex:

  - Female
  - Male

- Race:

  - American Indian or Alaska Native
  - Asian
  - Black or African American
  - Native Hawaiian or Other Pacific Islander
  - White
  - Multiracial
  - Other

- Ethnicity:

  - Hispanic or Latino
  - Not Hispanic or Latino

- Country for adult subjects:
  - United States
  - Bulgaria
  - Russia
  - Serbia
  - Ukraine
- Country for adolescent subjects:
  - United States
  - Serbia
- Geographic region:
  - US
  - Non-US
- Baseline Height (cm), as a continuous variable
- Baseline Weight (kg), as a continuous variable
- Baseline BMI (kg/m^2), as a continuous variable
- Baseline BMI (kg/m^2) category for adult subjects:
  - Underweight: <18.5 kg/m^2
  - Normal: ≥ 18.5 to <25.0 kg/m^2
  - Overweight: ≥ 25.0 to <30.0 kg/m^2
  - Obese: ≥ 30.0 kg/m^2
- Baseline Waist Circumference (cm), as a continuous variable
- Baseline PANSS Total Score, as a continuous variable
- Baseline PANSS Total Score categories:
  - < Overall median Baseline value
  - ≥ Overall median Baseline value
- Baseline PANSS Subscale Scores, as continuous variables
- Baseline PANSS Subscale Score categories:
  - < Overall median Baseline value
  - ≥ Overall median Baseline value

- Baseline PANSS Positive vs Negative Subscale Score categories:
  - Positive Subscale Score < Negative Subscale Score
  - Positive Subscale Score ≥ Negative Subscale Score
- Patient type based on Baseline UPSM factor scores:
  - Type 1: Prominently Disorganized
  - Type 2: Prominently Negative
  - Type 3: Prominently Hostile
  - Type 4: Prominently Positive
  - Type 5: Prominently Affective
- Baseline MPNS enrichment:
  - MPNS enriched
  - MPNS de-enriched
- Baseline CGI-S Score, as a continuous variable
- Baseline CGI-S Score categories:
  - <4
  - ≥4 to ≤5
  - >5

The following psychiatric history data will be summarized for the mITT population, SAF population, and PP population (adult subjects only) in separate tables. For the mITT and PP populations, the data will be presented by the randomized treatment group. For the SAF population, the data will be presented by the actual treatment group.

- Time since initial onset of schizophrenia (years) - calculated relative to date of informed consent for adult subjects, and relative to the later of (date of informed consent and date of informed assent) for adolescent subjects
- Time since initial onset of schizophrenia (years) categories for adult subjects:
  - <5 years
  - ≥5 to <10 years
  - ≥10 to <20 years
  - ≥20 years
- Age at initial onset of schizophrenia (years)
- Time since onset of current acute exacerbation of psychotic symptoms (days) - calculated relative to date of informed consent for adult subjects, and relative to the later of (date of informed consent and date of informed assent) for adolescent subjects

- DSM-5 schizophrenia subtype diagnosis:
  - 295.90 Schizophrenia
  - 293.89 Schizophrenia with Catatonia
- Number of prior hospitalizations for treatment of schizophrenia:
  - 0
  - 1
  - 2
  - 3
  - 4 or more
- Time since first hospitalization for treatment of schizophrenia (years) - calculated relative to date of informed consent for adult subjects, and relative to the later of (date of informed consent and date of informed assent) for adolescent subjects
- Age at first hospitalization for treatment of schizophrenia (years)
- Time since first antipsychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia (years) - calculated relative to date of informed consent for adult subjects, and relative to the later of (date of informed consent and date of informed assent) for adolescent subjects
- Age at first antipsychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia (years)
- Any other current psychiatric disorders:
  - Yes
  - No
- Time since onset of initial behavioral disturbance (years) (adolescent subjects only) - calculated relative to the later of (date of informed consent and date of informed assent)
- Age at onset of initial behavioral disturbance (years) (adolescent subjects only)
- Has subject ever taken an antipsychotic medication to treat any psychiatric disorders (adolescent subjects only):
  - Yes
  - No

Diagnosis and DSM-5 code for any other current psychiatric disorders will be summarized in a separate table. These other current psychiatric disorders will be coded using Medical Dictionary for Regulatory Activities (MedDRA) central coding dictionary, Version 22.0, and presented by System Organ Class (SOC) and Preferred Term (PT).

For adult subjects, healthcare resource utilization data collected at Baseline will be summarized

descriptively by actual treatment group for the SAF population. The frequency and percentage of subjects with physician's office visits, ER visits, and hospitalizations (for any reason and those related to schizophrenia) at Baseline (capturing the information during the past 3 months) will be summarized. The number of physician's office visits, ER visits, and hospitalizations (for any reason and those related to schizophrenia) per month at Baseline, as well as the average length of hospital stays (for any reason and those related to schizophrenia) at Baseline, will be summarized. Employment status at Baseline will be summarized. The frequency and percentage of subjects receiving unpaid care at Baseline, along with the average number of hours a caregiver spends per week helping the subject, will also be summarized.

11.1. DERIVATIONS

- BMI expressed in kg/m^2:

  Weight (kg)/ height $(m)^2$.

- Time since initial onset of schizophrenia, expressed in years:

  (Date of Informed Consent - Date of initial onset of schizophrenia <observed or imputed [see APPENDIX 2]>) / 365.25

  Note 1: For adolescent subjects, Date of Informed Consent should be replaced by: The Later of (Date of Informed Consent and Date of Informed Assent).

  Note 2: Round to one decimal place for each subject's calculated duration.

- Age at initial onset of schizophrenia, expressed in years:

  (Date of initial onset of schizophrenia <observed or imputed [see APPENDIX 2]> - Date of birth + 1) / 365.25

  Note: Round to one decimal place for each subject's calculated age.

- Time since onset of current acute exacerbation of psychotic symptoms, expressed in days:

  Date of Informed Consent - Date of onset of current acute exacerbation of psychotic symptoms <observed or imputed [see APPENDIX 2]>

  Note: For adolescent subjects, Date of Informed Consent should be replaced by: The Later of (Date of Informed Consent and Date of Informed Assent).

- Time since first hospitalization for treatment of schizophrenia, expressed in years:

(Date of Informed Consent – Date of first hospitalization for treatment of schizophrenia <observed or imputed [see APPENDIX 2]>) / 365.25

Note 1: For adolescent subjects, Date of Informed Consent should be replaced by: The Later of (Date of Informed Consent and Date of Informed Assent).

Note 2: Round to one decimal place for each subject's calculated duration.

Note 3: For subjects whose date of first hospitalization for treatment of schizophrenia is completely missing AND the number of prior hospitalizations for treatment of schizophrenia is 0, set the time since first hospitalization for treatment of schizophrenia to 0.

- Age at first hospitalization for treatment of schizophrenia, expressed in years:

  (Date of first hospitalization for treatment of schizophrenia <observed or imputed [see APPENDIX 2]> - Date of birth + 1) / 365.25

  Note: Round to one decimal place for each subject's calculated age.

- Time since first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia, expressed in years:

  (Date of Informed Consent - Start date of first anti-psychotic drug therapy of at least 2 weeks duration <observed or imputed [see APPENDIX 2]>) / 365.25

  Note 1: For adolescent subjects, Date of Informed Consent should be replaced by: The Later of (Date of Informed Consent and Date of Informed Assent).

  Note 2: Round to one decimal place for each subject's calculated duration.

- Age at first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia, expressed in years:

  (Start date of first anti-psychotic drug therapy of at least 2 weeks duration <observed or imputed [see APPENDIX 2]> - Date of birth + 1) / 365.25

  Note: Round to one decimal place for each subject's calculated age.

- Time since onset of initial behavioral disturbance, expressed in years:

  (The Later of [Date of Informed Consent and Date of Informed Assent] – Date of onset of initial behavioral disturbance <observed or imputed [see APPENDIX 2]>) / 365.25

  Note: Round to one decimal place for each subject's calculated duration.

- Age at onset of initial behavioral disturbance, expressed in years:

  (Date of onset of initial behavioral disturbance <observed or imputed [see APPENDIX 2]> - Date of birth + 1) / 365.25

  Note: Round to one decimal place for each subject's calculated age.

12. MEDICAL HISTORY

Medical and surgical history data will be presented separately for adult subjects and adolescent subjects.

Unless otherwise specified, the medical and surgical history summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, SEP-363856 Combined, and Total.

Medical and surgical history information, including both past and concomitant medical conditions and major surgical history, as collected on the "*Medical History*" CRF form, will be coded using MedDRA, Version 22.0, and presented by SOC and PT for the SAF population by the actual treatment group. Data will be sorted by SOC based on the internationally agreed order (APPENDIX 7) and by PT in decreasing frequency in the "SEP-363856 Combined" column.

13. MEDICATIONS

Medications data will be presented separately for adult subjects and adolescent subjects.

Unless otherwise specified, the medications summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, SEP-363856 Combined, and Total.

Medications will be coded to Anatomical Therapeutic Chemical (ATC) Levels and Preferred Names according to World Health Organization Drug (WHODRUG) dictionary, Version 01MAR2019.

Whenever available, the time information should be accounted for in the derivation of prior, concomitant, and post-treatment medications. See APPENDIX 2 for the handling of partial dates for medications. In the case where it is not possible to define a medication as prior, concomitant, or post treatment, the medication will be classified by the worst case; i.e., concomitant.

- Prior medications are medications which stopped prior to the first dose of study medication.

- Concomitant medications are medications which started at the same time of or after the first dose of study medication and at the same time of or before the last dose of study medication; or started prior to and ended at the same time of or after the first dose of study medication; or started at the same time of or prior to the last dose of study medication and marked as ongoing.

- Post-treatment medications are medications which started after the last dose of study medication.

Prior and concomitant medication use will be summarized by ATC Level 3 and Preferred Base Name for

the SAF population by the actual treatment group. Medications will be sorted by ATC Level 3 alphabetically and by Preferred Base Name in decreasing frequency in the "SEP-363856 Combined" column.

Prior, concomitant, and post-treatment medications will be provided in data listings.

Psychotropic and/or Sedating Medications taken by subjects prior to each visit as collected on the "*Timing of last dose of Psychotropic and/or Sedating Medications*" CRF form will be summarized by ATC Level 3 and Preferred Base Name for the SAF population by the actual treatment group and visit.

14. STUDY MEDICATION EXPOSURE

Exposure data will be presented separately for adult subjects and adolescent subjects.

Unless otherwise specified, the study medication exposure summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, SEP-363856 Combined, and Total.

Exposure to study medication data will be summarized for the SAF population by the actual treatment group.

The date/time of first dose of study drug and the date/time of last dose of study drug will be respectively derived as the earliest ("Date Dosing Started" & "Time Dosing Started") pair and the latest ("Date Dosing Ended" & "Time Dosing Ended") pair as collected on the "*Study Drug Administration / Drug Accountability*" CRF form. The start and end dates/times from blister cards with the number of tablets dispensed equal to the (number of tablets returned + number of tablets reported lost) are excluded from the derivation.

Duration of exposure (in days) will be summarized both as a continuous variable for the double-blind treatment period and categorically:

- Number and percentage of subjects with exposure ≥ 1, ≥ 3, ≥ 7, ≥ 14, ≥ 21, ≥ 28, ≥ 35, and ≥ 42 days
- Number and percentage of subjects with exposure for 1 - 2, 3 - 6, 7 - 13, 14 - 20, 21 - 27, 28 - 34, 35 - 41, and ≥ 42 days

Total person-years of exposure will be calculated for each treatment group and overall for all subjects.

Mean daily dose and modal daily dose will be calculated for the entire double-blind treatment period and summarized.

Lastly, the number of days that a subject received the 50 mg/day dose level and the 75 mg/day dose level will be summarized for the SAF population both as a continuous variable and categorically:

- Number and percentage of subjects with exposure to a particular dose level for 1 - 2, 3 - 6, 7 - 13, 14 - 20, 21 - 27, 28 - 34, 35 - 41, and ≥ 42 days

14.1. DERIVATIONS

- Per protocol, for subjects randomized to the 75 mg/day group, a titration card is dispensed at Visit 2 which contains 3 tablets of 50 mg dose level and 6 tablets of 75 mg dose level. Drug accountability data is not separately collected for the two dose levels at Visit 2. For subjects who were dispensed the titration card at Visit 2, the following assumptions will be made during analysis:
  - The subject is assumed to have received the 50 mg treatment from Day 1 to Day 3, and the 75 mg treatment on the remaining days during the Visit 2/Visit 3 treatment period, regardless of when Visit 3 occurred.
  - The 75 mg treatment is assumed to have started on Day 4 at the same time as the recorded dosing start time for Visit 2. For example, if the recorded dosing start date/time for Visit 2 is 01JUL2019 at 20:00, the 75 mg treatment will be assumed to have started on 04JUL2019 at 20:00 and the 50 mg treatment will be assumed to have ended on 03JUL2019 at 20:00.
  - Within the Visit 2/Visit 3 treatment period, if a subject missed any dose on Day 1 to Day 3 according to the "*Missed Doses*" CRF form, then the number of 50 mg tablets taken by the subject will be adjusted accordingly; if a subject missed any dose on or after Day 4 according to the "*Missed Doses*" CRF form, then the number of 75 mg tablets taken by the subject will be adjusted accordingly.
- Duration of exposure (days) = date of last dose of study drug – date of first dose of study drug + 1. Interruptions in exposure (i.e., missed doses) and dose changes (if any) are not considered in the calculation of overall exposure.
- Total person-years of exposure is the sum of all durations of exposure in days / 365.25.
- Mean daily dose (mg/day):

$$\frac{\sum \text{Dose per tablet for Visit } j * (\text{\# Tablets Dispensed for Visit } j - \text{\# Tablets Returned for Visit } j - \text{\# Tablets Lost for Visit } j)}{\text{Duration of Exposure}}$$

  At Visit 2, for subjects who were dispensed the titration card with mixed dose levels, please refer to the first bullet in this section for assumptions to be used in dose calculation.

  If the number of tablets dispensed, returned, and/or lost as collected on the "*Study Drug Administration / Drug Accountability*" CRF form is missing for one or more visits, the mean daily dose will be calculated based on visits with complete drug accountability data available. That is, the numerator of the formula above will only include visits with the number of tablets dispensed, returned, and lost available, and the denominator should be adjusted to exclude dosing periods covered by visits excluded from the calculation (i.e., Duration of Exposure – dosing periods [sum of (EXENDTC – EXSTDTC+1)] covered by visits with missing or incomplete accountability data). If the dose level of a visit is unknown, that visit should be excluded from the calculation as well in both the numerator and the denominator.
- Modal daily dose will be determined as the daily dose that is taken for the most time (in terms of number of days) among all doses taken. Data collected on the "*Missed Doses*" CRF form should be taken into

consideration when deriving the modal daily doses. A subject's modal daily dose may fall in one of the categories below:

- Placebo
- 50 mg/day
- 75 mg/day
- Tie between 50 mg/day and 75 mg/day (i.e., the subject was on 50 mg/day and 75 mg/day for the same amount of time) (if needed)
- Tie between placebo and 50 mg/day (if needed)
- Tie between placebo and 75 mg/day (if needed)
- Tie between placebo, 50 mg/day, and 75 mg/day (if needed)

15. STUDY MEDICATION COMPLIANCE

Compliance will be presented separately for adult subjects and adolescent subjects.

Unless otherwise specified, the study medication compliance summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, SEP-363856 Combined, and Total.

Compliance to study medication will be presented for the SAF population, by the actual treatment group.

Percent compliance will be calculated overall for the double-blind treatment period. Non-compliance is defined as less than 75% or more than 125% non-missing compliance for the double-blind treatment period. Subjects with missing compliance will not be classified as non-compliant. Compliance will be summarized both as a continuous variable and categorically (i.e., number and percentage of subjects with compliance < 75%, 75% - 125%, > 125%, and missing).

15.1. DERIVATIONS

Overall Compliance (%) to study medication in percentage will be calculated as follows:

$$\frac{\sum(\#\text{ Tablets Dispensed for Visit } j - \#\text{ Tablets Returned for Visit } j - \#\text{ Tablets Lost for Visit } j)}{\#\text{ Tablets should be taken per day} \times \text{Duration of Exposure}} \times 100\%$$

If the number of tablets dispensed, returned, and/or lost as collected on the "*Study Drug Administration / Drug Accountability*" CRF form is missing for one or more visits, the overall compliance will be calculated based on visits with complete drug accountability data available. That is, the numerator of the formula above will only include visits with the number of tablets dispensed, returned, and lost available, and the denominator should be adjusted to exclude dosing periods covered by visits excluded from the calculation (i.e., change "Duration of Exposure" to be Duration of Exposure – dosing periods [sum of (EXENDTC – EXSTDTC+1)] covered by visits with missing or incomplete accountability data).

16. EFFICACY OUTCOMES

The efficacy data will be analyzed and presented separately for adult subjects and adolescent subjects. In addition, efficacy variables of change from Baseline in PANSS total score and CGI-S score at Week 6 will be analyzed on combined data from the adult and adolescent subjects (see Section 16.4).

Unless otherwise specified, the efficacy analysis and summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, and SEP-363856 75 mg/day.

All analyses of the efficacy variables will be based on the mITT population and, for selected variables/analyses, the PP population (adult subjects only) by the randomized treatment group.

Efficacy data collected after an emergency treatment unblinding (see protocol Section 7.2.3) will not be used in any statistical analysis. These data will be listed in data listings only.

16.1. PRIMARY EFFICACY

The analyses of the primary efficacy variable will be performed on the mITT population of the adult subjects, unless otherwise specified.

16.1.1. PRIMARY EFFICACY VARIABLE & DERIVATION

The primary efficacy variable is change from Baseline in PANSS total score at Endpoint (Week 6).

The PANSS (Positive and Negative Syndrome Scale) is an interview-based measure of the severity of psychopathology in adults with psychotic disorders and comprises 30 items and 3 subscales. The positive subscale assesses hallucinations, delusions and related symptoms (7 items), the negative subscale assesses emotional withdrawal, lack of motivation and related symptoms (7 items), and the general psychopathology subscale assesses other symptoms such as anxiety, somatic concern and disorientation (16 items).

An anchored Likert scale from 1 to 7 (1 = absent, 7 = extreme, with values of 2 and above indicating the presence of progressively more severe symptoms) is used to score each item. PANSS total score will be equal to the sum of the 30 items and ranges between 30 and 210.

PANSS is assessed at these study visits: Visit 1, Visit 2, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, and Visit 9. The Baseline PANSS total score will be derived as described in Section 6.2. The change from Baseline in PANSS total score at Week 6, as well as at the other post-Baseline time points, will be derived as described in Section 6.7.

16.1.2. MISSING DATA METHODS FOR PRIMARY EFFICACY VARIABLE

Other than one supplementary analysis (see Section 16.1.5.4), the PANSS total score at a given visit will be set to missing if at least one PANSS item is missing at that visit. The primary efficacy variable, change from Baseline in PANSS total score at Week 6, will be set to missing if PANSS total score at Week 6 is missing or if Baseline PANSS total score is missing. The same applies to all other visits.

The primary analysis of the primary efficacy variable will use a mixed model for repeated measures (MMRM) based on observed data only (with early termination data mapped as described in Section 6.4). Missing data will not be imputed.

16.1.3. Primary Analysis of Primary Efficacy Variable

16.1.3.1. Estimand

The primary efficacy estimand is defined as the difference between each SEP-363856 dose level and placebo in the mean change of PANSS total score from Baseline to Week 6 in acutely psychotic adult subjects with schizophrenia as characterized by the study inclusion/exclusion criteria, in the hypothetical setting where the subjects were able to stay on study and remain on the study treatment for 6 weeks.

The four attributes of the primary efficacy estimand are as follows:

A. Population of interest: Acutely psychotic adult subjects with schizophrenia, as characterized by the inclusion/exclusion criteria of the study. For the efficacy analyses, the mITT population will be used to represent the population of interest.

B. Variable (or endpoint) of interest: Change from Baseline in PANSS total score to Week 6.

C. Intercurrent event: The intercurrent event that is deemed to have an impact on the interpretation of the variable of interest is early withdrawal from study treatment for any reason. This intercurrent event will be handled with the hypothetical strategy. That is, the treatment effect of interest concerns the outcomes had all subjects completed 6 weeks of study treatment. The efficacy data after the last on-treatment visit will not be collected as these data are irrelevant to the treatment effect of interest. Rather, these data will be implicitly predicted based on the assumptions about how the data would evolve after treatment withdrawal.

D. Population-level summary for the variable: The difference in the mean change of PANSS total score from Baseline to Week 6.

16.1.3.2. Justification for the estimand

The primary efficacy estimand defining the treatment effect of interest uses the hypothetical strategy specified in the International Conference on Harmonization (ICH) E9(R1) Addendum. The primary objective of the study is to assess the symptomatic effect of SEP-363856 compared to placebo in treating acutely psychotic adult subjects with schizophrenia. The estimand, or target of estimation, following the hypothetical strategy is the pharmacological effect seen, had no withdrawals from study treatment occurred. This hypothetical estimand is justifiable in this case, since the focus is on the pharmacological effect of the drug additional to no other effects. Subjects who withdraw from a symptomatic study treatment either could have lost their treatment effect had the subjects not taken any other symptomatic medication after withdrawal, or could have had their treatment effect masked had the subjects taken other symptomatic medications after withdrawal. This means that any observations taken after subjects stop study treatment will most likely not contribute relevant information about the pharmacological effect of the drug. Under the hypothetical strategy, the primary endpoint of the trial could be considered as a combination of the observed responses at Week 6 from on-treatment completers and the implicitly predicted responses at Week 6 for subjects who withdraw from study

treatment during the trial based on certain assumptions about how the unobserved efficacy outcome would evolve in the hypothetical setting of no treatment withdrawal.

16.1.3.3. Hypotheses and statistical model

The efficacy of SEP-363856 in terms of the PANSS total score will be evaluated using the following two null hypotheses,

- H_1: There is no difference in the mean change from Baseline in PANSS total score at Week 6 between the SEP-363856 50 mg/day treatment arm and Placebo.
- H_2: There is no difference in the mean change from Baseline in PANSS total score at Week 6 between the SEP-363856 75 mg/day treatment arm and Placebo.

The alternative hypothesis for each of the null hypotheses is that there is a difference. If at least one of the two null hypotheses is rejected indicating treatment effect of SEP-363856, the study will be considered positive.

The primary analysis of the primary efficacy variable will be performed on the mITT population of the adult subjects.

For the primary analysis of the primary efficacy endpoint, data will be analyzed using a mixed model for repeated measures (MMRM) under the missing-at-random (MAR) assumption. Under this assumption, the efficacy outcome of subjects in each treatment group after early discontinuation will exhibit the same future evolution as subjects in the same group remaining in the study. The MMRM model will include fixed factors for treatment, visit (Day 4, Weeks 1, 2, 3, 4, 5 and 6; as a categorical variable), country, and treatment-by-visit interaction, and include Baseline PANSS total score as a covariate. An unstructured covariance matrix will be used to model the within-subject correlation. Kenward-Roger approximation will be used to calculate the denominator degrees of freedom.

The main estimator of the primary efficacy estimand is the least squares (LS) mean difference in PANSS total score change from Baseline at Week 6 (each SEP-363856 group vs. placebo) from the primary analysis model of observed repeated measures data. Their standard errors, the two-sided 95% CIs, and the associated nominal p-values will be calculated from the MMRM model.

In addition, the following statistics will be reported in the MMRM table:

- The LS mean difference in PANSS total score change from Baseline on Day 4 and at Weeks 1 to 5, their standard errors, the two-sided 95% CIs, and the associated nominal p-values.
- The LS mean of PANSS total score change from Baseline at each time point for each treatment group, their standard errors, and the two-sided 95% CIs.
- Within group effect size at each time point, calculated as the LS mean of each treatment group at each time point divided by the model estimate of standard deviation, obtained as the square root of the corresponding diagonal element of the residual covariance matrix (R matrix from PROC MIXED).
- Between group effect size vs. placebo at each time point, calculated as the LS mean difference of each SEP-363856 group vs. placebo at each time point divided by the model estimate of standard deviation,

obtained as the square root of the corresponding diagonal element of the residual covariance matrix (R matrix from PROC MIXED).

In case the model above fails to converge, a spatial exponential covariance structure and a spatial power covariance structure along with an empirical sandwich estimator for the standard errors of the fixed effect parameters will be assumed sequentially. The first covariance structure to yield convergence will be used in the analysis. If the model fails to converge with all three structures specified above, the compound symmetry covariance structure will be assumed.

The normality and homoscedasticity assumptions underlying the primary MMRM model will be assessed graphically and included in the SAS outputs. Marginal studentized and Pearson-type residuals will be plotted against the predicted marginal mean values, respectively; the quantile-quantile (Q-Q) plots of these residuals versus the expected quantiles of the standard normal distribution will also be included in the SAS outputs to provide a graphical view of similarity and difference in the 2 distributions.

CCI

[redacted]

Adjusted point and 95% CI estimates for the treatment effect of each SEP-363856 group (vs. placebo) at Week 6 will be obtained using the method described in (Lawrence & Hung, 2003) and reported in a separate table.

Specifically, the MMRM model described above will be run separately on Stage 1 data and Stage 2 data to obtain the LS mean difference (vs. placebo) for each SEP-363856 group at Week 6. Let $\hat{\delta}_1^{(1)}$ and $\hat{\delta}_2^{(1)}$ denote the Stage 1 LS mean differences (vs. placebo) of the SEP-363856 50 mg/day and 75 mg/day groups at Week 6. Similarly, let $\hat{\delta}_1^{(2)}$ and $\hat{\delta}_2^{(2)}$ denote the Stage 2 LS mean differences (vs. placebo) of the SEP-363856 50 mg/day and 75 mg/day groups at Week 6. The adjusted point estimates, $\hat{\delta}_1$ and $\hat{\delta}_2$, of the treatment effect of SEP-363856 50 mg/day and 75 mg/day groups (vs. placebo) at Week 6 (δ_1 and δ_2) will be obtained as:

$$\hat{\delta}_1 = \frac{t\hat{\delta}_1^{(1)} + \sqrt{1-t}\sqrt{t^*-t}\hat{\delta}_1^{(2)}}{t + \sqrt{1-t}\sqrt{t^*-t}}$$

$$\hat{\delta}_2 = \frac{t\hat{\delta}_2^{(1)} + \sqrt{1-t}\sqrt{t^*-t}\hat{\delta}_2^{(2)}}{t + \sqrt{1-t}\sqrt{t^*-t}}$$

where t denotes the information fraction CCI [redacted] t^* denotes the maximum information and will be calculated as the ratio of the total number of randomized subjects at the end of the trial over the original sample size of 435.

The adjusted lower and upper bounds of the 95% CI for the treatment effect of SEP-363856 50 mg/day and 75 mg/day groups (vs. placebo) will be calculated as:

$$\text{Adjusted 95\% CI for } \delta_1 = \frac{t\hat{\delta}_1^{(1)} + \sqrt{1-t}\sqrt{t^*-t}\hat{\delta}_1^{(2)} \pm \hat{k}_1^{-1}\Phi^{-1}(\alpha)}{t + \sqrt{1-t}\sqrt{t^*-t}}$$

$$\text{Adjusted 95\% CI for } \delta_2 = \frac{t\hat{\delta}_2^{(1)} + \sqrt{1-t}\sqrt{t^*-t}\hat{\delta}_2^{(2)} \pm \hat{k}_2^{-1}\Phi^{-1}(\alpha)}{t + \sqrt{1-t}\sqrt{t^*-t}}$$

where $\Phi^{-1}(x)$ denotes the inverse cumulative distribution function of the standard normal distribution; α = 0.025 denotes the one-sided significance level.

The values of $\hat{k}_1$ and $\hat{k}_2$ will be calculated as follows:

$$\hat{k}_1 = \frac{1}{2} \times \frac{T_1^{(1)}}{\sqrt{t}\hat{\delta}_1^{(1)}} + \frac{1}{2} \times \frac{T_1^{(2)}}{\sqrt{t^*-t}\hat{\delta}_1^{(2)}}$$

$$\hat{k}_2 = \frac{1}{2} \times \frac{T_2^{(1)}}{\sqrt{t}\hat{\delta}_2^{(1)}} + \frac{1}{2} \times \frac{T_2^{(2)}}{\sqrt{t^*-t}\hat{\delta}_2^{(2)}}$$

where $T_1^{(1)}$ and $T_2^{(1)}$ are the Stage 1 t-statistics from the MMRM model for testing the treatment effect of SEP-363856 50 mg/day and 75 mg/day groups (vs. placebo) at Week 6; $T_1^{(2)}$ and $T_2^{(2)}$ are the Stage 2 t-statistics from the MMRM model for testing the treatment effect of SEP-363856 50 mg/day and 75 mg/day groups (vs. placebo) at Week 6.

The observed PANSS total score and the change from Baseline values will also be summarized descriptively for the mITT population by treatment group and visit.

LS Means (+/- Standard Error) of PANSS total score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

16.1.4. Sensitivity Analyses of Primary Efficacy Variable

16.1.4.1. Dropout profiles

Patterns of the observed data in the primary endpoint will be examined through graphical tools based on the reason and the timing of study treatment withdrawal.

Mean change from Baseline in PANSS total score at each time point will be plotted by the reason of early discontinuation (adverse event [separately for: either COVID-19 or geopolitical conflict related, neither COVID-19 nor geopolitical conflict related], lack of efficacy, lost to follow-up, withdrawal by subject, non-compliance with study drug, protocol deviation, death [separately for: either COVID-19 or geopolitical conflict related, neither COVID-19 nor geopolitical conflict related], pregnancy, other [separately for: either COVID-19 or geopolitical conflict related, neither COVID-19 nor geopolitical conflict related]) and for completers, separately for each treatment group. Similar reasons may be combined, depending on the number of subjects who discontinued under each reason. Reason pooling will be determined at the Blinded Data Review meeting prior to database lock and treatment unblinding.

Mean change from Baseline in PANSS total score at each time point will also be plotted by the timing of early discontinuation (Day 4 terminators, Week 1 terminators, Week 2 terminators, Week 3 terminators, Week 4 terminators, Week 5 terminators, Week 6 terminators) and for completers, separately for each

treatment group.

- Day 4 terminators: subjects who discontinued after Visit 2 but before or on Visit 3;
- Week 1 terminators: subjects who discontinued after Visit 3 but before or on Visit 4;
- Week 2 terminators: subjects who discontinued after Visit 4 but before or on Visit 5;
- Week 3 terminators: subjects who discontinued after Visit 5 but before or on Visit 6;
- Week 4 terminators: subjects who discontinued after Visit 6 but before or on Visit 7;
- Week 5 terminators: subjects who discontinued after Visit 7 but before or on Visit 8;
- Week 6 terminators: subjects who discontinued after Visit 8 but before Visit 9 (the EOT visit).

16.1.4.2. Pattern-mixture model with placebo-based multiple imputation (copy reference method implemented via sequential modeling)

The MMRM model used in the primary analysis of the primary endpoint makes the assumption that the unobserved PANSS data after study treatment withdrawal are MAR. That is, in the hypothetical setting of continued treatment with study drug, the subjects in each treatment group will exhibit the same future evolution of schizophrenia as subjects staying on treatment in their respective groups. However, the subjects who discontinued from study treatment may be different from subjects remaining on study treatment such that even if these former subjects had continued to receive study treatment their disease would've evolved according to a different trajectory. Sensitivity of the results from the primary MMRM analysis of the primary endpoint to the "missing data assumptions" (i.e., assumptions about how the unobserved PANSS total scores would've behaved) will be tested by using the pattern-mixture model (PMM) with a placebo-based multiple imputation method (O'Kelly & Ratitch, 2014). In this analysis, unobserved PANSS total scores after study treatment withdrawal (after mapping of the ET data) in the SEP-363856 50 mg/day and 75 mg/day treatment groups will be imputed based on the observed PANSS total score data of the placebo group, assuming that after study treatment withdrawal, subjects from the SEP-363856 50 mg/day and 75 mg/day treatment groups will exhibit the same future evolution of schizophrenia as subjects from the placebo group, and that subjects who discontinue from the placebo group will exhibit the same future evolution of schizophrenia as subjects in the placebo group remaining in the study. This approach does not assume that the subjects in the SEP-363856 groups will benefit from the experimental treatments after the time of discontinuation even if they had continued with the experimental treatments. Rather, it assumes that the subjects who withdraw from these two treatment groups will have correlations between time points for the PANSS total score like similar subjects from the placebo group.

Two separate imputation procedures are used to impute missing values. Firstly, the Markov Chain Monte Carlo (MCMC) method is used to perform partial imputation to obtain datasets with monotone missingness patterns. Then a sequential regression multiple imputation step is implemented to impute the monotone missing values.

Under the assumption that the PANSS total scores and dichotomized countries have a multivariate normal distribution, the MCMC method is used to impute only intermediate missing values assuming MAR (using the SAS MI procedure with the MCMC statement and the IMPUTE=MONOTONE option), by using a data augmentation algorithm, with each iteration n consisting of an imputation step and a posterior step. The imputation step uses a random draw of $\theta^{(n)}$, parameter of the joint imputation model, to sample missing values from a conditional distribution $P(Y_{mis}|x, y_{obs}, \theta^{(n)})$, obtaining $y_{mis}^{(n)}$, the subset of missing values that need to be filled in to achieve monotone missingness. The posterior step simulates a new draw of the parameter $\theta^{(n+1)}$ from the posterior distribution given the current monotone missing

data $P(\theta|x, y_{obs}, y_{mis}^{(n)})$ with a non-informative Jeffreys prior. Treatment group will be taken into account for this imputation (i.e., missing data at intermediate visits will be imputed for each treatment group separately). These steps are repeated to obtain 1000 datasets with monotone missingness. The random seed number is specified in the sample SAS code (APPENDIX 3).

The remaining monotone missing data will be imputed using sequential regression multiple imputation, where a separate univariate linear regression model is estimated for imputation of each variable (i.e., the PANSS total score at each post-Baseline time point). Missing values at a given time point in the placebo and the SEP-363856 50 mg/day and 75 mg/day treatment groups will be imputed from the same imputation model estimated from the observed data of the placebo group. Specifically, imputation of missing values in the placebo group will assume MAR. Missing values in the SEP-363856 50 mg/day and 75 mg/day groups at a given time point will be imputed using the imputation model of the placebo group, while conditioning on a subject's observed or imputed post-Baseline PANSS total scores at preceding time points. Each sequential regression model for imputation of missing values at a given time point will include explanatory variables for country, Baseline PANSS total score, and post-Baseline PANSS total scores at all preceding time points (Day 4/Visit 3, Week 1/Visit 4, Week 2/Visit 5, Week 3/Visit 6, Week 4/Visit 7, and Week 5/Visit 8). The SAS MI procedure with the MONOTONE REG statement is used to specify that the regression method will be used for the imputation, and the MNAR statement with MODEL option will be used to specify that only observations from the placebo group should be used to estimate the imputation model. The random seed number is specified in the sample SAS code (APPENDIX 3).

No rounding restriction will be applied to the imputed PANSS total scores. The imputed PANSS total scores must be within the range of 30 to 210.

Each of the 1000 imputed datasets will be analyzed using the same MMRM model as the primary efficacy analysis. Results from the analysis of each imputed dataset, i.e., the LS means of each treatment group, the LS mean treatment differences (vs. placebo), and their standard errors, will be combined using Rubin's imputation rules (using the SAS MIANALYZE procedure) to produce pooled LS mean and LS mean difference estimates, their standard errors and 95% CIs, and pooled p-values for the tests of null hypotheses of no treatment effect.

COVID-19 related analysis updates:

In the sequential regression multiple imputation step, if a subject was randomized to the SEP-363856 50 mg/day group or the SEP-363856 75 mg/day group and discontinued early due to COVID-19 (e.g., a COVID-19 adverse event, COVID-19 death, or other reasons related to COVID-19), their monotone missing data will be imputed under the MAR assumption, rather than using the imputation model estimated from the placebo group. This can be achieved by first multiply imputing the monotone missing data for all subjects in the SEP-363856 50 mg/day and 75 mg/day groups under the MAR assumption, then rendering the imputed monotone missing data of subjects who did not discontinue early due to COVID-19 to missing, then applying the classic copy reference imputation in these two groups.

Russia-Ukraine geopolitical conflict related analysis updates:

In the sequential regression multiple imputation step, if a subject was randomized to the SEP-363856 50 mg/day group or the SEP-363856 75 mg/day group and discontinued early due to the conflict (e.g., an adverse event related to the conflict, a death related to the conflict, or other reasons related to the conflict), their monotone missing data

will be imputed under the MAR assumption, rather than using the imputation model estimated from the placebo group. This can be achieved by first multiply imputing the monotone missing data for all subjects in the SEP-363856 50 mg/day and 75 mg/day groups under the MAR assumption, then rendering the imputed monotone missing data of subjects who did not discontinue early due to the conflict to missing, then applying the classic copy reference imputation in these two groups.

16.1.4.3. Jump to reference method implemented via sequential modeling

Another reference-based multiple imputation approach, jump to reference (J2R), will be used as a second sensitivity analysis to consider a missing-not-at-random (MNAR) mechanism for monotone missing data.

In this analysis, unobserved PANSS total scores after study treatment withdrawal (after mapping of the ET data) in the SEP-363856 50 mg/day and 75 mg/day treatment groups will be imputed based on the PANSS total score data of the placebo group, assuming that after study treatment withdrawal, subjects from the SEP-363856 50 mg/day and 75 mg/day treatment groups will have the same profile (individual mean response) as subjects from the placebo group. This approach assumes that any effect of SEP-363856 observed prior to discontinuation immediately disappears after discontinuation.

Two separate imputation procedures are used to impute missing values. Firstly, the Markov Chain Monte Carlo (MCMC) method is used to perform partial imputation to obtain datasets with monotone missingness patterns. This step is the same as the one described in Section 16.1.4.2. Then a sequential regression multiple imputation step is implemented to impute the monotone missing values.

In the sequential imputation step of this analysis, post-Baseline PANSS total scores in the SEP-363856 50 mg/day and 75 mg/day groups prior to withdrawal are not used as explanatory variables in the imputation model, and the missing outcome of a subject in the SEP-363856 50 mg/day or 75 mg/day group after withdrawal is assumed to be similar to that of subjects from the placebo group who have similar Baseline characteristics. This assumption therefore ignores any mean improvement in health that subjects may have gained due to SEP-363856 treatment up to the time of withdrawal. Missing values at a given time point in the placebo group are first imputed based on the MAR assumption conditioning on Baseline data and available post-Baseline data at all preceding visits. Then missing values at each time point in the SEP-363856 50 mg/day and 75 mg/day treatment groups will be imputed using the imputation model estimated from the full data of the placebo group, while conditioning on only the Baseline characteristics. Each sequential regression model for imputation of missing values at a given time point will include explanatory variables for country and Baseline PANSS total score. The SAS MI procedure with the MONOTONE REG statement is used to specify that the regression method will be used for the imputation, and the MNAR statement with MODEL option will be used to specify that only observations from the placebo group should be used to estimate the imputation model. The random seed number is specified in the sample SAS code (APPENDIX 3).

No rounding restriction will be applied to the imputed PANSS total scores. The imputed PANSS total scores must be within the range of 30 to 210.

Each of the 1000 imputed datasets will be analyzed using the same MMRM model as the primary efficacy analysis. Results from the analysis of each imputed dataset, i.e., the LS means of each treatment group, the LS mean treatment differences (vs. placebo), and their standard errors, will be combined using Rubin's imputation rules (using the SAS MIANALYZE procedure) to produce pooled LS mean and LS mean difference estimates, their standard errors and 95% CIs, and pooled p-values for

the tests of null hypotheses of no treatment effect.

COVID-19 related analysis updates:

In the sequential regression multiple imputation step, if a subject was randomized to the SEP-363856 50 mg/day group or the SEP-363856 75 mg/day group and discontinued early due to COVID-19 (e.g., a COVID-19 adverse event, COVID-19 death, or other reasons related to COVID-19), their monotone missing data will be imputed under the MAR assumption, rather than using the imputation model estimated from the placebo group. This can be achieved by first multiply imputing the monotone missing data for all subjects in the SEP-363856 50 mg/day and 75 mg/day groups under the MAR assumption, then rendering the imputed monotone missing data of subjects who did not discontinue early due to COVID-19 to missing, then applying the classic jump to reference imputation in these two groups.

Russia-Ukraine geopolitical conflict related analysis updates:

In the sequential regression multiple imputation step, if a subject was randomized to the SEP-363856 50 mg/day group or the SEP-363856 75 mg/day group and discontinued early due to the conflict (e.g., an adverse event related to the conflict, a death related to the conflict, or other reasons related to the conflict), their monotone missing data will be imputed under the MAR assumption, rather than using the imputation model estimated from the placebo group. This can be achieved by first multiply imputing the monotone missing data for all subjects in the SEP-363856 50 mg/day and 75 mg/day groups under the MAR assumption, then rendering the imputed monotone missing data of subjects who did not discontinue early due to the conflict to missing, then applying the classic jump to reference imputation in these two groups.

16.1.4.4. Tipping point analysis

Sensitivity to departures from the MAR assumption will also be investigated using a tipping point analysis. In this analysis, departures from MAR in the SEP-363856 50 mg/day and 75 mg/day groups will be assessed assuming that subjects who discontinue from study treatment have, on average, efficacy outcomes after discontinuation that are worse by some amount δ (i.e., a percentage of the LS mean treatment difference from the primary analysis based on observed data) compared to other similar subjects with observed data at the same time point (i.e., compared to a value which would have been assumed under MAR).

A series of analyses will be performed with increasing values of δ until the analysis conclusion of a statistically significant treatment effect no longer holds. The value of δ that overturns the primary analysis conclusion will represent a tipping point. An interpretation of clinical plausibility of the assumption underlying the tipping point will be provided. After one SEP-363856 group reaches the tipping point, the analyses will continue until the other SEP-363856 group also reaches the tipping point.

Intermediate (non-monotone) missing data will be imputed first based on the MAR assumption and a multivariate joint Gaussian imputation model using the MCMC method within each treatment group, as described earlier for the pattern-mixture model with placebo-based multiple imputation.

The remaining monotone missing data will be imputed using sequential regression multiple imputation,

where a separate regression model is estimated for imputation of each variable (i.e., PANSS total score at each post-Baseline time point). Each regression model will include explanatory variables for treatment, country, Baseline PANSS total score, and post-Baseline PANSS total scores at all preceding time points (Day 4/Visit 3, Week 1/Visit 4, Week 2/Visit 5, Week 3/Visit 6, Week 4/Visit 7, and Week 5/Visit 8). After the MAR-based imputations have been generated for PANSS total scores at each time point, the change from Baseline values at all visits based on the imputed PANSS total scores in the SEP-363856 50 mg/day and 75 mg/day groups will be penalized by a value of δ. This approach assumes that the marginal mean of unobserved subject measurements is worse by δ at each time point after discontinuation compared to the marginal mean of subjects with observed data at the same time points.

No rounding restriction will be applied to the imputed PANSS total scores. The imputed PANSS total scores must be within the range of 30 to 210.

A total of 1000 imputed datasets will be generated for each δ level. The random seed numbers for the partial imputation step and for the sequential regression multiple imputation step are specified in the sample SAS code (APPENDIX 3).

Each of the imputed and δ-adjusted datasets will be analyzed using the same MMRM model as the primary efficacy analysis. Results from the analysis of each imputed dataset at a given δ level, i.e., the LS mean treatment differences (vs. placebo) and their standard errors, will be combined using Rubin's imputation rules (using the SAS MIANALYZE procedure) to produce pooled LS mean difference estimates, their standard errors and 95% CIs, and pooled p-values for the tests of null hypotheses of no treatment effect.

Analyses will be conducted with different values of δ at each visit, which represents a percentage of the LS mean treatment difference at that visit from the primary analysis of observed data, starting at 5% with 5% increments, until either the tipping point is identified or 100% penalty is applied. The actual δ corresponding to each percentage increment will be presented in the table.

COVID-19 related analysis updates:

In the penalization step, if a subject was randomized to the SEP-363856 50 mg/day group or the SEP-363856 75 mg/day group and discontinued early due to COVID-19 (e.g., a COVID-19 adverse event, COVID-19 death, or other reasons related to COVID-19), their monotone missing data imputed under the MAR assumption will not be penalized.

Russia-Ukraine geopolitical conflict related analysis updates:

In the penalization step, if a subject was randomized to the SEP-363856 50 mg/day group or the SEP-363856 75 mg/day group and discontinued early due to the conflict (e.g., an adverse event related to the conflict, a death related to the conflict, or other reasons related to the conflict), their monotone missing data imputed under the MAR assumption will not be penalized.

16.1.5. Supplementary Analyses of Primary Efficacy Variable

16.1.5.1. Analysis of covariance

Change from Baseline in PANSS total score at each scheduled visit and at the LOCF endpoint will be analyzed using an analysis of covariance (ANCOVA) model. The model will include factors for treatment and country, and include Baseline PANSS total score as a covariate. The LS mean of each treatment group, LS mean differences (each SEP-383656 group vs. placebo), their standard errors and two-sided 95% CIs, and the nominal p-values for treatment differences will be obtained from the model.

Based on the ANCOVA analysis, within group effect size at a given time point will be calculated as the LS mean of each treatment group divided by the standard deviation, obtained as the standard error of the LS mean multiplied by the square root of the treatment group sample size at that time point. Between group effect size at a given time point will be calculated as the LS mean difference of each SEP-363856 group vs. placebo divided by the pooled standard deviation, obtained as the standard error of the LS mean difference divided by the square root of the sum of inverse treatment group sample sizes at that time point.

Baseline PANSS total score will also be analyzed by an ANCOVA model including factors for treatment and country. The nominal p-values for treatment differences will be obtained from the model.

16.1.5.2. Complete case analysis

The complete case analysis will be performed on the subset of adult subjects in the mITT population who completed the double-blind treatment period and have Week 6/Visit 9 PANSS total score data available. The MMRM analysis as described in Section 16.1.3.3 will be performed on these subjects.

16.1.5.3. Analysis on the per protocol population

The MMRM analysis as described in Section 16.1.3.3 will be performed on the PP population to evaluate the efficacy of the treatment for these subjects.

16.1.5.4. Analysis with missing PANSS item(s) imputed

Due to the use of electronic clinical outcome assessment (eCOA) technology and extensive data quality monitoring during the study, no partially completed PANSS assessments are expected. However, in the rare event of a partially completed PANSS assessment, missing PANSS item scores will be imputed as described below.

In contrast to all other analyses of the primary efficacy variable where missing PANSS item scores are not imputed and the corresponding PANSS total score is set to missing, in this supplementary analysis, if a PANSS assessment is partially available at a visit (i.e., one or more PANSS items are missing), the missing PANSS item(s) will be imputed. It should be noted that entirely missing PANSS assessments will not be filled in using imputation in this analysis.

The imputation will be performed by the MCMC method under the MAR assumption as described in Section 16.1.4. The only difference is that the MCMC statement will have the option IMPUTE=FULL.

For each PANSS item X that needs such imputation, MCMC imputation will be performed based on a multivariate normal distribution including variables for dichotomized countries, Baseline PANSS item X score, and all post-Baseline PANSS item X scores (Day 4/Visit 3, Week 1/Visit 4, Week 2/Visit 5, Week 3/Visit 6, Week 4/Visit 7, and Week 5/Visit 8, Week 6/Visit 9). The imputation will be done by treatment group. By using this method, those visits where entire PANSS assessments are missing will have item X filled in as well. When calculating PANSS total scores on the imputed datasets, the imputed values for those visits should be ignored.

A total of 1000 imputed datasets will be generated for each PANSS item to be imputed this way. Upon completion of the imputation for all individual PANSS items, the datasets for each PANSS item will be combined by the imputation number. PANSS total scores will be calculated for the visits where PANSS assessments are completely or partially available in the original data, using observed/imputed PANSS item scores. As stated earlier, for visits where PANSS assessments are entirely missing in the original data, the PANSS total score should be left as missing.

Each of the 1000 imputed datasets with PANSS total score calculated will be analyzed using the MMRM analysis as described in Section 16.1.3.3. Results from the analysis of each imputed dataset, i.e., the LS means of each treatment group, the LS mean treatment differences (vs. placebo), and their standard errors, will be combined using Rubin's imputation rules to produce pooled LS mean and LS mean difference estimates, their standard errors and 95% CIs, and pooled p-values.

This analysis will be performed on adult subjects.

16.1.6. Subgroup Analyses of Primary Efficacy Variable

For each of the subgroup factors listed in Section 7.5, change from Baseline in PANSS total score at Week 6 will be analyzed using the MMRM method.

For the subgroup factors other than country, the MMRM model will include fixed effects for treatment, subgroup, visit, country, Baseline PANSS total score, and treatment-by-subgroup, treatment-by-visit, subgroup-by-visit, and treatment-by-subgroup-by-visit interactions. For the subgroup factor of country, the MMRM model will include fixed effects for treatment, country, visit, Baseline PANSS total score, and treatment-by-country, treatment-by-visit, country-by-visit, and treatment-by-country-by-visit interactions.

Subgroups that do not have at least 2 mITT population subjects with change from Baseline in PANSS total score data available at Week 6/Visit 9 in each of the three treatment groups will be excluded from the analysis.

Estimates obtained from the MMRM model will be presented separately for each subgroup. The nominal p-value for the treatment-by-subgroup interaction at Week 6/Visit 9 will be presented. The presence of a significant interaction effect will be assessed at the 0.10 level for homogeneity of the treatment effect across the different categories of a subgroup factor. In case of a significant interaction effect, estimates by subgroup will be examined to determine the nature of the interaction (qualitative or quantitative). The MMRM results of all subgroup analyses will also be presented using forest plots.

The observed PANSS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit for each subgroup.

16.2. SECONDARY EFFICACY

The analyses of the secondary efficacy variable will be performed on the mITT population of the adult subjects, unless otherwise specified.

16.2.1. SECONDARY EFFICACY VARIABLE & DERIVATION

The secondary efficacy variable is change from Baseline in CGI-S score at Endpoint (Week 6).

The CGI-S (Clinical Global Impression-Severity) is a clinician-rated assessment of the subject's current illness state on a 7-point scale, where a higher score is associated with greater illness severity. The CGI-S score takes one of the following values: 1 (normal, not at all ill), 2 (borderline mentally ill), 3 (mildly ill), 4 (moderately ill), 5 (markedly ill), 6 (severely ill), 7 (among the most extremely ill patients).

CGI-S is assessed at these study visits: Visit 1, Visit 2, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, and Visit 9. The Baseline CGI-S score will be derived as described in Section 6.2. The change from Baseline in CGI-S score at Week 6, as well as at the other post-Baseline time points, will be derived as described in Section 6.7.

16.2.2. MISSING DATA METHODS FOR SECONDARY EFFICACY VARIABLE

The secondary efficacy variable, change from Baseline in CGI-S score at Week 6, will be set to missing if the CGI-S score at Week 6 is missing or if the Baseline CGI-S score is missing. The same applies to all other visits.

The primary analysis of the secondary efficacy variable will use a MMRM based on observed data only (with early termination data mapped as described in Section 6.4). Missing data will not be imputed.

16.2.3. PRIMARY ANALYSIS OF SECONDARY EFFICACY VARIABLE

16.2.3.1. Estimand

The secondary efficacy estimand is defined as the difference between each SEP-363856 dose level and placebo in the mean change of CGI-S score from Baseline to Week 6 in acutely psychotic adult subjects with schizophrenia as characterized by the study inclusion/exclusion criteria, in the hypothetical setting where the subjects were able to stay on study and remain on the study treatment for 6 weeks.

The four attributes of the secondary efficacy estimand are as follows:

A. Population of interest: Acutely psychotic adult subjects with schizophrenia, as characterized by the inclusion/exclusion criteria of the study. For the efficacy analyses, the mITT population will be used to represent the population of interest.

B. Variable (or endpoint) of interest: Change from Baseline in CGI-S score to Week 6.

C. Intercurrent event: The intercurrent event that is deemed to have an impact on the interpretation of the variable of interest is early withdrawal from study treatment for any reason. This intercurrent event

will be handled with the hypothetical strategy. That is, the treatment effect of interest concerns the outcomes had all subjects completed 6 weeks of study treatment. The efficacy data after the last on-treatment visit will not be collected as these data are irrelevant to the treatment effect of interest. Rather, these data will be implicitly predicted based on the assumptions about how the data would evolve after treatment withdrawal.

D. Population-level summary for the variable: The difference in the mean change of CGI-S score from Baseline to Week 6.

16.2.3.2. Justification for the estimand

Justification for the choice of the secondary efficacy estimand is similar to that of the primary efficacy estimand.

16.2.3.3. Hypotheses and statistical model

The efficacy of SEP-363856 in terms of the CGI-S score will be evaluated using the following two null hypotheses,

- H_3: There is no difference in the mean change from Baseline in CGI-S score at Week 6 between the SEP-363856 50 mg/day treatment arm and Placebo.
- H_4: There is no difference in the mean change from Baseline in CGI-S score at Week 6 between the SEP-363856 75 mg/day treatment arm and Placebo.

The alternative hypothesis for each of the null hypotheses is that there is a difference.

Change from Baseline in CGI-S score at Week 6 will be analyzed using a MMRM model similar to the model described in Section 16.1.3.3 for the primary efficacy variable, with Baseline CGI-S score as the covariate. The adjusted point and 95% CI estimates for the treatment effect of SEP-363856 groups (vs. placebo) at Week 6 will be calculated similarly as described in Section 16.1.3.3.

The observed CGI-S score and the change from Baseline values will also be summarized descriptively by treatment group and visit.

LS Means (+/- Standard Error) of CGI-S score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

16.2.4. Sensitivity Analyses of Secondary Efficacy Variable

Sensitivity analyses similar to the ones described in Section 16.1.4 will be performed for the secondary efficacy variable.

16.2.5. Supplementary Analyses of Secondary Efficacy Variable

Supplementary analyses similar to the ones described in Sections 16.1.5.1, 16.1.5.2, and 16.1.5.3 will be performed for the secondary efficacy variable. The complete case analysis will be performed on the subset of adult subjects in the mITT population who completed the double-blind treatment period and

have Week 6/Visit 9 CGI-S score data available.

16.2.6. Subgroup Analyses of Secondary Efficacy Variable

Subgroup analyses similar to the ones described in Section 16.1.6 will be performed for the secondary efficacy variable. The subgroup factor of Baseline patient type based on UPSM factor scores at Baseline and MPNS enrichment do not apply to the secondary efficacy variable.

The observed CGI-S score and the change from Baseline values will also be summarized descriptively by treatment group and visit for each subgroup.

16.3. Other Efficacy

The analyses of the other efficacy variables will be performed on the mITT populations of the adult subjects and/or the adolescent subjects, unless otherwise specified.

16.3.1. Other Efficacy Variables & Derivations

16.3.1.1. Change from Baseline in PANSS total score at each scheduled visit except Endpoint (Week 6) (adult subjects)

The derivation of this efficacy variable is described along with that of the primary efficacy variable in Section 16.1.1.

16.3.1.2. Change from Baseline in CGI-S score at each scheduled visit except Endpoint (Week 6) (adult subjects)

The derivation of this efficacy variable is described along with that of the secondary efficacy variable in Section 16.2.1.

16.3.1.3. Change from Baseline in PANSS total score at each scheduled visit (adolescent subjects)

Change from Baseline in PANSS total score at each scheduled visit among the adolescent subjects will be derived using the same method as described in Section 16.1.1 for the adult subjects.

16.3.1.4. Change from Baseline in CGI-S score at each scheduled visit (adolescent subjects)

Change from Baseline in CGI-S score at each scheduled visit among the adolescent subjects will be derived using the same method as described in Section 16.2.1 for the adult subjects.

16.3.1.5. Change from Baseline in PANSS subscale scores at each scheduled visit (adult subjects and adolescent subjects)

Individual items from the PANSS scale are summed to derive the following subscale scores:

- Positive subscale: delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution, hostility. This subscale score ranges from 7 to 49.
- Negative subscale: blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, stereotyped thinking. This subscale score ranges from 7 to 49.
- General psychopathology subscale: somatic concern, anxiety, guilt feelings, tension, mannerisms and posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgment and insight, disturbance of volition, poor impulse control, preoccupation, active social avoidance. This subscale score ranges from 16 to 112.

PANSS is assessed at these study visits: Visit 1, Visit 2, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, and Visit 9. The Baseline PANSS subscale scores will be derived as described in Section 6.2. The change from Baseline in PANSS subscale scores at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.6. Change from Baseline in PANSS Marder factor scores at each scheduled visit (adult subjects and adolescent subjects)

Individual items from the PANSS scale are summed to derive the following Marder factors (Marder, Davis, & Chouinard, 1997;58:538–46):

- Negative symptoms: blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, lack of spontaneity and flow of conversation, motor retardation, and active social avoidance. This Marder factor score ranges from 7 to 49.
- Positive symptoms: delusions, hallucinatory behavior, grandiosity, suspiciousness/persecution, stereotyped thinking, somatic concern, unusual thought content, and lack of judgment and insight. This Marder factor score ranges from 8 to 56.
- Disorganized thought: conceptual disorganization, difficulty in abstract thinking, mannerisms and posturing, poor attention, disturbance of volition, preoccupation, and disorientation. This Marder factor score ranges from 7 to 49.
- Uncontrolled hostility/excitement: excitement, hostility, uncooperativeness, and poor impulse control. This Marder factor score ranges from 4 to 28.
- Anxiety/depression: anxiety, guilt feelings, tension, and depression. This Marder factor score ranges from 4 to 28.

PANSS is assessed at these study visits: Visit 1, Visit 2, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, and Visit 9. The Baseline PANSS Marder factor scores will be derived as described in Section 6.2. The change from Baseline in PANSS Marder factor scores at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.7. Change from Baseline in PANSS UPSM factor scores and the UPSM total factor score at each scheduled visit (adult subjects and adolescent subjects)

The PANSS item scores of each subject at each visit will be transformed using the UPSM, to obtain the scores of 7 transformed PANSS factors (Hopkins S. , Ogirala, Loebel, & Koblan, 2018;44(3):593-602):

- POS: Positive
- DIS: Disorganized
- NAA: Negative apathy/avolition
- NDE: Negative deficit of expression
- HOS: Hostility
- ANX: Anxiety
- DEP: Depression

The transformation will be done as follows:

$$[\text{Transformed PANSS Factor Data}]_{(N\times 7)} = [\text{PANSS Data}]_{(N\times 30)} * [\text{UPSM}]_{(30\times 7)}$$

where

- $[\text{Transformed PANSS Factor Data}]_{(N\times 7)}$ is the transformed matrix with N sets of scores for the 7 transformed PANSS factors.
- $[\text{PANSS Data}]_{(N\times 30)}$ is a matrix with N PANSS assessments and 30 columns containing the scores of 30 PANSS items ordered in the same way as shown in UPSM.
- $[\text{UPSM}]_{(30\times 7)}$ is a matrix with 30 rows (one for each PANSS item) and 7 columns (one for each of the 7 transformed PANSS factors). This matrix is presented in APPENDIX 5.

Lastly, the UPSM total factor score will be calculated as the sum of the 7 UPSM factor scores.

PANSS is assessed at these study visits: Visit 1, Visit 2, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, and Visit 9. The Baseline PANSS UPSM factor scores and UPSM total factor score will be derived as described in Section 6.2. The change from Baseline in PANSS UPSM factor scores and UPSM total factor score at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.8. PANSS response at each scheduled visit (adult subjects and adolescent subjects)

PANSS response is defined as a 20% or greater improvement (i.e., decrease) in PANSS total score from Baseline.

The percent change in PANSS total score from Baseline will be calculated by:

$$\frac{\text{PANSS total score at a visit or the LOCF endpoint - PANSS total score at Baseline}}{\text{PANSS total score at Baseline - 30}} \times 100\%$$

For each subject, the responder indicator will be set to Y if the percent change is negative and the magnitude is equal to or greater than 20%. The indicator will be set to N if the percentage is negative but the magnitude is less than 20% or if the percentage is non-negative. The indicator will be set to missing if the percentage is missing.

In addition, PANSS response defined by two more stringent thresholds will be assessed; that is, having a 30% or greater and 50% or greater improvement in PANSS total score from Baseline.

PANSS response at all three thresholds will be derived for all post-Baseline time points.

16.3.1.9. Change from Baseline in BNSS total score and subscale scores at each scheduled visit (adult subjects)

The BNSS (Brief Negative Symptom Scale) is a rating scale that measures the current level of severity of negative symptoms in schizophrenia and schizoaffective disorder. The measure is comprised of 13 individual items organized into 6 subscales: blunted affect (items 9, 10, 11), alogia (items 12, 13), avolition (items 7, 8), anhedonia (items 1, 2, 3), asociality (items 5, 6), and distress (item 4). Each of the items is scored on a Likert-type 7-point scale from 0 to 6, where a value of 0 indicates the symptom is absent and a value of 6 means the symptom is a severe form. The subscale scores are calculated by summing the individual items within each subscale. The 13 items are also summed to provide a total score which ranges from 0 to 78.

BNSS is assessed at these study visits: Visit 2, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, and Visit 9. The Baseline BNSS subscale and total scores will be derived as described in Section 6.2. The change from Baseline in BNSS subscale and total scores at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.10. Change from Baseline in MADRS total score at each scheduled visit (adult subjects)

The MADRS (Montgomery-Asberg Depression Rating Scale) is a clinician-rated assessment of the subject's level of depression. The measure contains 10 items that measure apparent and reported sadness, inner tension, reduced sleep and appetite, difficulty concentrating, lassitude, inability to feel, and pessimistic and suicidal thoughts. Each item is scored in a range of 0 to 6 points, with higher scores indicating increased depressive symptoms. Total score will be equal to the sum of the 10 items (range between 0 and 60).

MADRS is assessed at these study visits: Visit 2, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, and Visit

9. The Baseline MADRS total score will be derived as described in Section 6.2. The change from Baseline in MADRS total score at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.11. Change from Baseline in BACS composite score and component test scores at each scheduled visit (adult subjects and adolescent subjects)

The BACS (Brief Assessment of Cognition in Schizophrenia) assesses 6 domains of cognition: verbal memory/learning, working memory, motor function, verbal fluency, speed of processing, and executive function. An electronic tablet-based version of the traditional BACS, called the BAC App, is used in this study. The BAC App was developed to allow standardized presentation of task instructions and stimuli, audio-recording of responses, and automatized scoring and data management.

The six domains of cognition assessed by BACS are listed below:

- Verbal Memory/Learning is assessed with the Verbal Memory task. Subjects are presented with a list of 15 words and asked to recall as many as possible. This procedure is repeated 5 times. The outcome measure is the number of words recalled.
- Working Memory is assessed with the Digit Sequencing task. Subjects are presented with auditory clusters of numbers (e.g., 936) of increasing length and asked to tell the rater the numbers in order from lowest to highest. The outcome measure is the number of correct responses.
- Motor Function is assessed with the Token Motor task. Subjects are presented with tokens and asked to drag them to a center container as quickly as possible for 60 seconds. The outcome measure is the number of tokens correctly dragged into the container.
- Verbal Fluency is assessed with the Semantic Fluency and Letter Fluency tasks. Subjects are given 60 seconds to generate as many words as possible in a given category (semantic) or for a given letter of the alphabet (letter). The outcome measure for each fluency test is the number of words generated.
- Speed of Processing is assessed with the Symbol Coding task. Subjects are provided a key and asked to fill the corresponding number beneath a series of symbols as quickly as possible within 90 seconds. The outcome measure is the number of correct items.
- Executive Function is assessed with the Tower of London task. Subjects are asked to give the minimum number of times the balls in one picture would need to be moved in order to make the arrangement of balls identical to that in the opposing picture. The outcome measure is the number of correct responses.

The raw scores of the 6 domains of cognition are transformed into component test T scores and then a composite T score summarizing all six domains are derived as described in (Keefe, et al., 2008). The component test T scores and the composite T score for each subject at each visit are provided by the BACS vendor for direct use in downstream statistical analyses.

BACS is assessed at these study visits: Visit 2 and Visit 9. The Baseline BACS component test T scores and composite T score will be derived as described in Section 6.2. The change from Baseline in BACS component test T scores and composite T score at each post-Baseline time point will be derived

as described in Section 6.7.

16.3.1.12. Change from Baseline in PSP total score and individual domain scores at each scheduled visit (adult subjects and adolescent subjects)

The PSP (Personal and Social Performance Scale) is a 100-point single-item rating scale of personal and social functioning. The 100-point rating scale is subdivided into 10 equal intervals (or 10-point categories). The rating is based on the assessment of a patient's functioning in four areas: 1) socially useful activities, 2) personal and social relationships, 3) self-care, and 4) disturbing and aggressive behaviors. Each area is evaluated using the degree of severity: Absent, Mild, Manifest, Marked, Severe and Very Severe. For the purpose of analysis, the following numerical values will be assigned to the degrees of severity:

0 = Absent

1 = Mild

2 = Manifest

3 = Marked

4 = Severe

5 = Very Severe

A PSP total score (range 1 to 100) is assigned by the rater based on the subject's functioning in the four areas.

Higher PSP total scores indicate better functioning. Scores of 1-30 indicate functioning so poor that intensive support or supervision is needed; scores of 31-70 indicate varying degrees of difficulty; and scores of 71-100 reflect only mild difficulties.

PSP is assessed at these study visits: Visit 2 and Visit 9. The Baseline PSP total score will be derived as described in Section 6.2. The change from Baseline in PSP total score at each post-Baseline time point will be derived as described in Section 6.7.

In addition, the following binary outcomes based on PSP total score will be derived:

- PSP total score ≥71 at Baseline and each scheduled visit (Week 6/Visit 9)
- Improvement of ≥1 PSP 10-point category from Baseline to each scheduled visit (Week 6/Visit 9)

For each subject, the indicator for each of the binary outcomes described above will be set to Y if the subject satisfied the condition, and N if the subject failed to satisfy the condition. The indicator will be set to missing if the data necessary for the derivation is missing (e.g., the PSP total score is missing at a particular time point).

16.3.1.13. Change from Baseline in EQ-5D-5L VAS, index value and dimension score at each scheduled visit (adult subjects and adolescent subjects)

The EQ-5D-5L (EuroQol-5 Dimensions – 5 Levels) is a standardized instrument developed by the EuroQol Group as a measure of health-related quality of life that can be used in a wide range of health conditions and treatments. The EQ-5D-5L consists of two parts: a) the EQ-5D-5L descriptive system, and b) the EQ VAS.

The EQ-5D-5L descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: level 1 (no problems), level 2 (slight problems), level 3 (moderate problems), level 4 (severe problems), and level 5 (extreme problems/unable to do). The patient is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number that expresses the level selected for that dimension (i.e., the dimension score).

The dimension scores for the five dimensions can be combined into a 5-digit code that describes the patient's health state. An index value (a weighted scoring of the 5 dimension scores with a possible range from less than 0 [where 0 is the value of a health state equivalent to dead; negative values representing values as worse than dead] to 1 [the value of full health]) will be assigned to each observed health state using the US standard value set as defined in APPENDIX 6.

The EQ VAS records the patient's self-rated health on a vertical visual analogue scale from 0 to 100, where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. The VAS can be used as a quantitative measure of health outcome that reflect the patient's own judgment.

EQ-5D-5L is assessed at these study visits: Visit 2 and Visit 9. The Baseline EQ-5D-5L VAS and index value and dimension scores will be derived as described in Section 6.2. The change from Baseline in EQ-5D-5L VAS and index value at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.14. Change from Baseline in UPSA-B total score and subscale scores at each scheduled visit (adult subjects)

The UPSA-B (University of California San Diego (UCSD) Performance-based Skills Assessment – Brief Version) assesses everyday functioning in persons with serious mental illness. The UPSA-B is a measure of functional capacity in which patients are asked to role-play tasks in 2 areas of functioning: communication and finances.

The raw score of the financial subscale is the sum of the 10 financial items and ranges from 0 to 11, and the raw score of the communication subscale is the sum of 9 communication items and ranges from 0 to 9. Each subscale score is calculated by dividing the raw score by the highest possible raw score of that subscale and then multiplying by 50, so both subscale scores range from 0 to 50. The UPSA-B total score, calculated as the sum of two subscale scores, ranges from 0 to 100. Higher scores reflect better performance.

UPSA-B is assessed at these study visits: Visit 2 and Visit 9. The Baseline UPSA-B total score will be derived as described in Section 6.2. The change from Baseline in UPSA-B total score at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.15. Change from Baseline in MSQ score at each scheduled visit (adult subjects and adolescent subjects)

The MSQ is a single-item, patient-rated, rater administered questionnaire that requires the subject to use a 7-point, Likert-type scale to rate how satisfied they are with their current antipsychotic medication. The subject will be asked the following question: "Overall, how satisfied are you with your current antipsychotic medication".

Subjects will select 1 of 7 potential responses based on their level of satisfaction from extremely dissatisfied (1) to extremely satisfied (7) as follows:

(1) Extremely dissatisfied

(2) Very dissatisfied

(3) Somewhat dissatisfied

(4) Neither dissatisfied nor satisfied

(5) Somewhat satisfied

(6) Very satisfied

(7) Extremely satisfied

MSQ is assessed at these study visits: Visit 1 and Visit 9. The Baseline MSQ score will be derived as described in Section 6.2. The change from Baseline in MSQ score at each post-Baseline time point will be derived as described in Section 6.7.

16.3.1.16. Tobacco use (adult subjects)

Information regarding the subject's tobacco use are recorded in the CRF. Data collected include the type of tobacco used, approximate amount, and time period during which tobacco was / is being used.

Tobacco use is assessed at these study visits: Visit 1 and Visit 9.

16.3.2. Missing Data Methods for Other Efficacy Variables

With the exception of one supplementary analysis for BNSS total score (see Section 16.3.3.9) and MADRS total score (see Section 16.3.3.10), any individual missing item in any scale will not be imputed.

For derived scores that depend on more than one individual item (e.g., PANSS total score, PANSS subscale scores, PANSS Marder factor scores, PANSS UPSM factor scores and UPSM total factor score, BNSS total score, BNSS subscale scores, MADRS total score, EQ-5D-5L index value, and UPSA-B total score), if one or more items are missing at a visit, the derived score will be set to missing. The corresponding change from Baseline value at a given post-Baseline time point will be set to missing if the Baseline derived score is missing or if the derived score at that time point is missing.

For PANSS response, any subject with a missing PANSS total score at Baseline or at any post-Baseline time point will have their PANSS response set to missing for that time point.

For PSP binary variables based on the PSP total score, if the PSP total score is missing at Baseline or

at any post-Baseline time point, the affected binary variable will be set to missing.

16.3.3. Analysis of Other Efficacy Variables

16.3.3.1. Change from Baseline in PANSS total score at each scheduled visit except Endpoint (Week 6) (adult subjects)

This efficacy variable is analyzed along with the primary efficacy variable as described in Sections 16.1.3, 16.1.4, 16.1.5, and 16.1.6.

16.3.3.2. Change from Baseline in CGI-S score at each scheduled visit except Endpoint (Week 6) (adult subjects)

This efficacy variable is analyzed along with the secondary efficacy variable as described in Sections 16.2.3, 16.2.4, 16.2.5, and 16.2.6.

16.3.3.3. Change from Baseline in PANSS total score at each scheduled visit (adolescent subjects)

This efficacy variable will be analyzed using the MMRM method as described in Section 16.1.3.3 on the mITT population.

The observed PANSS total score and the change from Baseline values will be summarized descriptively by treatment group and visit. This summary will also be repeated for subjects who completed the study.

LS Means (+/- Standard Error) of PANSS total score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

16.3.3.4. Change from Baseline in CGI-S score at each scheduled visit (adolescent subjects)

This efficacy variable will be analyzed using the MMRM method as described in Section 16.2.3.3 on the mITT population.

The observed CGI-S score and the change from Baseline values will be summarized descriptively by treatment group and visit. This summary will also be repeated for subjects who completed the study.

LS Means (+/- Standard Error) of CGI-S score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

16.3.3.5. Change from Baseline in PANSS subscale scores at each scheduled visit (adult subjects and adolescent subjects)

For both adult subjects and adolescent subjects, change from Baseline in each of the PANSS subscale scores at each scheduled visit will be analyzed using a MMRM model similar to the model described in

Section 16.1.3.3, with the respective Baseline PANSS subscale score as the covariate. In addition, for adult subjects, change from Baseline in each of the PANSS subscale scores at each scheduled visit and at the LOCF endpoint will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with the respective Baseline PANSS subscale score as the covariate.

For both adult subjects and adolescent subjects, the observed PANSS subscale scores and the change from Baseline values will also be summarized descriptively by treatment group and visit.

LS Means (+/- Standard Error) of PANSS subscale scores change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

16.3.3.6. Change from Baseline in PANSS Marder factor scores at each scheduled visit (adult subjects and adolescent subjects)

For adult subjects, change from Baseline in each of the PANSS Marder factor scores at each scheduled visit will be analyzed using a MMRM model similar to the model described in Section 16.1.3.3, with the respective Baseline PANSS Marder factor score as the covariate. In addition, change from Baseline in each of the PANSS Marder factor scores at each scheduled visit and at the LOCF endpoint will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with the respective Baseline PANSS Marder factor score as the covariate.

For both adult subjects and adolescent subjects, the observed PANSS Marder factor scores and the change from Baseline values will be summarized descriptively by treatment group and visit.

For adult subjects, LS Means (+/- Standard Error) of PANSS Marder factor scores change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

16.3.3.7. Change from Baseline in PANSS UPSM factor scores and the UPSM total factor score at each scheduled visit (adult subjects and adolescent subjects)

For adult subjects, change from Baseline in each of the PANSS UPSM factor scores and the total factor score at each scheduled visit will be analyzed using a MMRM model similar to the model described in Section 16.1.3.3, with the respective Baseline PANSS UPSM factor score or the total factor score as the covariate. In addition, change from Baseline in each of the PANSS UPSM factor scores and the total factor score at each scheduled visit and at the LOCF endpoint will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with the respective Baseline PANSS UPSM factor score or the total factor score as the covariate.

For adult subjects, for each of the UPSM factor scores and the total factor score, the 95% CI of the ANCOVA-based within group effect size of each treatment group at Week 6/Visit 9 will be calculated by multiplying the lower and upper bounds of the 95% CI of the non-centrality parameter of the t-distribution associated with the t-test for the LS mean by the square root of inverse treatment group sample size at Week 6/Visit 9. The 95% CI of the ANCOVA-based between group effect size for each SEP-363856 group vs. placebo at Week 6/Visit 9 will be calculated by multiplying the lower and upper bounds of the 95% CI of the non-centrality parameter of the t-distribution associated with the t-test for the LS mean difference by the square root of the sum of inverse treatment group sample sizes at Week 6/Visit 9. These 95% CIs will only be presented in a figure that shows a side-by-side comparison of the Marder factor scores and PANSS total score vs. the UPSM factor scores and total factor score. (95% CI for the Marder factor scores and the PANSS total score effect sizes at Week 6/Visit 9 will be calculated

similarly.)

For both adult subjects and adolescent subjects, the observed PANSS UPSM factor scores and the total factor score as well as the change from Baseline values will be summarized descriptively by treatment group and visit.

For adult subjects, LS Means (+/- Standard Error) of PANSS UPSM factor scores change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

16.3.3.8. PANSS response at each scheduled visit (adult subjects and adolescent subjects)

The analyses described below will be applied to all three thresholds: 20% or greater improvement, 30% or greater improvement, and 50% or greater improvement in the PANSS total score from Baseline.

For adult subjects, PANSS response at each scheduled visit and at the LOCF endpoint will be analyzed using a logistic regression model with responder indicator as the dependent variable and include factors for treatment and region, and include Baseline PANSS total score as a covariate. The Number Needed to Treat (NNT) will be provided:

- The NNT for each SEP-363856 group will be derived as:

$$NNT = \frac{1}{\text{Risk Reduction (RR)}} = \frac{1}{\text{PANSS Response Rate}_{\text{SEP-363856 xx mg}} - \text{PANSS Response Rate}_{\text{Placebo}}}$$

  Only positive NNT results will be presented. The NNT results will be provided in whole numbers with any fractional values rounded up to the nearest whole number. The 95% CI of NNT will also be presented and are computed by taking the reciprocal of the 95% CI lower and upper bounds of the RR when both bounds are positive. The lower confidence limit will be rounded down to the largest whole number that is less than the computed estimate, and the upper confidence limit will be rounded up to the smallest whole number that is greater than the computed estimate.

For both adult subjects and adolescent subjects, the number and percentage of subjects who achieve a PANSS response will be summarized descriptively by treatment group and visit.

Lastly, for both adult subjects and adolescent subjects, the proportion of subjects achieving a given percentage change threshold in PANSS total score from Baseline at the LOCF endpoint will be calculated for each treatment group. This calculation will be performed at multiple thresholds, starting from -100% and increases at 5% increments until all subjects are accounted for in all treatment groups.

16.3.3.9. Change from Baseline in BNSS total score and subscale scores at each scheduled visit (adult subjects)

Change from Baseline in BNSS total score at each scheduled visit will be analyzed using a MMRM model similar to the model described in Section 16.1.3.3, with Baseline BNSS total score as the covariate. In addition, change from Baseline in BNSS total score at each scheduled visit and at the LOCF endpoint will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline BNSS total score as the covariate.

Change from Baseline in each of the BNSS subscale scores will be analyzed using the MMRM method and the ANCOVA method similarly to the BNSS total score.

The observed BNSS total score and subscale scores and the change from Baseline values will also be summarized descriptively by treatment group and visit.

LS Means (+/- Standard Error) of BNSS total score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

Lastly, as a supplementary analysis, individual BNSS items that are missing in partially completed BNSS assessments will be filled in using the MCMC imputation method as described for PANSS in Section 16.1.5.4. The BNSS total scores will then be calculated based on the observed/imputed item scores and analyzed using a MMRM model similar to the model described in Section 16.1.3.3. Model estimates from each MMRM analysis will then be combined using Rubin's rules.

16.3.3.10. Change from Baseline in MADRS total score at each scheduled visit (adult subjects)

Change from Baseline in MADRS total score at each scheduled visit will be analyzed using a MMRM model similar to the model described in Section 16.1.3.3, with Baseline MADRS total score as the covariate. In addition, change from Baseline in MADRS total score at each scheduled visit and at the LOCF endpoint will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline MADRS total score as the covariate.

The observed MADRS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit.

LS Means (+/- Standard Error) of MADRS total score change from Baseline over time based on MMRM estimates will be plotted as described in the figure shell.

Lastly, as a supplementary analysis, individual MADRS items that are missing in partially completed MADRS assessments will be filled in using the MCMC imputation method as described for PANSS in Section 16.1.5.4. The MADRS total scores will then be calculated based on the observed/imputed item scores and analyzed using a MMRM model similar to the model described in Section 16.1.3.3. Model estimates from each MMRM analysis will then be combined using Rubin's rules.

16.3.3.11. Change from Baseline in BACS composite score and component test scores at each scheduled visit (adult subjects and adolescent subjects)

For adult subjects, change from Baseline in BACS composite T score at each scheduled visit (Week 6/Visit 9) and the LOCF endpoint will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline BACS composite T score as the covariate.

Change from Baseline in each of the BACS component test T scores will be analyzed using the ANCOVA method similarly to the BACS composite T score.

For both adult subjects and adolescent subjects, the observed BACS composite T score and component test T scores and the change from Baseline values will be summarized descriptively by treatment group and visit.

16.3.3.12. Change from Baseline in PSP total score and individual domain scores at each scheduled visit (adult subjects and adolescent subjects)

For adult subjects, change from Baseline in PSP total score at each scheduled visit (Week 6/Visit 9) and the LOCF endpoint will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline PSP total score as the covariate.

Change from Baseline in each of the PSP individual domain scores will be analyzed using the ANCOVA method similarly to the PSP total score.

For both adult subjects and adolescent subjects, the observed PSP total score and individual domain scores and the change from Baseline values will be summarized descriptively by treatment group and visit.

For adult subjects, each binary outcome listed below at Week 6/Visit 9 and the LOCF endpoint will be analyzed using a logistic regression model with event indicator as the dependent variable and include factors for treatment group and region and include Baseline PSP total score as a covariate. NNT (see Section 16.3.3.8) will also be provided.

- PSP total score ≥71 at Baseline and each scheduled visit (Week 6/Visit 9)
- Improvement of ≥1 PSP 10-point category from Baseline to each scheduled visit (Week 6/Visit 9)

For both adult subjects and adolescent subjects, the number and percentage of subjects satisfying each of the above conditions will also be summarized descriptively by treatment group and visit.

In addition, for both adult subjects and adolescent subjects, the number and percentage of subjects that fall in each of the following PSP categories will be summarized descriptively by treatment group and visit:

- Total score 100-71 (mild to no impairment).
- Total score 70-51 (moderate impairment)
- Total score 50-31 (marked impairment)
- Total score 30-1 (severe impairment)

For adult subjects, the treatment difference in the frequency distribution of the PSP categories at Week 6/Visit 9 and the LOCF endpoint will be assessed by using a Chi-squared test. If >20% of the cells have expected frequencies less than 5, Fisher's exact test will be used instead of the Chi-squared test.

16.3.3.13. Change from Baseline in EQ-5D-5L VAS, index value and dimension score at each scheduled visit (adult subjects and adolescent subjects)

For adult subjects, change from Baseline in EQ-5D-5L VAS and index value at each scheduled visit (Week 6/Visit 9) and the LOCF endpoint will each be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline EQ-5D-5L VAS and index value as the respective covariate.

For both adult subjects and adolescent subjects, the observed EQ-5D-5L VAS and index value and the change from Baseline values will be summarized descriptively by treatment group and visit.

For both adult subjects and adolescent subjects, the number and percentage of subjects reporting each

level of problem under each of the 5 dimensions (i.e., the frequency distribution of the dimension scores) will be summarized descriptively by treatment group and visit. For adult subjects, the treatment difference in the frequency distribution of each of the 5 dimensions at Week 6/Visit 9 and the LOCF endpoint will be assessed by using a Chi-squared test. If >20% of the cells have expected frequencies less than 5, Fisher's exact test will be used instead of the Chi-squared test.

For both adult subjects and adolescent subjects, the EQ-5D health state at a given post-Baseline time point relative to the health state at Baseline will be categorized into:

- Better: If the health state at the post-Baseline time point is better in at least one dimension and is no worse in any other dimension than the health state at Baseline.
- Worse: If the health state at the post-Baseline time point is worse in at least one dimension and is no better in any other dimension than the health state at Baseline.
- Same: If the health state is exactly the same between the post-Baseline time point and Baseline.
- Mixed: If the health state at the post-Baseline time point is better in one dimension but worse in another dimension than the health state at Baseline.

The frequency distribution of the post-Baseline categorized EQ-5D health state relative to the Baseline will be summarized descriptively by treatment group and visit. For adult subjects, the treatment difference in the frequency distribution at Week 6/Visit 9 and the LOCF endpoint will be assessed by using a Chi-squared test. If >20% of the cells have expected frequencies less than 5, Fisher's exact test will be used instead of the Chi-squared test.

16.3.3.14. Change from Baseline in UPSA-B total score and subscale scores at each scheduled visit (adult subjects)

Change from Baseline in UPSA-B total score at each scheduled visit (Week 6/Visit 9) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline UPSA-B total score as the covariate.

Change from Baseline in each of the UPSA-B subscale scores will be analyzed using the ANCOVA method similarly to the UPSA-B total score.

The observed UPSA-B total score and subscale scores and the change from Baseline values will also be summarized descriptively by treatment group and visit.

16.3.3.15. Change from Baseline in MSQ score at each scheduled visit (adult subjects and adolescent subjects)

The analysis of MSQ data will be limited to subjects who were being treated with an antipsychotic medication at the time of screening or had been treated with antipsychotic medications within 30 days prior to the Screening visit. These subjects will be identified at the Blinded Data Review meeting prior to database lock and treatment unblinding.

For adult subjects, change from Baseline in MSQ score at each scheduled visit (Week 6/Visit 9) will be

analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline MSQ score as the covariate.

For both adult subjects and adolescent subjects, the observed MSQ score and the change from Baseline values will be summarized descriptively by treatment group and visit. In addition, the frequency distribution of the MSQ score will be summarized descriptively by treatment group and visit.

16.3.3.16. Tobacco use (adult subjects)

Tobacco use data will be summarized descriptively by treatment group and visit.

For each tobacco type, the amount being used at Week 6/Visit 9 in comparison with the amount being used at Baseline will be classified as "increased", "decreased", or "unchanged" for every subject, based on the reported amount used in a given period. If a subject quit using a particular type of tobacco since Baseline, the amount used for that tobacco type will be classified as "decreased". If a subject newly started or restarted using a particular type of tobacco since Baseline, the amount used for that tobacco type will be classified as "increased".

Then for subjects whose changes in amount for all tobacco types between Baseline and Week 6/Visit 9 are not in opposite directions, a subject's overall tobacco consumption at Week 6/Visit 9 in comparison with Baseline will be classified as "increased", "decreased", or "unchanged" based on the following:

- If the change in amount for each tobacco type is either "increased" or "unchanged", the subject's overall consumption will be classified as "increased".
- If the change in amount for each tobacco type is either "decreased" or "unchanged", the subject's overall consumption will be classified as "decreased".
- If the change in amount for all tobacco types is "unchanged", the subject's overall consumption will be classified as "unchanged".

The number and percentage of subjects in each overall consumption amount change category will be summarized by treatment group.

In addition, for subjects who reported using "Cigarettes" at either Baseline or Week 6/Visit 9 or at both time points, the number of cigarettes used per day will be derived for both time points. The following conversion will be applied if necessary:

- Amount: 1 Pack = 20 Cigarettes.
- Time period: 1 Week = 7 Days; 1 Month = 30 Days.

The amount of cigarette used per day and the change from Baseline values will be summarized by treatment group and visit.

16.4. Combined Adult and Adolescent Efficacy Analyses

PANSS total scores from the adult and adolescent subjects in the mITT population will be combined. Change from Baseline in PANSS total score at Week 6 will be analyzed using a MMRM model with fixed effects for treatment, visit (Day 4, Weeks 1, 2, 3, 4, 5 and 6; as a categorical variable), country, treatment-by-visit interaction, Baseline PANSS total score, and cohort indicator (adult vs. adolescent). An unstructured covariance matrix will be used to model the within-subject correlation. Kenward-Roger

approximation will be used to calculate the denominator degrees of freedom. In case this model fails to converge, a spatial exponential covariance structure and a spatial power covariance structure along with an empirical sandwich estimator for the standard errors of the fixed effect parameters will be assumed sequentially. The first covariance structure to yield convergence will be used in the analysis. If the model fails to converge with all three structures specified above, the compound symmetry covariance structure will be assumed.

The observed PANSS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit.

CGI-S score from the adult and adolescent subjects in the mITT population will be combined. Change from Baseline in CGI-S score at Week 6 will be analyzed using a MMRM model with fixed effects for treatment, visit (Day 4, Weeks 1, 2, 3, 4, 5 and 6; as a categorical variable), country, treatment-by-visit interaction, Baseline CGI-S score, and cohort indicator (adult vs. adolescent). An unstructured covariance matrix will be used to model the within-subject correlation. Kenward-Roger approximation will be used to calculate the denominator degrees of freedom. In case this model fails to converge, a spatial exponential covariance structure and a spatial power covariance structure along with an empirical sandwich estimator for the standard errors of the fixed effect parameters will be assumed sequentially. The first covariance structure to yield convergence will be used in the analysis. If the model fails to converge with all three structures specified above, the compound symmetry covariance structure will be assumed.

The observed CGI-S score and the change from Baseline values will also be summarized descriptively by treatment group and visit.

17. SAFETY OUTCOMES

The safety data will be analyzed and presented separately for adult subjects and adolescent subjects. In addition, selected adverse event summaries will be performed on combined data from the adult and adolescent subjects (see Section 17.8).

Unless otherwise specified, the safety analysis and summary tables will include the following columns: Placebo, SEP-363856 50 mg/day, SEP-363856 75 mg/day, and SEP-363856 Combined.

All analyses of the safety outcomes will be based on the SAF Population, by the actual treatment group.

Safety data will be used in analysis irrespective of emergency treatment unblinding (see protocol Section 7.2.3).

17.1. ADVERSE EVENTS AND PRE-TREATMENT EVENTS

Adverse events (AEs) and pre-treatment events will be coded using MedDRA central coding dictionary, Version 22.0.

Any COVID-19 related Adverse Events and pre-treatment events will be identified using a pre-defined search:

Table 2: Predefined search criteria for COVID-19 related adverse events or pre-treatment events.

Lower Level Term	Lower Level Term Code	Preferred Term	Preferred Term Code	Search Criteria for COVID-19 Related Adverse Events or Pre-treatment Events
Coronavirus test positive	1007025	Coronavirus test positive	10070255	Preferred Term Code = 10070255 or 10053983
Coronavirus infection	10051905	Corona virus infection	10053983	

Any adverse events or pre-treatment events related to the Russia-Ukraine geopolitical conflict will be identified by the reported term containing "BCP22".

AEs are defined as untoward medical occurrences that started at the same time of or after the first dose of study drug. Untoward medical occurrences that started prior to the first dose of study drug are pre-treatment events.

Whenever available, the time information should be accounted for in the derivation of AEs vs. pre-treatment events. In the case where time is not available, untoward medical occurrences that started on or after the day of the first dose of study drug will be considered AEs; those that started before the day of the first dose of study drug will be considered pre-treatment events.

See APPENDIX 2 for handling of partial dates for AEs. In the case where it is unclear whether an untoward medical occurrence is an AE or a pre-treatment event, the algorithm uses a conservative approach where the untoward medical occurrence is classified by the worst case; i.e., AE.

AEs (including serious adverse events (SAEs)) are collected into the clinical database until the last study visit. For subjects who do not roll over to study 361-303, the last study visit will be Visit 10 (the follow-up visit) which per protocol should occur 7 (± 2) days after the last dose of study drug. For subjects continuing into study 361-303, the last 361-301 study visit will be Visit 9 (the end of treatment visit) which per protocol should occur the day following the subject's last dose of study drug. If an AE (or a pre-treatment event) started in 361-301 and was ongoing at rollover, this adverse event (pre-treatment event) will be marked Ongoing in the 361-301 database. It will also be re-entered into the 361-303 database and its outcome will be monitored and updated in the 361-303 database.

For both adult subjects and adolescent subjects, overall summary of the incidence of all AEs, AEs related to COVID-19, AEs related to geopolitical conflict, study medication-related AEs, severe AEs, serious AEs, AEs leading to discontinuation from study, AEs leading to study medication withdrawal, AEs leading to study medication interruption, and AEs leading to death will be provided by treatment group. For adult subjects only, this overall incidence summary will also be separately presented for the following subgroups: geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category.

Listings will be provided for all AEs, AEs related to COVID-19, AEs related to geopolitical conflict, study medication-related AEs, severe AEs, serious AEs, AEs leading to discontinuation from the study, AEs leading to study medication withdrawal, AEs leading to study medication interruption, AEs leading to death, AEs of potential drug abuse and dependence, extrapyramidal AEs, and AEs subject to additional monitoring (ESAM; adolescent subjects only). A listing of the pre-treatment events will also be presented. When complete event start date and complete event end date are available, duration of AEs/pre-treatment events will be calculated as: event end date – event start date + 1. Duration will be

presented in data listings.

For all summaries, each subject will be counted only once within each category (e.g., an AE type, a severity level, a relationship category, a SOC, a high level term (HLT), and a PT). If not otherwise specified, all summaries will present the number and percentage of subjects as well as the number of events. For summaries by SOC and PT, AEs will be sorted by SOC based on the internationally agreed order (see APPENDIX 7) and then by PT in decreasing frequency in the "SEP-363856 Combined" column. For summaries by SOC, HLT, and PT, AEs will be sorted by SOC based on the internationally agreed order and then by HLT and PT in decreasing frequency in the "SEP-363856 Combined" column.

COVID-19 related pre-treatment events and AEs and geopolitical conflict related pre-treatment events and AEs will be displayed similarly as any other pre-treatment events and AEs.

17.1.1. ALL AEs

For adult subjects, all AEs will be summarized by PT, by SOC and PT, as well as by SOC, HLT, and PT. The summary by SOC and PT will also be presented for the following subgroups: geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category. For adolescent subjects, all AEs will be summarized by SOC and PT.

For both adult subjects and adolescent subjects, summary tables (by SOC and PT) will be generated for those AEs starting after the last dose of study drug and those AEs starting more than 1 day after the last dose of study drug.

For adult subjects, AEs reported by ≥ 2.0% (without rounding) of subjects in any treatment group will be summarized by SOC and PT.

For both adult subjects and adolescent subjects, non-serious AEs reported by > 5.0% (without rounding) of subjects in any treatment group will be summarized by SOC and PT.

For both adult subjects and adolescent subjects, the summary by SOC and PT will be broken down further by maximum severity and by strongest relationship to study medication. These summaries are described in the sections below.

17.1.1.1. Severity

Severity is classed as mild/ moderate/ severe (increasing severity). AEs with a missing severity will be classified as severe.

If a subject reported an AE more than once within the same SOC/ PT with different severity levels, the subject will be assigned to a severity level for that SOC/ PT based on the worst case severity (i.e., maximum severity). Event counts will not be included in this summary.

In a separate table, severe AEs will be summarized by SOC and PT.

17.1.1.2. Relationship to study medication

Relationship to study medication, as indicated by the Investigator, is classed as "not related"/ "possible"/ "probable"/ "definite" (increasing strength of relationship). A "related" AE is defined as an AE with a relationship to study medication as "possible", "probable" or "definite". AEs with a missing relationship to

study medication will be regarded as related to the study medication. For this summary, AEs will be presented in 2 categories, related and not related.

If a subject reported an AE more than once within the same SOC/ PT in different relationship categories, the subject will be assigned to a category for that SOC/ PT based on the worst case relationship (i.e., strongest relationship). Event counts will not be included in this summary.

In a separate table, study medication-related AEs will be summarized by SOC and PT.

17.1.1.3. Study medication dose level at AE onset (adolescent subjects)

For this summary, the table will have the following columns: Placebo, SEP-363856 50 mg/day, and SEP-363856 75 mg/day. The columns are not mutually exclusive; each subject will be counted in a column if they received that dose level at least once during the study.

Study medication dose at AE onset will be determined by the last dose level the subject received prior to AE onset. In case of partial or missing AE start date, the start date will be imputed as described in APPENDIX 2. The imputed start date will then be used to determine the study medication dose at AE onset (see rules described in APPENDIX 2).

If a subject reported multiple AEs under different dose levels, the subject will be counted in each dose level (column) under which they reported an AE. Under a given dose level (column), if a subject reported an AE more than once within the same SOC/PT, the subject will only be counted once under that dose level (column) for that SOC/PT. Event counts will not be included in this summary.

17.1.2. AEs Leading to Discontinuation from Study

AEs leading to discontinuation from the study are those AEs with "Caused Study Discontinuation" = "Yes" on the "*Adverse Events*" CRF form.

For both adult subjects and adolescent subjects, AEs leading to discontinuation from the study will be summarized by SOC and PT.

17.1.3. AEs Leading to Study Medication Withdrawal

AEs leading to permanent withdrawal from the study medication are those AEs with "Action Taken with Study Treatment" = "Drug Withdrawn" on the "*Adverse Events*" CRF form.

For both adult subjects and adolescent subjects, AEs leading to study medication withdrawal will be summarized by SOC and PT.

17.1.4. AEs Leading to Study Medication Interruption

AEs leading to study medication interruption are those AEs with "Action Taken with Study Treatment" = "Drug Interrupted" on the "*Adverse Events*" CRF form.

For both adult subjects and adolescent subjects, AEs leading to study medication interruption will be

summarized by SOC and PT.

17.1.5. Serious Adverse Events

SAEs are those AEs recorded as "Serious" on the "*Adverse Events*" CRF form.

For both adult subjects and adolescent subjects, SAEs will be summarized by SOC and PT. For adult subjects only, the summary will also be presented for the following subgroups: geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category.

Another table will summarize SAEs for European Union Drug Regulating Authorities Clinical Trials Database (EudraCT), including the number of causally related events.

In a separate table, SAEs starting within 7 days after the last dose of study drug will be summarized by SOC and PT as well.

17.1.6. Adverse Events Leading to Death

AEs leading to death are those AEs with "Outcome" = "Fatal" on the "*Adverse Events*" CRF form.

For adult subjects, AEs leading to death will be summarized by SOC and PT.

17.1.7. Adverse Events of Potential Drug Abuse and Dependence

AEs associated with potential drug abuse and dependence will be identified as described in APPENDIX 8.

For both adult subjects and adolescent subjects, these AEs will be summarized by PT only.

17.1.8. Extrapyramidal Adverse Events

Extrapyramidal AEs will be identified by MedDRA SMQ 20000095 Extrapyramidal syndrome as described in APPENDIX 9.

For both adult subjects and adolescent subjects, these AEs will be summarized by PT only.

17.1.9. Adverse Events Subject to Additional Monitoring (Adolescent Subjects Only)

Adverse events subject to additional monitoring (ESAM) are those AEs with "Was the AE an ESAM?" = "Yes" on the "*Adverse Events*" CRF. ESAM events will be summarized by PT.

17.1.10. Adverse Events by Subgroups

The subgroup factors of interest for AE summaries in adult subjects include: geographic region, sex, age group, number of prior hospitalizations for treatment of schizophrenia, duration of schizophrenia, and BMI category (see Section 7.5). AE by subgroup summaries are described in the individual sections above.

17.1.11. Additional Information Collected on Select Adverse Events

Additional information is collected for the non-serious psychiatric AEs that led to discontinuation from the study as well as all serious psychiatric AEs within the study.

1. Could the psychiatric AE be accounted for by an exacerbation of the underlying mental illness? Describe how the symptoms or behaviors of the psychiatric AE are characteristic of or similar to those typically experienced by the patient and/or how they are atypical/different.
2. Describe any new psychosocial stressors that may have contributed to the event.
3. Describe any adverse reactions to other concomitant medications that may have accounted for / contributed to the event.
4. Describe any recreational drug use that may have accounted for / contributed to the event. Please provide results of any recent drug screens.
5. Describe any other medical conditions that could manifest with psychiatric symptoms that might have accounted for or contributed to the event.
6. Were there any new physical or neurological symptoms that emerged at the same time as worsening of psychiatric symptoms? Please provide any details of the medical review of body systems at the time of the event.

The above information is recorded in separate trackers and not part of the CRF. This information will be presented in separate data listings only.

17.2. Laboratory Evaluations

Results from the central laboratory to be reported for this study include Hematology, Chemistry (including lipid panel and thyroid panel), Urinalysis, Urine drug screening, Serology panel, Serum pregnancy (β-HcG) (in female subjects only), Urine pregnancy (in female subjects only), Follicle stimulating hormone (FSH) (in female adult subjects with suspected menopause and in female adolescent subjects), Luteinizing hormone (LH) (in female adolescent subjects only), Estradiol (in female adolescent subjects only) and Testosterone (in male adolescent subjects only).

Serum and urine pregnancy results in both adult and adolescent female subjects, FSH level in adult female subjects, serology panel in both adult and adolescent subjects, and any unexpected lab parameters not specified in protocol Section 22 (APPENDIX III. CLINICAL LABORATORY TESTS) will only be listed. Laboratory parameters prespecified in protocol Section 22 under the categories of "HEMATOLOGY", "BLOOD CHEMISTRIES" (plus HOMA-IR), "URINALYSIS", and "URINE DRUG SCREENING" in both adult and adolescent subjects, as well as the hormone parameters in adolescent subjects (FSH, LH, estradiol, testosterone) will be summarized in tables as well as presented in listings.

Listing presentations will use both standard international (SI) Units and conventional units. Table summaries will also be provided using both SI units and conventional units.

Quantitative laboratory measurements reported as "< X", i.e., below the lower limit of quantification (BLQ), or "> X", i.e., above the upper limit of quantification (ULQ), will be converted to X for the purpose of quantitative summaries, but they will be presented as recorded, i.e., as "< X" or "> X" in the listings.

For both adult subjects and adolescent subjects, the following summaries will be provided:

- By-visit summary of observed values and change from Baseline values for quantitative measurements in hematology, chemistry, and urinalysis. Serum prolactin results will be summarized overall and separately by sex. Glucose, insulin, HOMA-IR and lipid panel results (total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides) will be summarized by fasting status: fasting only and overall (fasting, non-fasting, or fasting status unknown combined). Change from Baseline for glucose, insulin, HOMA-IR and lipid panel results will only be calculated if post-Baseline fasting status is matching Baseline fasting status.

- By-visit summary of the number and percentage of subjects in each outcome category for qualitative measurements in urinalysis (as applicable) and for urine drug screening results. Urine drug screening results will be reported as "Positive"/ "Negative".

- Shift in laboratory results (chemistry, hematology, urinalysis) from Baseline to Week 6/Visit 9 and LOCF Endpoint according to the reference range criteria. The existing reference range indicators provided by the central laboratory will be mapped as needed to categories of "Normal" (within the reference range) / "Abnormal" (outside the reference range) for urinalysis non-pH results, and to categories of "Low" (below the reference range) / "Normal" (within the reference range) / "High" (above the reference range) for chemistry and hematology results as well as urinalysis pH results.

- Number and percentage of subjects with at least one potentially clinically significant (PCS) laboratory value (see APPENDIX 10) post Baseline. The period of evaluation includes both the double-blind treatment period and the double-blind follow-up period, including unscheduled visits. Subjects will be counted in a particular PCS category if they met that PCS criteria at least once post Baseline, regardless of their Baseline value. For adolescent subjects, the PCS criteria will be applied based on age at study entry.

In addition, for adolescent subjects, the following summaries will be provided:

- By-visit summary of observed values and change from Baseline values for FSH, LH, and estradiol for female adolescent subjects, and testosterone for male adolescent subjects.

- Shift in hormone levels from Baseline to Week 6/Visit 9 and LOCF Endpoint according to the reference range criteria.

All laboratory data will be provided in data listings, with the values outside the reference ranges flagged. In addition, separate listings will be provided to present the laboratory data that met the PCS criteria.

Boxplots will be created to present Baseline and Week 6/Visit 9 values by treatment group for lipid parameters (total cholesterol, LDL, HDL, and triglycerides), glucose, insulin, and HOMA-IR by fasting status: fasting only and overall (fasting, non-fasting, or fasting status unknown combined). In addition, boxplots will be created to present Baseline and Week 6/Visit 9 prolactin values by treatment group by

sex: Overall, males, females. Lastly, the values of HbA1c will be presented for Baseline and Week 6/Visit 9 by treatment group in boxplots as well. Each of these boxplots will be repeated to present the change from Baseline values.

17.2.1. Laboratory Specific Derivations

- Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) will be calculated for each visit:

  HOMA-IR = Glucose (mg/dL) × Insulin (mU/L) / 405

  The following conversion factors will be used if needed:

  Glucose (mg/dL) = Glucose (mmol/L) × 18.015588;

  Insulin (mU/L) = Insulin (pmol/L) × (1/6).

17.2.2. Laboratory Reference Ranges

Laboratory reference range indicators will be provided by the laboratory vendor and used in statistical analyses. Only if a reference range indicator is missing in the data transfer will it be derived in the analysis step as described below.

- Quantitative laboratory measurements (that are not urinalysis erythrocytes or urinalysis leukocytes) will be compared with the relevant laboratory reference ranges in original units and categorized as:
  - Low: Below the lower limit of the laboratory reference range.
  - Normal: Within the laboratory reference range (upper and lower limit included).
  - High: Above the upper limit of the laboratory reference range.
- For laboratory parameters with categorical outcomes as well as urinalysis erythrocytes and urinalysis leukocytes, if the result is within the reference range, the indicator is "NORMAL"; if the result is not within range, the indicator is "ABNORMAL".

17.3. ECG Evaluations

Data from the centrally over-read ECG (Electrocardiogram) results will be included in the reporting of this study.

The following ECG parameters will be reported for this study:

- PR Interval (msec)
- RR Interval (msec)

- QRS Duration (msec)
- QRS Axis (deg)
- QT Interval (msec)
- QTcF Interval (msec) (Fridericia's Correction of QT interval)
- QTcB Interval (msec) (Bazett's Correction of QT interval)
- Heart Rate (bpm)
- Overall assessment of ECG as determined by the central over-read:
  - Normal
  - Abnormal, Insignificant
  - Abnormal, Potentially Significant
  - Abnormal, Significant
  - Exclusion Alert (only given for the Screening visit). In table summaries, the category of "Exclusion Alert" will be combined into the category of "Abnormal, Significant".
  - Not Evaluable
- ECG findings

ECG findings will only be listed. Other ECG data will be summarized in tables as well as presented in listings.

For both adult subjects and adolescent subjects, the following summaries will be provided:

- By-visit summary of observed values and change from Baseline values for quantitative measurements.
- By-visit summary of ECG overall assessment results as determined by the central over-read ("Normal", "Abnormal, Insignificant", "Abnormal, Potentially Significant", "Abnormal, Significant", "Not Evaluable").
- Shift in ECG overall assessment as determined by the central over-read from Baseline to Week 1/Visit 4, Week 6/Visit 9, and LOCF endpoint.
- Number and percentage of subjects who met each of the QTc interval prolongation criteria (see Section 17.3.1). The period of evaluation includes both the double-blind treatment period and the double-blind follow-up period, including unscheduled visits.
- Number and percentage of subjects with at least one PCS ECG value (see Section 17.3.2) post Baseline. The period of evaluation includes both the double-blind treatment period and the double-blind follow-up period, including unscheduled visits. Subjects will be counted in a particular PCS category if they met that PCS criteria at least once post Baseline, regardless of their Baseline value. For adolescent subjects, the PCS criteria will be applied based on age at study entry.

All ECG parameters, overall assessment as determined by the central over-read, and findings will be provided in a data listing. In addition, separate listings will be generated to present the QTc interval data of subjects who met at least one QTc prolongation criterion and the ECG data that met the PCS criteria.

17.3.1. QTc Interval Prolongation Criteria

QTc interval prolongation in adult subjects will be identified in accordance with the following predefined criteria (same criteria apply to both QTcF and QTcB):

- > 450 msec at any post-Baseline time point (including unscheduled visits) not present at Baseline
- > 480 msec at any post-Baseline time point (including unscheduled visits) not present at Baseline
- > 500 msec at any post-Baseline time point (including unscheduled visits) not present at Baseline
- ≥ 30 msec increase from Baseline for at least one post-Baseline measurement (including unscheduled visits) and < 60 msec increase from Baseline for all post-Baseline measurements (including unscheduled visits)
- ≥ 60 msec increase from Baseline for at least one post-Baseline measurement (including unscheduled visits)

QTc interval prolongation in adolescent subjects (12 to <18 years) will be identified in accordance with the following predefined criteria (same criteria apply to both QTcF and QTcB):

- > 460 msec at any post-Baseline time point (including unscheduled visits) not present at Baseline
- ≥ 60 msec increase from Baseline for at least one post-Baseline measurement (including unscheduled visits)

17.3.2. ECG Potentially Clinically Significant Criteria

Potentially clinically significant ECG measurements will be identified in accordance with the following predefined PCS criteria:

Table 3: Predefined ECG PCS criteria for adult subjects.

ECG Parameter	PCS Low	PCS High
Heart Rate (beats/min)	--	≥ 100
PR Interval (msec)	--	≥ 210
QRS Interval (msec)	--	≥ 120

Table 4: Predefined ECG PCS criteria for adolescent subjects.

ECG Parameter	Age (years)	PCS Low	PCS High
Heart Rate (beats/min)	12 to <16	< 50	> 105
	≥ 16	< 50	> 100
PR Interval (msec)	12 to <16	--	> 180
	≥ 16	--	> 200
QRS interval (msec)	12 to <16	--	> 110
	≥ 16	--	> 120

17.4. VITAL SIGNS

The following vital sign measurements will be reported for this study:

- Supine and Standing Systolic Blood Pressure (mmHg)
- Supine and Standing Diastolic Blood Pressure (mmHg)
- Supine and Standing Pulse Rate (bpm)
- Respiratory Rate (breaths/min)
- Temperature (°C)
- Height (cm)[§]
- Weight (kg)
- BMI (kg/m^2)
- Waist Circumference (cm)

[§]Height will be summarized together with the other vital sign measures for adolescent subjects only. For adult subjects, height will be summarized as part of the Baseline characteristics only.

For adult subjects, the following summaries will be provided:

- By-visit summary of observed values and change from Baseline values for vital sign measurements, including Week 7/Follow-up/Visit 10.

- Number and percentage of subjects with at least one PCS vital sign value (see Section 17.4.2) post Baseline. The period of evaluation includes both the double-blind treatment period and the double-blind follow-up period, including unscheduled visits. Subjects will be counted in a particular PCS category if they met that PCS criteria at least once post Baseline, regardless of their Baseline value.

- Number and percentage of subjects with orthostatic hypotension and/or orthostatic tachycardia (see Section 17.4.1). The data will be summarized for Baseline and the overall post-Baseline period (which covers both the double-blind treatment period and the double-blind follow-up period, including unscheduled visits), as well as by visit, including Week 7/Follow-up/Visit 10.

- By-visit summary of BMI category (see Section 7.5) and shift in BMI category from Baseline to each post-Baseline time point.

- By-visit summary of observed values and change from Baseline values for vital signs measurements by BMI category (see Section 7.5).

For adolescent subjects, the following summaries will be provided:

- By-visit summary of observed values and change from Baseline values for vital sign measurements, including Week 7/Follow-up/Visit 10.

- Number and percentage of subjects with at least one PCS vital sign value (see Section 17.4.2) post Baseline. The period of evaluation includes both the double-blind treatment period and the double-blind follow-up period, including unscheduled visits. Subjects will be counted in a particular PCS category if they met that PCS criteria at least once post Baseline, regardless of their Baseline value.

- Number and percentage of subjects with orthostatic hypotension and/or orthostatic tachycardia (see Section 17.4.1). The data will be summarized for Baseline and the overall post-Baseline period (which covers both the double-blind treatment period and the double-blind follow-up period, including unscheduled visits), as well as by visit, including Week 7/Follow-up/Visit 10.

All vital signs data will be provided in a data listing. In addition, a separate listing will be generated to present the vital signs data that met the PCS criteria. All occurrences of orthostatic hypotension and orthostatic tachycardia will also be presented in a listing.

Boxplots will be created to present weight data by time point and treatment group. The boxplots will be repeated to present the change from Baseline values.

17.4.1. Vital Sign Specific Derivations

- BMI expressed in kg/m^2 = Weight (kg)/ height $(m)^2$.

  For adult subjects, the height collected at Visit 1 will be used to derive BMI where needed throughout the study.

For adolescent subjects, the height collected at Visit 1 and at Visit 9/EOT/ET will be used to derive BMI at these two visits; for visits in between Visit 1 and Visit 9/EOT/ET where BMI needs to be derived, BMI will be derived using a linear interpolated value of height (assuming the height collected at Visit 9/EOT/ET is no less than the height collected at Visit 1). BMI will be missing at visits that would rely on interpolated height if 1) Height at Visit 1 or Visit 9/EOT/ET is missing or 2) Height at Visit 9/EOT/ET is lower than height at Visit 1.

- Interpolated Height (cm) for Date X = Height at Visit 1 + (Height at Visit 9/EOT/ET – Height at Visit 1) x (Date X – Date of Height assessment at Visit 1) / (Date of Height assessment at Visit 9/EOT/ET – Date of Height assessment at Visit 1)

- Orthostatic hypotension is defined as a decrease of ≥ 20 mmHg in systolic blood pressure or ≥ 10 mmHg in diastolic blood pressure after a subject has been standing for at least 2 to 4 minutes, compared to the systolic blood pressure and diastolic blood pressure measured in the supine position, respectively.

- Orthostatic tachycardia is defined as a heart rate increase of ≥ 20 bpm after a subject has been standing for at least 2 to 4 minutes compared to the heart rate measured in the supine position, and a heart rate of > 100 bpm after the subject has been standing for at least 2 to 4 minutes.

17.4.2. Vital Sign Potentially Clinically Significant Criteria

Potentially clinically significant vital sign measurements will be identified in accordance with the following predefined PCS criteria:

Table 5: Predefined vital sign PCS criteria for adult subjects.

Vital Sign Parameter	PCS Low	PCS High
Systolic Blood Pressure (Supine, Standing) (mmHg)	Value ≤ 90 and ≥ 20 decrease from Baseline	Value ≥ 180 and ≥ 20 increase from Baseline
Diastolic Blood Pressure (Supine, Standing) (mmHg)	Value ≤ 50 and ≥ 15 decrease from Baseline	Value ≥ 105 and ≥ 15 increase from Baseline
Pulse Rate (Supine, Standing) (beats/min)	Value ≤ 50 and ≥ 15 decrease from Baseline	Value ≥ 120 and ≥ 15 increase from Baseline
Weight (kg)	≥ 7% decrease from Baseline	≥ 7% increase from Baseline
Temperature (°C)	NA	Value ≥ 38.3°C and ≥ 0.8°C increase from Baseline

Table 6: Predefined vital sign PCS criteria for adolescent subjects.

Vital Sign Parameter	PCS Low	PCS High
Systolic Blood Pressure (Supine, Standing) (mmHg)	Value ≤ 90 and ≥ 20 decrease from Baseline	Value ≥ 135 and ≥ 20 increase from Baseline
Diastolic Blood Pressure (Supine, Standing) (mmHg)	Value ≤ 50 and ≥ 15 decrease from Baseline	Value ≥ 90 and ≥ 15 increase from Baseline
Pulse Rate (Supine, Standing) (beats/min)	Value ≤ 50 and ≥ 15 decrease from Baseline	Value ≥ 120 and ≥ 15 increase from Baseline
Temperature (°C)	NA	Value ≥ 38.3°C and ≥ 0.8°C increase from Baseline

17.5. PHYSICAL EXAMINATION

As all physical and neurological findings will be recorded as medical history or AEs, no specific analysis of physical and neurological examination will be performed.

17.6. OTHER SAFETY ASSESSMENTS

17.6.1. COLUMBIA SUICIDE SEVERITY RATING SCALE (C-SSRS)

The C-SSRS is a tool designed to systematically assess and track suicidal behavior and suicidal ideation for lifetime, one month prior to the screening visit for suicidal ideation and 6 months prior to the screening visit for suicidal behavior, and throughout the study. The strength of this suicide classification system is in its ability to comprehensively identify suicidal events while limiting the over-identification of suicidal behavior. The C-SSRS Baseline/Screening Version is used at the screening visit and the C-SSRS Since Last Visit Version is used from Visit 2 and onward. Subjects with Type 4 (active suicidal ideation with some intent to act, without specific plan) or Type 5 (active suicidal ideation with specific plan and intent) suicidal ideation during the study will be discontinued from the study and referred to a mental health professional.

C-SSRS includes two main sections: Suicidal Ideation and Suicidal Behavior.

The following outcomes are C-SSRS categories and have binary responses (yes/no). The categories are re-ordered from the scale to facilitate the definitions of the C-SSRS endpoints, and to provide clarity in the presentation of the results.

- Suicidal ideation is measured by 5 categories, representing 5 subtypes of suicidal ideation with increasing severity:
  - Category 1: Wish to be Dead
  - Category 2: Non-specific Active Suicidal Thoughts

- Category 3: Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act
- Category 4: Active Suicidal Ideation with Some Intent to Act, without Specific Plan
- Category 5: Active Suicidal Ideation with Specific Plan and Intent

- Suicidal behavior is measured by 5 categories, representing 5 subtypes of suicidal behavior:

  - Category 6: Preparatory Acts or Behavior
  - Category 7: Aborted Attempt
  - Category 8: Interrupted Attempt
  - Category 9: Actual Attempt (non-fatal)
  - Category 10: Completed Suicide

The 10 categories above are not mutually exclusive. Subjects will be counted in each category for which they have an event.

Self-injurious behavior without suicidal intent is a non-suicide-related C-SSRS outcome, and also has a binary response (yes/no).

For the purpose of C-SSRS analysis, "Baseline" and the overall "post-Baseline" periods are defined as follows.

Time point	Study Visit	C-SSRS Version	Derivation Rule
Baseline	Visit 1	Baseline/Screening – Past 1 Month for Suicidal Ideation / Past 6 Months for Suicidal Behavior	Most severe outcome
	Visit 2*	Since Last Visit	
Post-Baseline	All post-Baseline visits up to and including Visit 10 (the follow-up visit), including unscheduled visits	Since Last Visit	Most severe outcome

* Note: The Visit 2 C-SSRS assessment must be administered prior to the first dose of study medication in order to be used in the C-SSRS Baseline derivation.

The following C-SSRS composite endpoints will be derived for each time point of interest (i.e., Baseline, overall post-Baseline, and each scheduled visit including Week 7/Follow-up/Visit 10) as follows:

- Any suicidal ideation: A "yes" answer to any one of the 5 suicidal ideation questions on C-SSRS (Categories 1-5).

- Any suicidal behavior: A "yes" answer to any one of the 5 suicidal behavior questions on the C-SSRS (Categories 6-10).

- Any suicidality: A "yes" answer to any one of the 10 suicidal ideation and behavior questions on the C-SSRS (Categories 1-10).

For each subject, the suicidal ideation score at each time point of interest (i.e., Baseline, overall post-Baseline, the LOCF endpoint, and each scheduled visit including Week 7/Follow-up/Visit 10) is defined as the maximum suicidal ideation category (1-5) present for the time point of interest. If no ideation is present a score of 0 is assigned.

The number and percentage of subjects with any suicidality, any suicidal ideation and subtypes of ideation, any suicidal behavior and subtype of behavior, and any non-suicidal self-injurious behavior will be presented for:

- Baseline (as defined above)
- The overall post-Baseline period (as defined above)
- Each scheduled visit: Screening/Visit 1 (lifetime; past 1 month for ideation/past 6 months for behavior), Randomization/Visit 2, Day 4/Visit 3, Week1/Visit 4, Week 2/Visit 5, Week 3/Visit 6, Week 4/Visit 7, Week 5/Visit 8, Week 6/Visit 9, and Week 7/Follow-up/Visit 10.

For adult subjects, difference between each SEP-363856 treatment group, as well as the two SEP-363856 groups combined, against the placebo group for the proportion of subjects with any suicidality, any suicidal behavior, and any suicidal ideation at Baseline and during the overall post-Baseline period will be evaluated using Fisher's Exact test.

Shift in suicidal ideation score from Baseline to the overall post-Baseline period, to each of the scheduled visits (Day 4/Visit 3, Week1/Visit 4, Week 2/Visit 5, Week 3/Visit 6, Week 4/Visit 7, Week 5/Visit 8, Week 6/Visit 9, and Week 7/Follow-up/Visit 10), and to the LOCF endpoint will be presented.

Intensity of ideation for the most severe ideation subtype is measured in terms of frequency, duration, controllability, deterrents, and reasons for ideation. Each is measured with responses ranging from 1 to 5 for frequency and duration, and from 0 to 5 for controllability, deterrents, and reasons for ideation. The ideation intensity total score is the sum of responses to the five items and can range from 2 to 25 for subjects with endorsed suicidal ideation. For subjects with endorsed suicidal ideation, if one or more of these five items are missing at an assessment, the total score will be set to missing. If a subject did not endorse any suicidal ideation, a score of 0 for the ideation intensity total score will be given.

Actual lethality associated with actual attempts is rated on a 6-point scale from 0 = 'No physical damage or very minor physical damage' to 5 = 'Death'. Potential lethality of actual attempts (if actual lethality = 0) is rated on a 3-point scale from 0 = 'Behavior not likely to result in injury' to 2 = 'Behavior likely to result in death despite available medical care'.

Responses to each C-SSRS question will be listed. The ideation intensity total score and the actual lethality and potential lethality of actual attempts will only be presented in data listings.

17.6.2. Abnormal Involuntary Movement Scale (AIMS)

The AIMS is a clinician-rated assessment of abnormal movements consisting of unobtrusive observation of the subject at rest (with shoes removed) and several questions or instructions directed toward the subject. It contains seven items related to: facial, lip, jaw, and tongue movements (items 1 - 4), upper and lower extremity movements (items 5 - 6), and trunk movements (item 7). Three other items assess the subject at a global level (items 8 - 10), and two items assess dental status (items 11 - 12).

The (non-global) AIMS total score is the sum of items 1 through 7. (Items 8 through 12 are not used in AIMS total score calculation.) The possible range for AIMS total score is 0 to 28. Higher values of the AIMS total score indicate increased severity in abnormal movement. If one or more of the 7 items contributing to AIMS total score calculation are missing at a visit, the total score will be set to missing for that visit.

AIMS total score at each visit is classified as 'abnormal' if: either at least two items (out of items 1 - 7) have a response of 'Mild' or higher (i.e., item score ≥2); or at least one item (out of items 1 - 7) has a response of 'Moderate' or higher (i.e., item score ≥3). Otherwise, the non-missing AIMS total scores is classified as 'normal'.

Item 8 of AIMS represents the global severity score. Post-Baseline AIMS global severity scores will be classified as 'worsened', 'unchanged', or 'improved', relative to a subject's Baseline response to item 8. A higher score than that of the Baseline would be classified as 'worsened'. Conversely, a lower score would be classified as 'improved'. If the score is equal to that of Baseline, the score will be classified as 'unchanged'.

AIMS is assessed at these study visits: Visit 2 and Visit 9.

For adult subjects, change from Baseline in AIMS total score at each scheduled visit (Week 6/Visit 9) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline AIMS total score as the covariate. In addition, the ANCOVA analysis will be repeated for subgroups of subjects based on whether the subject took concomitant medications for treatment of movement disorders during the study. The list of medications will be determined by a review of the coded medication terms before database lock and study unblinding.

For both adult subjects and adolescent subjects, the observed AIMS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit. In addition, for adult subjects only, the observed AIMS total score and the change from Baseline values will be summarized descriptively by the subgroups of concomitant medication use for treatment of movement disorders. For the subgroup analysis, the ANCOVA analysis will be performed for a given time point only if there are at least 2 safety population subjects with data available in each of the three treatment groups at that time point.

For both adult subjects and adolescent subjects, shift from Baseline in AIMS total score category (Normal/Abnormal) to each post-Baseline scheduled visit (Week 6/Visit 9) and to the overall post-Baseline period (including both the double-blind treatment period and the double-blind follow-up period) will be summarized descriptively by treatment group.

The observed AIMS global severity score and the change from Baseline values will be summarized descriptively by treatment group and visit. In addition, the frequency distribution of the AIMS global severity item will be summarized descriptively by treatment group and visit. Post-Baseline changes in

AIMS global severity score (Worsened/Unchanged/Improved) will also be summarized descriptively by treatment group and visit.

17.6.3. BARNES AKATHISIA RATING SCALE (BARS)

The BARS is a rating scale geared toward assessment of neuroleptic-induced akathisia, though it can be used to measure akathisia associated with other drugs as well. The BARS consists of four items, including one item assessing objective restlessness (item 1), two items targeting subjective restlessness (awareness and related distress; items 2 - 3), and one global clinical assessment of akathisia item (item 4). The objective and subjective items are anchored and utilize a 4-point scale. The global assessment item has a 6-point scale (from absence of akathisia through severe akathisia).

The BARS total score is the sum of items 1 through 3 and ranges from 0 to 9. Higher values of the BARS total score indicate higher severity of akathisia. If one or more of items 1 to 3 are missing at a visit, the BARS total score will be set to missing for that visit.

The post-Baseline BARS Global Clinical Assessment of Akathisia responses will be classified as 'worsened', 'unchanged', or 'improved', relative to a subject's Baseline response to this item. A higher score than that of the Baseline would be classified as 'worsened'. Conversely, a lower score would be classified as 'improved'. If the score is equal to that of Baseline, the score will be classified as 'unchanged'.

BARS is assessed at these study visits: Visit 2 and Visit 9.

For adult subjects, change from Baseline in BARS total score at each scheduled visit (Week 6/Visit 9) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline BARS total score as the covariate. In addition, the ANCOVA analysis will be repeated for subgroups of subjects based on whether the subject took concomitant medications for treatment of movement disorders during the study.

For both adult subjects and adolescent subjects, the observed BARS total score and the change from Baseline values will also be summarized descriptively by treatment group and visit. In addition, for adult subjects only, the observed BARS total score and the change from Baseline values will be summarized descriptively by the subgroups of concomitant medication use for treatment of movement disorders. For the subgroup analysis, the ANCOVA analysis will be performed for a given time point only if there are at least 2 safety population subjects with data available in each of the three treatment groups at that time point.

For adult subjects, change from Baseline in BARS global clinical assessment score at each scheduled visit (Week 6/Visit 9) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline BARS global clinical assessment score as the covariate.

For both adult subjects and adolescent subjects, post-Baseline changes in BARS global clinical assessment score (Worsened/Unchanged/Improved) will be summarized descriptively by treatment group and visit.

Lastly, for both adult subjects and adolescent subjects, the observed BARS item scores and the change from Baseline values will be summarized descriptively by treatment group and visit. In addition, the frequency distribution of each BARS item will be summarized descriptively by treatment group and visit.

17.6.4. Simpson-Angus Scale (SAS)

The SAS is a clinician-rated assessment of neuroleptic-induced Parkinsonism consisting of 10 items. Items are anchor-based, rated on a 5-point scale (ranging between 0 and 4), and address rigidity, gait (bradykinesia), tremor, akathisia, shoulder shaking, glabellar tap, and salivation.

SAS mean score is defined as the average of all 10 items and ranges between 0 and 4. Lower values of the SAS mean score indicate milder symptoms. If one or more of the SAS items are missing at a visit, the SAS mean score will be set to missing for that visit.

The SAS mean score at each visit will be classified as 'abnormal' if it exceeds 0.3 (Rush, et al., 2000). Otherwise, the non-missing SAS mean score will be classified as 'normal'.

SAS is assessed at these study visits: Visit 2 and Visit 9.

For adult subjects, change from Baseline in SAS mean score at each scheduled visit (Week 6/Visit 9) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline SAS mean score as the covariate. In addition, the ANCOVA analysis will be repeated for subgroups of subjects based on whether the subject took concomitant medications for treatment of movement disorders during the study.

For both adult subjects and adolescent subjects, the observed SAS mean score and the change from Baseline values will also be summarized descriptively by treatment group and visit. In addition, for adult subjects only, the observed SAS mean score and the change from Baseline values will be summarized descriptively by the subgroups of concomitant medication use for treatment of movement disorders. For the subgroup analysis, the ANCOVA analysis will be performed for a given time point only if there are at least 2 safety population subjects with data available in each of the three treatment groups at that time point.

For both adult subjects and adolescent subjects, shift from Baseline in SAS mean score category (Normal/Abnormal) to each post-Baseline scheduled visit (Week 6/Visit 9) and to the overall post-Baseline period (including both the double-blind treatment period and the double-blind follow-up period) will be summarized descriptively by treatment group.

17.6.5. Pittsburgh Sleep Quality Index (Adult Subjects Only)

The Pittsburgh Sleep Quality Index (PSQI) consists of 19 self-rated questions and 5 questions rated by the bed partner or roommate (if one is available). It is used to measure the quality and patterns of sleep in adults. Only self-rated questions are included in the scoring. It differentiates "poor" from "good" sleep quality by measuring seven "component" scores, each of which has a range of 0-3 points: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction due to sleepiness over the last month.

The seven component scores are then summed to yield one global PSQI score, with a range of 0-21 points, "0" indicating no difficulty and "21" indicating severe difficulties in all areas (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).

The PSQI scoring algorithm as downloaded from the University of Pittsburgh Sleep and Chronobiology Center is inserted in APPENDIX 12. The seven component scores and the PSQI global score will be derived according to this algorithm. If one or more of the component scores are missing at a visit, the

PSQI global score will be set to missing for that visit.

PSQI is assessed at these study visits: Visit 2 and Visit 9.

Change from Baseline in PSQI global score at each scheduled visit (Week 6/Visit 9) will be analyzed using an ANCOVA model similar to the model described in Section 16.1.5.1, with Baseline PSQI global score as the covariate. In addition, the observed PSQI global score and the change from Baseline values will be summarized descriptively by treatment group and visit.

17.6.6. Tanner Staging (Adolescent Subjects Only)

Tanner staging is a scale of physical development which can be used in children, adolescents, and adults. The scale defines physical measurements of development based on external primary and secondary sex characteristics, such as the size of the breasts, genitalia, testicular volume, and development of pubic and axillary hair.

Tanner staging is assessed at these study visits: Visit 2 and Visit 9.

The frequency distribution of the Tanner stages will be tabulated by treatment group and visit. Shift in the Tanner stages from Baseline to Week 6/Visit 9 will also be tabulated by treatment group.

17.6.7. Menstrual Cyclicity (Female Adolescent Subjects Only)

Menstrual cyclicity is assessed at these study visits: Visit 2 and Visit 9.

Change in the frequency of menstrual cycle over the past year or since last visit will be tabulated by treatment group and visit.

Shift in the frequency of menstrual cycle from Baseline (capturing the approximate frequency over the past year) to Week 6/Visit 9 (capturing the approximate frequency since last visit) will be tabulated by treatment group.

Change in the nature of menstrual cycle over the past year and since last visit will also be tabulated by treatment group and visit.

17.6.8. Healthcare Resource Utilization (Adolescent Subjects Only)

Healthcare resource utilization is assessed at these study visits: Visit 2 and Visit 9.

The frequency and percentage of subjects with physician's office visits, ER visits, and hospitalizations (for any reason and those related to schizophrenia) at Baseline and at Week 6/Visit 9 (capturing the information during the past 3 months) will be summarized. The number of physician's office visits, ER visits, and hospitalizations (for any reason and those related to schizophrenia) per month at Baseline and at Week 6/Visit 9, as well as the average length of hospital stays (for any reason and those related to schizophrenia) at Baseline and at Week 6/Visit 9, will be summarized. Employment status at Baseline and at Week 6/Visit 9 will be summarized. The frequency and percentage of subjects receiving unpaid care at Baseline and at Week 6/Visit 9, along with the average number of hours a caregiver spends per week helping the subject, will also be summarized.

The change in the number of physician's office visits, ER visits, and hospitalizations per month, the average length of hospital stays, and the average number of hours a caregiver spends per week helping the subject from Baseline at Week 6/Visit 9 will be summarized.

Shift from Baseline to Week 6/Visit 9 in whether the subjects receive unpaid care will also be summarized.

17.7. Subgroup Analysis of Safety Variable(s)

The subgroup analyses for AE data, vital signs data, and AIMS/BARS/SAS scales are described in their respective sections.

17.8. Combined Adult and Adolescent Safety Analyses

AE data from adult subjects and adolescent subjects in the SAF population will be combined. AE overall incidence summaries will be provided on the combined data. In addition, the AE by SOC and PT summary will be provided on the combined data.

CCI [redacted]

19. Data Not Summarized or Presented

The variables and/or domains not summarized or presented are:

- Subject initials
- Any data collected on screen failures other than disposition, basic demographics, and pre-treatment events.
- Any data collected during previously failed screening(s) for randomized subjects who were screened more than once except Adverse Events.

These domains and/or variables will not be summarized or presented but will be available in the clinical study database and SDTM datasets.

20. REFERENCES

Buysse, D., Reynolds, C., Monk, T., Berman, S., & Kupfer, D. (1989). The Pittsburgh Sleep Quality Index (PSQI): A new instrument for psychiatric research and practice. *Psychiatry Research, 28(2)*, 193-213.

Dmitrienko, A., & Tamhane, A. (2011). Mixtures of multiple testing procedures for gatekeeping applications in clinical trials. *Statistics in Medicine*.

Dmitrienko, A., & Tamhane, A. (2013). General theory of mixture procedures for gatekeeping. *Biometrical Journal*, 402–419.

Hopkins, S., Ogirala, A., Loebel, A., & Koblan, K. (2018;44(3):593-602). Transformed PANSS factors intended to reduce pseudospecificity among symptom domains and enhance understanding of symptom change in antipsychotic-treated patients with schizophrenia. *Schizophrenia Bull*.

Hopkins, S., Ogirala, A., Loebel, A., & Koblan, K. (2020). Characterization of specific and distinct patient types in clinical trials of acute schizophrenia using an uncorrelated PANSS score matrix transform (UPSM). *Psychiatry Research*.

Keefe, R., Philip, H., Terry, G., James, G., Trina, W., Courntey, K., & Kirsten, H. (2008). Norms and standardization of the Brief Assessment of Cognition in Schizophrenia (BACS). *Schizophrenia Reaseach*, 108-115.

Kordzakhia, G., Brechenmacher, T., Ishida, E., Dmitrienko, A., Zheng, W., & Li, D. (2018). An enhanced mixture method for constructing gatekeeping procedures in clinical trials. *JOURNAL OF BIOPHARMACEUTICAL STATISTICS*, VOL. 28, NO. 1, 113-128.

Lawrence, J., & Hung, H. J. (2003). Estimation and Confidence Intervals after Adjusting the Maximum Information. *Biometrical Journal*, 143-152.

Marder, S., Davis, J., & Chouinard, G. (1997;58:538–46). The effects of risperidone on the five dimensions of schizophrenia. *J Clin Psychiatry* .

O'Kelly, M., & Ratitch, B. (2014). *Clinical Trial with Missing Data - A Guide for Practitioners.* John Wiley & Sons.

Rush, A., Pincus, H., First, M., Blacker, D., Endicott, J., Keith, S., . . . Zarin, D. (2000). *Handbook of Psychiatric Measures.* American Psychiatric Association.

Sugitani, T., Posch, M., Bretz, F., & Koenig, F. (2018). Flexible alpha allocation strategies for confirmatory adaptive enrichment clinical trials with a prespecified subgroup. *Statistics in Medicine*, 1-16.

Wassmer, G., & Brannath, W. (2016). *Group sequential and confirmatory adaptive designs in clinical trials.* New York: Springer.

APPENDIX 1. PROGRAMMING CONVENTIONS FOR OUTPUTS

IQVIA OUTPUT CONVENTIONS

Where applicable, the appendix_compilation_working_Guidelines_21Jun2017 Global Final.pdf document – provided by SMPA – will be followed.

In addition, the following output conventions are to be followed:

- General presentation:
  - The first row in the body of the table or listing should be blank
  - The left-hand column should start in column 1. No indenting or centering of the output should occur.
  - Rounding should be done with the SAS function ROUND.
  - Numbers in tables should be rounded, not truncated.
  - Alphanumeric output should be left aligned.
  - Numbers should be decimal point aligned.
  - Whole numbers should be right aligned.
  - Text values should be left aligned.
  - The first letter of a text entry should be capitalized.
  - The width of the entire output should match the linesize (134)
- Univariate Statistics: If the raw data has N decimal places, then the summary statistics should have the following decimal places:
  - Minimum and maximum: N
  - Mean, median, Q1, and Q3: N + 1
  - SD: N + 2
  - For lab data only, in the rare case where raw data has more than 3 decimal places, summary statistics will be presented for the scenario of N = 3. All decimals will be presented in Listings.
  - For CGI-S score, 2 decimal places will be presented for mean, median, Q1, Q3, LS mean, LS mean difference, and 95% CI; 3 decimal places will be presented for SD and SE; 0 decimal places will be presented for min and max. 0 decimal places will be presented in listings.
  - For UPSM scores, 3 decimal places will be presented for mean, median, Q1, Q3, LS mean, LS mean difference, and 95% CI; 4 decimal places will be presented for SD and SE; 2 decimal places will be presented for min and max. Up to 2 decimal places will be presented in Listings. No rounding will be applied in the ADaM datasets.
  - For the following calculated parameters, no rounding will be applied in the ADaM datasets. The N values noted below will be used to determine the number of decimal places to be reported in outputs (tables, listings, and figures as applicable):
    - BMI: N = 1

- Frequencies and percentages (n and %):
  - Percent values should be reported inside parentheses, with one space between the count (n) and the left parenthesis of the percentage. Parentheses should be justified to accept a maximum of 100.0 as a value and padded with blank space if the percent is less than 100.0.
  - Percentages will be reported to one decimal place, except cases where percent <100.0% but >99.9% will be presented as '>99.9%' (e.g., 99.99% is presented as >99.9%); and cases where percent < 0.1% will be presented as '<0.1%' (e.g., 0.08% is presented as <0.1%). Rounding will be applied after the <0.1% and >99.9% rule.
  - Where counts are zero, no percentage should appear in the output.
- Confidence Intervals:
  - Confidence intervals and estimates are presented to one place more than the raw data, and standard errors to two places more than the raw data.
  - Confidence intervals should be justified so that parentheses displayed on consecutive lines of a table "line up".
  - Boundary values of confidence intervals should be separated by a comma.
  - Boundary values should be padded as necessary to accept negative values and to allow alignment of the decimal place.
- P-values should be reported to three decimal places, except values <1.000 but >0.999 will be presented as '>0.999' (e.g., 0.9998 is presented as >0.999); and values <0.001 will be presented as '<0.001' (e.g., 0.0009 is presented as <0.001). Rounding will be applied after the <0.001 and >0.999 rule.
- Ratios should be reported to one more decimal place than the raw data.
- Spacing must be a minimum of 1 blank space between columns (preferably 2).
- Missing values:
  - A "0" should be used to indicate a zero frequency.
  - A blank will be used to indicate missing data in an end-of-text table or subject listing.
- Figures:
  - Figures should be provided in RTF files using the SAS Output Delivery System (ODS), as Computer Graphics Metafile (CGM) formatted graphical output generated by SAS.
  - The CGM file itself should contain the title or footer.
  - The image should be clear and of high quality when viewed in the Word document, and when printed.
  - In general, boxes around the figures should be used.
- Footers should be defined as follows:
  - A continuous line of underscores ('_') will follow the body of the table or listing prior to any footnotes at the bottom of the page.

- Table footnotes should be defined using compute statements in the proc report and should appear directly after the body of the table.
- If text wraps across more than one line (for a note), the first letter for all lines of text after the first one will be indented to align beneath the first letter of the text in the first line.

DATES & TIMES

Depending on data available, dates and times will take the form yyyy-mm-ddThh:mm:ss .

SPELLING FORMAT

English US.

PRESENTATION OF TREATMENT GROUPS

For outputs, treatment groups will be represented as follows and in that order:

Treatment Group	For Tables (Column Order)	For Listings and Graphs (Order)
Placebo	Placebo (1)	Placebo (L3; G1)
SEP-363856 50 mg/day	SEP-363856 50 mg/day (2)	SEP-363856 50 mg/day (L1; G2)
SEP-363856 75 mg/day	SEP-363856 75 mg/day (3)	SEP-363856 75 mg/day (L2; G3)
	SEP-363856 Combined (4)	
	Total (5)	

LISTINGS

All listings will be ordered by the following (unless otherwise indicated in the template):

- Actual treatment group, displaying active dose first [50 mg/day then 75 mg/day] and then placebo. Randomized subjects who did not receive any study medication will be presented at the end and labelled "Not Treated".
- Subject ID.
- Visit (where applicable)
- Original date/time (where applicable).

APPENDIX 2. PARTIAL DATE CONVENTIONS

The actual dates as collected on the CRF will be presented in the listings. Imputed dates will not be presented in the listings unless otherwise specified.

ALGORITHM FOR ADVERSE EVENTS

As a general rule, if the start date of an AE is available and the start time of the AE is not available, the AE will be considered to have started after the study drug dose administered on the day of the AE start date.

In case of partial or missing AE start and/or end dates, impute partial or missing event start and/or end dates (if not ongoing) using the algorithm below. If an AE has some missing components in both the start and end dates, first impute the end date.

AE end date imputation

- If year and month (YYYY-MM) of AE end date are known, then impute the missing day to be the earlier of (last day of the month; date of last contact).
- If only year (YYYY) of AE end date is known, then impute the missing month and day to be the earlier of (31st December; date of last contact).
- If AE end date is completely missing and AE is not ongoing, then impute AE end date to be date of last contact.

AE start date imputation

- If year and month (YYYY-MM) of AE start date are known and YYYY-MM = year and month of 361-301 study med start date, then impute AE start date to be the earlier of (361-301 study med start date; full or imputed AE end date [if non-missing]).
- If year and month (YYYY-MM) of AE start date are known and YYYY-MM ≠ year and month of 361-301 study med start date, then impute AE start date to be YYYY-MM-01.
- If only year (YYYY) of AE start date is known and YYYY = year of 361-301 study med start date, then impute AE start date to be the earlier of (361-301 study med start date; full or imputed AE end date [if non-missing]).
- If only year (YYYY) of AE start date is known and YYYY ≠ year of 361-301 study med start date, then impute AE start date to be YYYY-01-01.
- If AE start date is completely missing, then impute AE start date to be the earlier of (361-301 study med start date; full or imputed AE end date [if non-missing]).

Using the full or imputed event dates, assign events into pre-treatment events vs. AE as described below.

If both event start date/time and 361-301 study med start date/time are available:

- If event start date/time < 361-301 study med start date/time, then pre-treatment event.

- If event start date/time ≥ 361-301 study med start date/time, then AE.

If (event start date is available and time is not available) and/or (361-301 study med start date is available and time is not available):

- If event start date < 361-301 study med start date, then pre-treatment event.
- If event start date ≥ 361-301 study med start date, then AE.

ALGORITHM FOR PRIOR / CONCOMITANT / POST-TREATMENT MEDICATIONS

In case of partial or missing medication start and/or stop dates, impute the partial or missing dates using the algorithm below.

If a medication has some missing components in both the start and stop dates, first impute the stop date.

Impute stop date as latest possible date

- If only day unknown, impute to the earlier of (last day of the month; date of 361-301 last contact).
- If month and day unknown, impute to the earlier of (31st December; date of 361-301 last contact).
- If stop date is completely unknown and medication is not ongoing, impute to date of 361-301 last contact.

Impute start date as earliest possible date

CRF questions: 'Started prior to first dose?' = Yes; 'Started after last dose of study medication?' = No.

- If only day unknown, impute to the later of (first day of the month; date of birth [if full date is available]).
- If month and day unknown, impute to the later of (1st January; date of birth [if full date is available]).
- If start date is completely unknown, impute to the earlier of (date of informed consent*; full or imputed medication stop date [if not missing]).

*For adolescents, use max(date of informed consent, date of informed assent).

CRF questions: 'Started prior to first dose?' = No; 'Started after last dose of study medication?' = Yes.

- If only day unknown, impute to the later of (first day of the month; 361-301 study med end date + 1).
- If month and day unknown, impute to the later of (1st January; 361-301 study med end date + 1).
- If start date is completely unknown, impute to 361-301 study med end date + 1.

CRF questions: 'Started prior to first dose?' = No; 'Started after last dose of study medication?' = No.

- If only day unknown, impute to the later of (first day of the month; 361-301 study med start date).
- If month and day unknown, impute to the later of (1st January; 361-301 study med start date).
- If start date is completely unknown, impute to 361-301 study med start date.

Then assign a medication into prior, concomitant, or post-treatment

The concept of "date" below should also include time information whenever time is available for both comparators.

- If medication stop date < 361-301 study med start date, assign as prior.

- If (medication stop date ≥ 361-301 study med start date or medication is ongoing) and medication start date ≤ 361-301 study med end date, assign as concomitant.
- If medication start date > 361-301 study med end date, assign as post-treatment.

Overriding rule

For the case where the medication start date is known and is equal to 361-301 study med end date and the medication start time is unknown, or the case where the imputed medication start date is equal to 361-301 study med end date:

- If CRF question '*Started after last dose of study medication?*' = *No*, then assign as concomitant.
- If CRF question '*Started after last dose of study medication?*' = *Yes*, then assign as post-treatment.

PARTIAL DATE IMPUTATION RULES FOR INITIAL ONSET OF SCHIZOPHRENIA

For subjects with partial onset date of schizophrenia, impute the onset date using the following rules:

- If only day unknown, impute as the earlier of: 15th of the month, or date of ICF*.
- If both month and day unknown, impute as the earlier of: June 30th of the year, or date of ICF*.

*For adolescent subjects, the later of the ICF date and IAF date should be used.

PARTIAL DATE IMPUTATION RULES FOR CURRENT ONSET OF ACUTE EXACERBATION

For subjects with partial onset date of acute exacerbation, impute the onset date using the following rules:

- If only day unknown and the known year and month is earlier than the year and month of ICF*, impute as the later of: 15th of the month, or date of initial onset of schizophrenia (actual or imputed).
- If only day unknown and the known year and month is the same as the year and month of ICF*, impute as the later of: earlier of (date of ICF*, 15th of the month), or date of initial onset of schizophrenia (actual or imputed).
- If both month and day unknown and the known year is earlier than the year of ICF*, impute as the later of: June 30th of the year, or date of initial onset of schizophrenia (actual or imputed).
- If both month and day unknown and the known year is the same as the year of ICF*, impute as the later of: earlier of (date of ICF*, June 30th of the year), or date of initial onset of schizophrenia (actual or imputed).

*For adolescent subjects, the later of the ICF date and IAF date should be used.

PARTIAL DATE IMPUTATION RULES FOR FIRST HOSPITALIZATION

For subjects with partial date of first hospitalization for treatment of schizophrenia, impute the date using the following rules:

- If only day unknown, impute as the earlier of: 15th of the month, or date of ICF*.
- If both month and day unknown, impute as the earlier of: June 30th of the year, or date of ICF*.

*For adolescent subjects, the later of the ICF date and IAF date should be used.

For subjects whose date of first hospitalization for treatment of schizophrenia is completely missing AND the number of prior hospitalizations for treatment of schizophrenia is 0, impute the date of first hospitalization to be the "*Date of admission for this study hospitalization*" collected on the "*Psychiatric Hospitalization (HOSP)*" CRF form.

PARTIAL DATE IMPUTATION RULES FOR FIRST ANTI-PSYCHOTIC DRUG THERAPY

For subjects with partial start date for the first anti-psychotic drug therapy of at least 2 weeks duration intended for treatment of schizophrenia, impute the start date using the following rules:

- If only day unknown, impute as the earlier of: 15th of the month, or date of ICF*.
- If both month and day unknown, impute as the earlier of: June 30th of the year, or date of ICF*.

*For adolescent subjects, the later of the ICF date and IAF date should be used.

PARTIAL DATE IMPUTATION RULES FOR ONSET OF INITIAL BEHAVIORAL DISTURBANCE

For adolescent subjects with partial onset date of initial behavioral disturbance, impute the onset date using the following rules:

- If only day unknown, impute as the earlier of: 15th of the month, or the later of (date of ICF and date of IAF).
- If both month and day unknown, impute as the earlier of: June 30th of the year, or the later of (date of ICF and date of IAF).

RULES FOR ASSIGNING DOSEON/DOSEA

- In general, DOSEON/DOSEA should be the dose level immediately before the start of an AE or an assessment. In case the AE or the assessment start date/time coincides with the first dosing start date/time of the study, the DOSEON/DOSEA should be assigned to the dose level associated with that first dosing start date/time. In case the AE or the assessment start date/time coincides with a dosing start date/time other than the first dosing start date/time (collected or imputed for Day 4 as specified in Section 14.1), the DOSEON/DOSEA should be assigned to the dose level associated with the previous dosing start date/time.

- In case of missing AE start time, missing assessment (start) time, and/or missing dosing start time (after imputation for Day 4 as specified in Section 14.1), DOSEON/DOSEA should be assigned using the algorithm in the table below.

Scenario	Data	Rules
Dosing start date and start time both available	Adverse Events	If AE start date is available and AE start time is missing, dose on the same day as AE start should be assigned as DOSEON.
	Scales/Questionnaires, Vitals, Labs, ECG	If assessment start date is available and assessment start time is missing, dose on the previous day of the assessment should be assigned as DOSEA.
Dosing start date available but start time missing	Adverse Events	Regardless of whether AE start time is available, dose on the same day as AE start should be assigned as DOSEON.
	Scales/Questionnaires, Vitals, Labs, ECG	Regardless of whether assessment start time is available, dose on the previous day of the assessment should be assigned as DOSEA.

- In case of partial or missing AE start date, the imputed AE start date will be used for the purpose of assigning DOSEON.

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

ccl

APPENDIX 4. LOCAL P-VALUES FOR INTERSECTION HYPOTHESES CALCULATED USING HOCHBERG-BASED GATEKEEPING PROCEDURE

The local p-values for the intersection hypotheses will be calculated using the Hochberg-based gatekeeping procedure constructed using the enhanced mixture method (Kordzakhia, et al., 2018). Specifically:

- Let r_1 and r_2 denote the combined one-sided p-values associated with Family F1 hypotheses H_1 and H_2, respectively; let r_3 and r_4 denote the combined one-sided p-values associated with Family F2 hypotheses H_3 and H_4, respectively. (The combined one-sided p-values are obtained as described in Section 7.4.)
- Let $r_{(1)}$ and $r_{(2)}$ denote the ordered p-values in Family F1, i.e., $r_{(1)} = r_1$ and $r_{(2)} = r_2$ if $r_1 < r_2$, and $r_{(1)} = r_2$ and $r_{(2)} = r_1$ otherwise; let $r_{(3)}$ and $r_{(4)}$ denote the ordered p-values in Family F2, i.e., $r_{(3)} = r_3$ and $r_{(4)} = r_4$ if $r_3 < r_4$, and $r_{(3)} = r_4$ and $r_{(4)} = r_3$ otherwise.
- Let γ denote the truncation parameter of the truncated Hochberg procedure.

The local p-values $r(I)$ for the intersection hypotheses $H(I)$ will be calculated as shown in the table below.

Intersection Hypothesis $H(I)$	Local p-value $r(I)$
$H_1 \cap H_2 \cap H_3 \cap H_4$	$\min(2r_{(1)}, r_{(2)})$
$H_1 \cap H_2 \cap H_3$	$\min(2r_{(1)}, r_{(2)})$
$H_1 \cap H_2 \cap H_4$	$\min(2r_{(1)}, r_{(2)})$
$H_1 \cap H_2$	$\min(2r_{(1)}, r_{(2)})$
$H_1 \cap H_3 \cap H_4$	$\min(2r_1/(1+\gamma), 2r_4/(1-\gamma))$
$H_1 \cap H_3$	r_1
$H_1 \cap H_4$	$\min(2r_1/(1+\gamma), 2r_4/(1-\gamma))$
H_1	r_1
$H_2 \cap H_3 \cap H_4$	$\min(2r_2/(1+\gamma), 2r_3/(1-\gamma))$
$H_2 \cap H_3$	$\min(2r_2/(1+\gamma), 2r_3/(1-\gamma))$
$H_2 \cap H_4$	r_2
H_2	r_2
$H_3 \cap H_4$	$\min(2r_{(3)}, r_{(4)})$

H_3	r_3
H_4	r_4

APPENDIX 5. UNCORRELATED PANSS SCORE MATRIX (UPSM)

PANSS	UPSM-POS	UPSM-DIS	UPSM-NAA	UPSM-NDE	UPSM-HOS	UPSM-ANX	UPSM-DEP
PANSS01	0.5792730597	-0.1547126840	-0.0828932650	0.0071927220	-0.0593031510	-0.0735449620	0.0020484408
PANSS02	0.0292444390	0.1975824582	-0.0260173260	-0.0234753800	-0.0368756010	-0.0012396240	-0.0361645050
PANSS03	0.2065788330	-0.0179419820	-0.0250663450	-0.0133031880	-0.0300507070	0.0001506005	0.0293001724
PANSS04	-0.0336790630	0.0115284348	0.0011652392	-0.0723891460	0.1379358628	0.1108194656	-0.1045224460
PANSS05	-0.0341508580	-0.0301875430	-0.0041019560	-0.0233459100	-0.0069204000	-0.0313277060	0.0308288417
PANSS06	0.3537254634	-0.0626270750	0.0477329954	0.0012126712	0.0192067437	-0.0161398140	0.0063264235
PANSS07	-0.0383468990	-0.1767919370	-0.0299340700	0.0314652864	0.5025411101	-0.0997121200	0.0573604084
PANSS08	-0.0054230270	-0.0291400280	0.0568702938	0.2474176209	-0.0388464000	0.0188235393	-0.0091524870
PANSS09	-0.0315765690	-0.0243925850	0.3317907576	-0.0228204580	-0.0507096280	-0.0145653830	0.0112689069
PANSS10	-0.0742072890	-0.0401313020	-0.0097485120	0.0161513666	0.0245536353	-0.0176161520	-0.0172218040
PANSS11	-0.0943532590	-0.0856364190	0.4611503804	-0.0286825100	-0.0189062390	-0.0185825180	-0.0130433890
PANSS12	0.0043338689	0.1062496353	0.0255910591	-0.0301470410	-0.0133497570	0.0096065791	-0.0686802390
PANSS13	0.0041274699	0.0051521898	0.0009558861	0.2576813501	-0.0085004640	0.0194235006	-0.1037459520
PANSS14	-0.0111267300	0.1462268689	-0.0276416260	0.0023017188	-0.0055291270	-0.0118427800	0.0040128786
PANSS15	-0.0356272010	0.0552508287	-0.0382627720	0.0110152489	-0.0309176290	0.0444944076	0.1059845189
PANSS16	-0.0331052830	-0.0821894470	-0.0327376640	-0.0533178140	-0.0386473380	0.4576579818	0.1197800301
PANSS17	-0.0368854600	-0.0004363100	-0.0020681500	-0.0407976460	-0.0272172130	-0.0253163640	0.2459654614
PANSS18	-0.0931367690	-0.0332617600	-0.0132943930	0.0231904701	-0.0287529750	0.5123850161	-0.0312522560
PANSS19	-0.0455199430	0.0494113554	-0.0324174560	0.1026255664	-0.0136676190	0.0293507269	-0.0441735260
PANSS20	-0.0344751890	-0.0688197670	-0.0412738350	0.0381793764	0.0042219619	-0.0635101090	0.4514426846
PANSS21	-0.0348890020	-0.0366137810	-0.0779782830	0.4409895205	-0.0073240410	-0.0192655290	0.0464131877
PANSS22	-0.0803690920	0.0334025939	-0.0088488890	-0.0200483170	0.2858700784	-0.0567167860	-0.0531076130
PANSS23	0.1428966744	0.0939213700	-0.0326143600	-0.0367524640	-0.0675856980	-0.0209072840	-0.0177890070
PANSS24	-0.0383047770	-0.0324584080	-0.0255393890	-0.0180115340	-0.0266180700	-0.0210068530	-0.0176029110
PANSS25	-0.1036311520	0.2814367260	-0.0478918640	0.0029986238	0.0037656449	-0.0226520240	0.0401351054

PANSS26	0.0142987589	0.1548635741	-0.0306089330	-0.0331581690	0.0262295986	-0.0576293550	-0.0626180490
PANSS27	-0.0573513270	0.1867914227	-0.0143489160	0.0581534153	-0.0145494330	-0.0371788310	0.0455412078
PANSS28	-0.0748387810	0.0166272025	-0.0267498020	-0.0031632780	0.2546669938	-0.0201249190	-0.0076420280
PANSS29	-0.0520812460	0.2912295497	0.0029775475	-0.0324350460	-0.0442337350	-0.0047991290	0.0567191230
PANSS30	-0.0112030990	-0.0007246980	0.2860136812	-0.0606201430	0.0183598393	-0.0302347770	0.0370748725

APPENDIX 6. EQ-5D-5L INDEX VALUE CALCULATION

EQ-5D-5L health states, defined by the EQ-5D-5L descriptive system, may be converted into a single index value using an appropriate EQ-5D-5L value set. If a standard EQ-5D-5L value set is not available, but an EQ-5D-3L value set is available, a "crosswalk" value set can be used to derive the index value. For multiregional trials, EuroQol recommends applying a single standard value set (or crosswalk value set) to all study sites. For this study, the US EQ-5D-5L standard value set will be used for all countries.

Please refer the following EuroQol website for EQ-5D-5L value sets and further information.

https://euroqol.org/publications/key-euroqol-references/value-sets/

APPENDIX 7. INTERNATIONALLY AGREED ORDER FOR SYSTEM ORGAN CLASS

Internationally Agreed Order
Infections and infestations
Neoplasms benign, malignant and unspecified (incl cysts and polyps)
Blood and lymphatic system disorders
Immune system disorders
Endocrine disorders
Metabolism and nutrition disorders
Psychiatric disorders
Nervous system disorders
Eye disorders
Ear and labyrinth disorders
Cardiac disorders
Vascular disorders
Respiratory, thoracic and mediastinal disorders
Gastrointestinal disorders
Hepatobiliary disorders
Skin and subcutaneous tissue disorders
Musculoskeletal and connective tissue disorders
Renal and urinary disorders
Pregnancy, puerperium and perinatal conditions
Reproductive system and breast disorders
Congenital, familial and genetic disorders
General disorders and administration site conditions
Investigations
Injury, poisoning and procedural complications
Surgical and medical procedures
Social circumstances
Product issues

APPENDIX 8. ADVERSE EVENTS OF POTENTIAL DRUG ABUSE AND DEPENDENCE

To ensure comprehensive and consistent selection of terminology used for analyses of drug abuse and dependence in ongoing / planned studies of SEP-363856, MedDRA PTs were identified from the following sources:

- FDA Guidance for Industry: Assessment of Abuse Potential of Drugs (CDER, 2017; noted that the Guidance reflects MedDRA version 20.0 terminology)
- MedDRA version 22.0 SMQ: Drug abuse and dependence [20000101], Broad
- FDA FMQ: Study Agent Abuse Potential, Broad (released at FDA public workshop "Advancing Premarket Safety Analytics", held September 14, 2022)

Description:

Preferred terms were tabulated using MedDRA version 22.0 from the sources listed above. All PTs within the FDA Abuse Potential Guidance were included. All PTs listed in the MedDRA version 22.0 SMQ for Drug abuse and dependence [20000101] were included. For the FDA Study Agent Abuse Potential FMQ: No associated MedDRA PT was found for the term "Hypnogogic hallucination", and this is therefore not included. SMPA evaluates 'Drug withdrawal' as a unique medical concept using MedDRA version 22.0 SMQ for Drug withdrawal [20000102] (Broad); any overlapping PTs from the Drug withdrawal SMQ which are listed in the FDA Study Agent Abuse Potential FMQ are not included. All other PTs listed in the FDA FMQ were included.

The table below depicts the preferred terms by source.

Table 7: Drug Abuse and Dependence Preferred Terms Using MedDRA v 22.0

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
-	-	Accidental overdose	10000381	Accidental overdose	10000381
-	-	-	-	Acute psychosis	10001022
Aggression	10001488	-	-	-	-
Behavioural addiction	10081939	-	-	-	-
Confusional state	10010305	-	-	-	-
-	-	-	-	Delusion of grandeur	10012241
-	-	-	-	Delusional perception	10012258
Dependence	10012335	Dependence	10012335	Dependence	10012335
-	-	-	-	Depersonalisation	10012357
-	-	-	-	Derealisation disorder	10077810
-	-	-	-	Detoxification	10061814
-	-	-	-	Disinhibition	10013142
Disorientation	10013395	-	-	-	-
-	-	Disturbance in social behaviour	10061108	-	-
Dizziness	10013573	-	-	-	-
Dopamine	10067468	Dopamine	10067468	-	-

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
dysregulation syndrome		dysregulation syndrome			
-	-	Drug abuse	10013654	Drug abuse	10013654
-	-	Drug abuser	10061111	Drug abuser	10061111
-	-	Drug dependence	10013663	Drug dependence	10013663
Drug dependence, antepartum	10013675	Drug dependence, antepartum	10013675	Drug dependence, antepartum	10013675
Drug dependence, postpartum	10013676	Drug dependence, postpartum	10013676	Drug dependence, postpartum	10013676
-	-	Drug detoxification	10052237	Drug detoxification	10052237
-	-	Drug diversion	10066053	Drug diversion	10066053
-	-	Drug level above therapeutic	10061132	-	-
-	-	Drug level increased	10013722	-	-
-	-	Drug screen	10050837	-	-
-	-	Drug screen positive	10049177	-	-
Drug tolerance	10052804	Drug tolerance	10052804	-	-
Drug tolerance decreased	10052805	Drug tolerance decreased	10052805	-	-
Drug tolerance increased	10052806	Drug tolerance increased	10052806	-	-
Drug use disorder	10079381	Drug use disorder	10079381	Drug use disorder	10079381
-	-	Drug use disorder, antepartum	10079382	Drug use disorder, antepartum	10079382
-	-	Drug use disorder, postpartum	10079383	Drug use disorder, postpartum	10079383
-	-	-	-	Energy increased	
Euphoric mood	10015535	-	-	Euphoric mood	10015535
Feeling abnormal	10016322	-	-	-	-
Feeling drunk	10016330	-	-	Feeling drunk	10016330
-	-	-	-	Feeling jittery	10016338
Feeling of relaxation	10016352	-	-	Feeling of relaxation	10016352
-	-	-	-	Flight of ideas	10016777
Hallucination	10019063	-	-	Hallucination	10019063
Hallucination, auditory	10019070	-	-	Hallucination, auditory	10019070
Hallucination, gustatory	10019071	-	-	Hallucination, gustatory	10019071
Hallucination, olfactory	10019072	-	-	Hallucination, olfactory	10019072
Hallucination, synaesthetic	10062824	-	-	Hallucination, synaesthetic	10062824
Hallucination, tactile	10019074	-	-	Hallucination, tactile	10019074
Hallucination, visual	10019075	-	-	Hallucination, visual	10019075
Hallucinations, mixed	10019079	-	-	Hallucinations, mixed	10019079

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
Inappropriate affect	10021588	-	-	Hallucination, gustatory	10019071
-	-	-	-	Hypersomnia	10020765
-	-	-	-	Hypervigilance	10048533
-	-	-	-	Hypnagogic hallucination	10020927
-	-	-	-	Hypnogogic hallucination	No such code
-	-	-	-	Hypnopompic hallucination	10020928
-	-	-	-	Inappropriate affect	10021588
-	-	-	-	Infant sedation	10082187
-	-	-	-	Intentional misuse of drug delivery system	10081675
-	-	Intentional overdose	10022523	Intentional overdose	10022523
-	-	Intentional product misuse	10074903	Intentional product misuse	10074903
-	-	Intentional product use issue	10076308	-	-
-	-	-	-	Mania	10026749
-	-	Maternal use of illicit drugs	10026938	-	-
-	-	Medication overuse headache	10072720	-	-
-	-	-	-	Mixed delusion	10076429
Mood altered	10027940	-	-	Mood altered	10027940
Mood swings	10027951	-	-	-	-
-	-	Narcotic bowel syndrome	10072286	-	-
-	-	Needle track marks	10028896	-	-
-	-	Neonatal complications of substance abuse	10061862	-	-
-	-	-	-	Neonatal oversedation	10050395
-	-	Overdose	10033295	-	-
-	-	-	-	Paranoia	10033864
-	-	-	-	Post-injection delirium sedation syndrome	10072851
-	-	Prescription drug used without a prescription	10076639	-	-
-	-	Prescription form tampering	10067669	Prescription form tampering	10067669
-	-	-	-	Psychomotor hyperactivity	10037211

FDA Guidance 2017		SMQ 20000101		FDA FMQ	
PT	Code	PT	Code	PT	Code
Psychotic disorder	10061920	-	-	-	-
		Reversal of opiate activity	10039004	-	-
-	-	-	-	Sedation	10039897
-	-	-	-	Sedation complication	10079741
Somnolence	10041349	-	-	Somnolence	10041349
-	-	-	-	Somnolence neonatal	10041350
-	-	-	-	Stupor	10042264
-	-	Substance abuse	10066169	Substance abuse	10066169
-	-	Substance abuser	10067688	Substance abuser	10067688
-	-	Substance dependence	10076595	Substance dependence	10076595
-	-	Substance use	10070964	-	-
Substance use disorder	10079384	Substance use disorder	10079384	Substance use disorder	10079384
-	-	Substance-induced mood disorder	10072387	Substance-induced mood disorder	10072387
-	-	Substance-induced psychotic disorder	10072388	Substance-induced psychotic disorder	10072388
-	-	-	-	Suspected product tampering	10079404
Thinking abnormal	10043431	-	-	-	-
-	-	Toxicity to various agents	10070863	-	-
-	-	-	-	Transient psychosis	10056326
-	-	-	-	Withdrawal hypertension	10048007

APPENDIX 9. EXTRAPYRAMIDAL ADVERSE EVENTS

To ensure comprehensive and consistent selection of terminology used for analyses of extrapyramidal signs and symptoms in ongoing / planned studies of SEP-363856, MedDRA PTs were identified from the following source:

- MedDRA version 22.0 SMQ: Extrapyramidal syndrome [20000095], Broad, including all 4 sub-SMQs (Akathisia [20000096], Dyskinesia [20000097], Dystonia [20000098], and Parkinson-like events [20000099])

Description:

All PTs listed in the MedDRA version 22.0 SMQ for Extrapyramidal syndrome [20000095] were included. The table below depicts the PTs by sub-SMQ.

Table 8: Extrapyramidal Syndrome SMQ Using MedDRA v 22.0

Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
Akathisia	10001540	-	-	-	-	-	-
-	-	-	-	-	-	Akinesia	10001541
-	-	Athetosis	10003620	-	-	-	-
-	-	Ballismus	10058504	-	-	-	-
-	-	-	-	-	-	Bradykinesia	10006100
-	-	Buccoglossal syndrome	10006532	-	-	-	-
-	-	Chorea	10008748	-	-	-	-
-	-	Choreoathetosis	10008754	-	-	-	-
-	-	-	-			Cogwheel rigidity	10009848
-	-	Dopamine dysregulation syndrome	10067468	-	-	-	-
-	-	-	-	Dopa-responsive dystonia	10080034	-	-
-	-	Dyskinesia	10013916	-	-	-	-
-	-	Dyskinesia neonatal	10013922	-	-	-	-
-	-	Dyskinesia oesophageal	10013924	-	-	-	-
-	-			Dystonia	10013983		
-	-			Dystonic tremor	10073210		
-	-	-	-	Early onset primary dystonia	10076668	-	-
-	-	-	-	Emprosthotonus	10014566	-	-

Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
-	-	-	-	-	-	Freezing phenomenon	10060904
-	-	Grimacing	10061991	-	-	-	-
-	-	-	-	-	-	Hypertonia	10020852
-	-	-	-	-	-	Hypertonia neonatal	10048615
-	-	-	-	-	-	Hypokinetic dysarthria	10082243
-	-	-	-	Meige's syndrome	10027138		
-	-	-	-	-	-	Muscle rigidity	10028330
-	-	Oculogyric crisis	10030071	Oculogyric crisis	10030071		
-	-	-	-	-	-	On and off phenomenon	10030312
-	-	-	-	Opisthotonus	10030899	-	-
-	-			Oromandibular dystonia	10067954	-	-
-	-	-	-	-	-	Parkinsonian crisis	10048868
-	-	-	-	-	-	Parkinsonian gait	10056242
-	-	-	-	-	-	Parkinsonian rest tremor	10056437
-	-	-	-	-	-	Parkinsonism	10034010
-	-	-	-	-	-	Parkinsonism hyperpyrexia syndrome	10071243
-	-	-	-	-	-	Parkinson's disease	10061536
-	-	-	-	-	-	Parkinson's disease psychosis	10074835
-	-	Pharyngeal dyskinesia	10070912	-	-	-	-
-	-	-	-	Pharyngeal dystonia	10081226	-	-
-	-	-	-	Pleurothotonus	10035628	-	-
-	-	-	-			Propulsive gait	10082328
-	-	Protrusion tongue	10037076	-	-	-	-
-	-	Rabbit syndrome	10068395	-	-	-	-
-	-	Respiratory dyskinesia	10057570	-	-	-	-
-	-	-	-	-	-	Resting tremor	10071390
-	-	-	-	Spasmodic dysphonia	10067672	-	-

Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
-	-	Tardive dyskinesia	10043118	-	-	-	-
-	-	-	-	Torticollis	10044074	-	-
-	-	-	-	Trismus	10044684	-	-
-	-	-	-	Writer's cramp	10072249	-	-
-	-	Abnormal involuntary movement scale	10075002	-	-	-	-
-	-	-	-	-	-	Action tremor	10072413
-	-	-	-	Blepharospasm	10005159		
-	-	-	-	-	-	Bradyphrenia	10050012
-	-	Chronic tic disorder	10076661	Chronic tic disorder	10076661	-	-
-	-	Complex tic	10076663	Complex tic	10076663	-	-
-	-	Drooling	10013642	Drooling	10013642	Drooling	10013642
-	-	-	-	-	-	Dysphonia	10013952
Extrapyramidal disorder	10015832	Extrapyramidal disorder	10015832	Extrapyramidal disorder	10015832	Extrapyramidal disorder	10015832
-	-	-	-	Facial spasm	10063006	-	-
-	-	-	-	-	-	Fine motor skill dysfunction	10076288
-	-	-	-	-	-	Gait disturbance	10017577
-	-	-	-	Gait inability	10017581	-	-
Hyperkinesia	10020651	-	-	-	-	-	-
Hyperkinesia neonatal	10020652	-	-	-	-	-	-
-	-	-	-	-	-	Hypokinesia	10021021
-	-	-	-	-	-	Hypokinesia neonatal	10021022
-	-	-	-	-	-	Laryngeal tremor	10078751
-	-	-	-	Laryngospasm	10023891	-	-
-	-	-	-	-	-	Micrographia	10057333
-	-	-	-	-	-	Mobility decreased	10048334
Motor dysfunction	10061296	Motor dysfunction	10061296	Motor dysfunction	10061296	Motor dysfunction	10061296
Movement disorder	10028035	Movement disorder	10028035	Movement disorder	10028035	Movement disorder	10028035
-	-	Muscle twitching	10028347	-	-	-	-
-	-	-	-	Muscle contractions involuntary	10028293	-	-
-	-	-	-	Muscle spasms	10028334	-	-

Akathisia		Dyskinesia		Dystonia		Parkinson-like	
PT	Code	PT	Code	PT	Code	PT	Code
-	-	-	-	Muscle spasticity	10028335	-	-
-	-	-	-	Muscle tightness	10049816	-	-
-	-	-	-	Muscle tone disorder	10072889	Muscle tone disorder	10072889
-	-	-	-	Muscle twitching	10028347	-	-
-	-	-	-	Musculoskeletal stiffness	10052904	Musculoskeletal stiffness	10052904
-	-	-	-	Oesophageal spasm	10030184	-	-
-	-	-	-	Oropharyngeal spasm	10031111	-	-
-	-	-	-	Posture abnormal	10036436	-	-
-	-	-	-	-	-	Postural reflex impairment	10067206
-	-	-	-	-	-	Postural tremor	10073211
-	-			Posturing	10036437	-	-
-	-	Provisional tic disorder	10076694	Provisional tic disorder	10076694	-	-
Psychomotor hyperactivity	10037211	-	-	-	-	-	-
		-	-	-	-	Reduced facial expression	10078576
Restlessness	10038743	-	-	-	-	-	-
-	-	-	-	Risus sardonicus	10039198	-	-
-	-	Secondary tic	10076702	Secondary tic	10076702	-	-
-	-	Tic	10043833	Tic	10043833	-	-
-	-	-	-	Tongue spasm	10043981	-	-
-	-	-	-	Torticollis psychogenic	10044076	-	-
-	-	-	-	-	-	Tremor	10044565
-	-	-	-	-	-	Tremor neonatal	10044575
-	-	-	-	Uvular spasm	10050908	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	Walking disability	10053204

APPENDIX 10. PREDEFINED POTENTIALLY CLINICALLY SIGNIFICANT (PCS) CRITERIA IN SI UNITS

STANDARD ADULT PCS CRITERIA FOR LABORATORY PARAMETERS – SI UNITS

Category Parameter Name Age/Sex Restriction, if any	PCS Low	PCS High
HEMATOLOGY		
WBC	≤ 2.8 × 10^9/L	≥ 16 × 10^9/L
Neutrophils (abs)	< 0.5 × 10^9/L	> 13.5 × 10^9/L
Lymphocytes (abs)	N/A	> 12 × 10^9/L
Monocytes (abs)	N/A	> 2.5 × 10^9/L
Eosinophils (abs)	N/A	> 1.6 × 10^9/L
Basophils (abs)	N/A	> 1.6 × 10^9/L
Neutrophils (relative)	≤ 0.15	> 0.85
Lymphocytes (relative)	N/A	≥ 0.75
Monocytes (relative)	N/A	≥ 0.15
Eosinophils (relative)	N/A	≥ 0.10
Basophils (relative)	N/A	≥ 0.10
Hemoglobin		
Male	≤ 115 g/L	≥ 190 g/L
Female	≤ 95 g/L	≥ 175 g/L
Hematocrit		
Male	≤ 0.37	≥ 0.60
Female	≤ 0.32	≥ 0.54
RBC	≤ 3.5 × 10^{12}/L	≥ 6.4 × 10^{12}/L
Platelet Count	≤ 75 × 10^9/L	≥ 700 × 10^9/L
SERUM CHEMISTRY		
Sodium	< 130 mmol/L	> 150 mmol/L
Potassium	< 3 mmol/L	> 5.5 mmol/L
Chloride	≤ 90 mmol/L	≥ 118 mmol/L
Calcium	< 1.75 mmol/L	≥ 3.1 mmol/L
Phosphate	< 0.65 mmol/L	> 1.65 mmol/L
Bicarbonate	< 15.1 mmol/L	> 34.9 mmol/L
Magnesium	< 0.4 mmol/L	> 1.23 mmol/L
AST	N/A	≥ 3 × ULN
ALT	N/A	≥ 3 × ULN
Alkaline Phosphatase	N/A	≥ 1.5 × ULN
CK	N/A	> 2.5 × ULN
Creatinine	N/A	≥ 177 umol/L
BUN	N/A	≥ 10.7 mmol/L
Total bilirubin	N/A	≥ 34.2 umol/L OR > 2 × ULN
Total protein	≤ 45 g/L	≥ 100 g/L
Albumin	≤ 25 g/L	N/A
Total Cholesterol	N/A	> 7.76 mmol/L
HDL-Cholesterol	< 0.78 mmol/L	N/A

LDL-Cholesterol	N/A	> 4.9 mmol/L
Triglycerides	N/A	> 3.42 mmol/L
Uric acid		
Male	N/A	> 595 umol/L
Female	N/A	> 476 umol/L
Glucose	< 2.78 mmol/L	> 13.9 mmol/L
HbA1c	N/A	≥ 0.075
Prolactin	N/A	≥ 5 × ULN
URINALYSIS		
RBC	N/A	> 25 hpf
WBC	N/A	> 25 hpf

STANDARD ADOLESCENT PCS CRITERIA FOR LABORATORY PARAMETERS – SI UNITS

Category Parameter Name Age/Sex Restriction, if any	PCS Low	PCS High
HEMATOLOGY		
WBC		
≥12 to <18 years	< 2.63 × 10^9/L	> 15.00 × 10^9/L
Neutrophils (abs)		
≥12 to <18 years	< 1.0 × 10^9/L	> 10.15 × 10^9/L
Lymphocytes (abs)		
≥12 to <18 years	< 0.8 × 10^9/L	> 7 × 10^9/L
Monocytes (abs)		
Male (≥12 to <18 years)	N/A	> 2.7 × 10^9/L
Female (≥12 to <18 years)	N/A	> 1.92 × 10^9/L
Eosinophils (abs)		
≥12 to <18 years	N/A	> 0.7 × 10^9/L
Basophils (abs)		
≥13 to <18 years	N/A	> 0.7 × 10^9/L
Neutrophils (relative)		
≥13 to <18 years	< 0.368	> 0.934
Lymphocytes (relative)		
≥13 to <18 years	< 0.129	> 0.646
Monocytes (relative)		
Male (≥12 to <18 years)	N/A	> 0.16
Female (≥12 to <18 years)	N/A	> 0.14
Eosinophils (relative)		
Male (≥12 to <18 years)	N/A	> 0.065
Female (≥12 to <18 years)	N/A	> 0.143
Basophils (relative)		
≥12 to <18 years	N/A	> 0.035
Hemoglobin		
Male (≥12 to <18 years)	≤ 115 g/L	≥ 207 g/L
Female (≥12 to <18 years)	≤ 95 g/L	≥ 190 g/L
Hematocrit		
Male (≥12 to <18 years)	< 0.28	> 0.6
Female (≥12 to <18 years)	< 0.28	> 0.56
RBC		
Male (≥12 to <18 years)	< 4.25 × 10^{12}/L	> 6.65 × 10^{12}/L
Female (≥12 to <18 years)	< 3.85 × 10^{12}/L	> 5.85 × 10^{12}/L
Platelet Count		
≥12 to <18 years	< 100 × 10^9/L	> 500 × 10^9/L
SERUM CHEMISTRY		
Sodium		
≥13 to <18 years	≤ 125 mmol/L	> 150 mmol/L
Potassium		
≥13 to <18 years	≤ 3 mmol/L	≥ 6.0 mmol/L
Chloride		
≥13 to <18 years	≤ 90 mmol/L	≥ 118 mmol/L
Calcium		

≥13 to <18 years	< 2.1 mmol/L	> 3.1 mmol/L
Phosphate		
≥13 to ≤15 years	< 1 mmol/L	> 2.08 mmol/L
>15 to <18 years	< 0.71 mmol/L	> 1.76 mmol/L
Bicarbonate		
>12 to <18 years	< 15.1 mmol/L	> 34.9 mmol/L
Magnesium		
≥12 to <18 years	< 0.4 mmol/L	> 1.23 mmol/L
AST		
≥13 to <18 years	N/A	≥ 2 × ULN
ALT		
≥13 to <18 years	N/A	≥2 × ULN
Alkaline Phosphatase		
≥13 to <18 years	N/A	≥ 3 × ULN
CK		
≥13 to <18 years	N/A	≥ 2 × ULN
Creatinine		
≥13 to ≤16 years	N/A	> 132.6 umol/L
>16 to <18 years	N/A	> 176.8 umol/L
BUN		
≥13 to <18 years	N/A	≥ 10.7 mmol/L
Total bilirubin		
≥13 to <18 years	N/A	≥ 30 umol/L
Direct bilirubin		
≥13 to <18 years	N/A	≥ 10 umol/L
Total protein		
≥13 to <18 years	≤ 45 g/L	≥ 100 g/L
Albumin		
≥13 to <18 years	≤ 20 g/L	N/A
Total Cholesterol		
≥13 to <18 years	N/A	> 10.34 mmol/L
HDL-Cholesterol		
≥13 to <18 years	< 0.78 mmol/L	N/A
LDL-Cholesterol		
≥13 to <18 years	N/A	> 3.3 mmol/L
Triglycerides		
Male (≥13 to ≤15 years)	N/A	> 1.85 mmol/L
Male (>15 to <18 years)	N/A	> 2.2 mmol/L
Female (≥13 to ≤15 years)	N/A	> 5.7 mmol/L
Female (>15 to <18 years)	N/A	> 1.84 mmol/L
Uric acid		
≥13 to <18 years	N/A	> 1.5 × ULN
Glucose		
≥13 to <18 years	< 2.5 mmol/L	> 10 mmol/L
HbA1c		
≥13 to <18 years	N/A	> 0.07
URINALYSIS		
RBC		
≥13 to <18 years	N/A	> 25 hpf
WBC		
≥13 to <18 years	N/A	> 25 hpf

Protein		
≥13 to <18 years	N/A	≥ 2+
Ketone		
≥13 to <18 years	N/A	≥ 2+
Glucose		
≥13 to <18 years	N/A	≥ 2+

APPENDIX 12. PSQI SCORING SHEET

PSQI scoring reference as defined by BUYSSE is provided in following website:

https://www.sleep.pitt.edu/instruments/#psqi

Pittsburgh Sleep Quality Index (PSQI)

Form Administration Instructions, References, and Scoring

Form Administration Instructions

The range of values for questions 5 through 10 are all 0 to 3.

Questions 1 through 9 are not allowed to be missing except as noted below. If these questions are missing then any scores calculated using missing questions are also missing. Thus it is important to make sure that all questions 1 through 9 have been answered.

In the event that a range is given for an answer (for example, '30 to 60' is written as the answer to Q2, minutes to fall asleep), split the difference and enter 45.

Reference

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research* 28:193-213, 1989.

Scores – reportable in publications

On May 20, 2005, on the instruction of Dr. Daniel J. Buysse, the scoring of the PSQI was changed to set the score for Q5J to 0 if either the comment or the value was missing. This may reduce the DISTB score by 1 point and the PSQI Total Score by 1 point.

PSQIDURAT **DURATION OF SLEEP**

IF Q4 $\geq$ 7, THEN set value to 0
IF Q4 < 7 and $\geq$ 6, THEN set value to 1
IF Q4 < 6 and $\geq$ 5, THEN set value to 2
IF Q4 < 5, THEN set value to 3
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIDISTB **SLEEP DISTURBANCE**

IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) = 0, THEN set value to 0

IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) $\geq$ 1 and $\leq$ 9, THEN set value to 1

IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 9 and $\leq$ 18, THEN set value to 2

IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 18, THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQILATEN **SLEEP LATENCY**

First, recode Q2 into Q2new thusly:
IF Q2 ≥ 0 and ≤ 15, THEN set value of Q2new to 0
IF Q2 > 15 and ≤ 30, THEN set value of Q2new to 1
IF Q2 > 30 and ≤ 60, THEN set value of Q2new to 2
IF Q2 > 60, THEN set value of Q2new to 3
Next
IF Q5a + Q2new = 0, THEN set value to 0
IF Q5a + Q2new ≥ 1 and ≤ 2, THEN set value to 1
IF Q5a + Q2new ≥ 3 and ≤ 4, THEN set value to 2
IF Q5a + Q2new ≥ 5 and ≤ 6, THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIDAYDYS **DAY DYSFUNCTION DUE TO SLEEPINESS**

IF Q8 + Q9 = 0, THEN set value to 0
IF Q8 + Q9 ≥ 1 and ≤ 2, THEN set value to 1
IF Q8 + Q9 ≥ 3 and ≤ 4, THEN set value to 2
IF Q8 + Q9 ≥ 5 and ≤ 6, THEN set value to 3
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIHSE **SLEEP EFFICIENCY**

Diffsec = Difference in seconds between day and time of day Q1 and day Q3
Diffhour = Absolute value of diffsec / 3600
newtib =IF diffhour > 24, then newtib = diffhour – 24
IF diffhour ≤ 24, THEN newtib = diffhour
(NOTE, THE ABOVE JUST CALCULATES THE HOURS BETWEEN GNT (Q1) AND GMT (Q3))
tmphse = (Q4 / newtib) * 100

IF tmphse ≥ 85, THEN set value to 0
IF tmphse < 85 and ≥ 75, THEN set value to 1
IF tmphse < 75 and ≥ 65, THEN set value to 2
IF tmphse < 65, THEN set value to 3
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQISLPQUAL **OVERALL SLEEP QUALITY**

Q6
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIMEDS **NEED MEDS TO SLEEP**

Q7
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQI **TOTAL**

DURAT + DISTB + LATEN + DAYDYS + HSE + SLPQUAL + MEDS
Minimum Score = 0 (better); Maximum Score = 21 (worse)

Interpretation: TOTAL ≤ 5 associated with good sleep quality
TOTAL > 5 associated with poor sleep quality

APPENDIX 13. CLASSIFICATION OF PATIENT TYPE FROM UPSM FACTOR SCORES

Guided machine learning via linear support vector machine (L-SVM) algorithm in MATLAB will be used to classify subjects into 5 patient types based on UPSM factor scores. There are 5 distinct patient types described in the table below.

TYPE	PATIENT TYPE
1	Prominently Disorganized
2	Prominently Negative
3	Prominently Hostile
4	Prominently Positive
5	Prominently Affective

The classification will occur in two steps:

- Step 1: Train L-SVM in MATLAB to classify subjects into 1 of 5 patient types using 7 columns of UPSM data. Training dataset is given in the table below.
- Step 2: Use the now trained classifier function in MATLAB to classify subjects into 1 of 5 patient types using 7 columns of UPSM data.

Table 9: Training Dataset

UPSM-HOS	UPSM-DIS	UPSM-POS	UPSM-NAA	UPSM-ANX	UPSM-NDE	UPSM-DEP	TYPE
0.110138	1.960813	0.478927	3.298293	1.382828	2.114771	0.391504	1
1.431769	1.616874	3.310726	2.225812	0.541127	1.542821	0.22721	4
0.537462	2.293898	3.358519	2.713077	2.582309	1.584137	2.762624	5
1.458801	0.51371	3.162632	4.179415	2.367169	0.687056	2.014098	5
0.491282	1.47429	0.583566	2.633944	4.227873	1.12837	3.735909	5
2.124307	2.621508	2.553096	1.81619	1.463642	0.857061	1.801388	3
0.229749	4.356682	3.900132	2.980611	1.59104	2.825456	2.487569	1
0.65872	1.492003	3.98728	1.558729	1.721153	1.716735	2.567419	4
4.311785	3.13258	3.26397	-0.53456	3.583895	0.246863	3.063737	3
1.673673	2.982224	2.381804	0.168301	2.017634	2.223616	2.420761	3
-0.28911	1.117716	3.325504	4.394722	0.710643	2.619891	1.77449	4
-0.40258	1.164411	3.68884	2.699136	3.395212	2.032147	2.131544	5
0.120462	2.660464	3.395254	2.078197	2.900268	0.261296	2.725002	4
1.361992	3.411795	4.64508	0.18819	1.223746	2.532468	1.366811	4
3.667904	3.136446	2.321715	2.125103	3.409371	1.537432	-0.2218	3
4.879887	3.475862	2.076838	-0.59349	1.113849	1.688076	0.123996	3
-0.02164	2.41729	2.779121	3.079331	2.108443	1.951256	1.676715	1
-0.3092	2.157215	2.674034	2.803489	1.084307	0.996332	1.994321	4
0.196083	2.475004	2.878793	1.351682	1.201559	0.816825	2.181635	4
0.030238	3.526967	4.532129	0.380547	0.326149	1.986222	1.517082	4
2.275873	2.640193	3.251667	0.839343	2.051567	0.58417	2.170745	3
0.664909	2.042059	2.76595	2.366495	1.440192	0.733822	2.402925	5
1.243306	1.337145	4.074218	2.793057	2.698381	2.51747	3.318289	5
3.22947	2.860181	3.577492	3.502082	2.628584	0.298051	3.390157	5
0.901195	1.663412	2.142304	3.688469	1.330552	2.56257	2.640387	5
2.593164	3.648882	3.709823	3.206283	1.011247	1.094186	3.558644	3
-0.51118	2.448093	2.437806	1.15006	2.797663	3.063268	2.065887	1
-0.11226	1.666885	2.743509	1.415346	0.850013	2.305111	1.401516	4

0.461343	2.627467	4.224476	0.273361	1.87481	0.626399	1.981483	4
2.984818	3.119943	1.817018	0.766638	2.093436	1.529787	0.320228	3
3.77918	4.634406	1.565869	3.283619	0.239241	1.954698	0.044583	2
2.144653	2.782737	3.498727	0.538967	1.545457	0.710868	0.792113	3
0.894321	4.51713	0.328192	4.038478	0.461848	4.202648	0.153093	2
-0.36753	4.43122	3.945508	3.314841	3.447207	2.09228	1.277813	1
-0.54075	4.778543	0.863248	4.518782	2.584591	3.675675	1.102248	1
0.567503	3.24148	3.050335	3.616151	2.485309	1.23559	1.194027	1
-0.14361	3.811718	1.934878	4.106673	2.496619	1.883645	1.255909	1
2.074899	4.309083	3.67494	2.931829	2.158336	1.564656	0.532635	2
-0.19755	3.56726	2.443049	2.469007	2.522924	2.551866	4.876176	1
1.77413	1.53753	2.847139	1.882985	0.272108	1.812518	3.542881	5
1.620442	2.629055	2.66762	-0.09426	2.112038	0.781558	3.528088	3
0.284396	1.770956	2.033619	2.009207	3.469858	0.528655	2.227344	5
3.932854	4.528324	2.861762	1.430475	2.837778	1.200249	2.254885	3
-0.56969	0.692111	4.179689	2.437995	1.95239	1.874127	3.146663	5
4.750689	2.427282	4.856594	3.187711	1.452157	-0.41915	0.793141	3
3.405697	1.355663	3.002656	3.832785	3.044058	1.05007	2.012123	5
3.246586	1.094777	3.274349	3.670523	2.797322	0.536438	3.19334	5
-0.73954	2.073529	3.517236	4.06399	3.114689	3.682423	3.860445	5
-0.52019	1.761008	4.510467	2.327021	2.304678	3.148164	2.974405	4
2.014756	2.407895	2.295336	2.006102	1.24862	3.567501	2.040139	2
0.617758	2.661608	1.536687	3.738151	1.672221	2.392486	-0.23323	2
2.207155	1.517604	2.625454	1.804154	0.763335	0.901574	1.873668	3
1.23422	2.210916	2.561197	2.528093	1.527851	1.183324	0.255261	4
0.021092	1.402188	2.331655	1.812051	2.72359	0.272525	2.258971	5
-0.954	5.328812	2.839309	3.194626	2.923765	1.602491	3.133907	1
3.167057	3.125152	1.146554	4.533739	1.648505	1.456163	2.409444	2
0.076614	2.337764	1.24781	1.632617	2.307237	1.494694	0.092505	1
1.769865	3.050355	3.584774	3.050455	0.435454	0.965985	1.414732	4
-0.14345	2.274485	3.363205	2.516223	1.298419	0.84683	0.939489	4
0.73008	2.109659	1.353254	2.267853	1.683644	1.547878	2.385081	1
1.99611	2.845866	2.776477	2.253987	2.519993	1.293208	0.830398	3
0.070748	2.973237	2.458206	2.670777	0.933532	0.498741	0.68469	4
0.876838	1.702267	2.500296	1.205238	1.988358	1.73428	1.88312	5
2.539879	1.866446	1.194986	2.380642	1.503776	2.970662	0.607604	2
1.394134	3.329297	3.029867	2.34767	2.089692	0.610036	3.175958	5
1.370158	3.673851	0.853038	2.542066	2.93799	2.377451	1.666476	1
1.873059	1.656544	2.282509	0.870666	2.632208	0.4312	1.362965	3
2.587309	1.766566	1.972871	2.451865	2.200703	1.026357	0.802177	3
3.83788	1.83301	2.241711	3.814479	1.270124	0.82664	0.010026	3
1.139727	1.009246	2.171023	2.861618	1.94202	1.469105	2.310987	5
0.399375	1.269958	3.185143	3.451366	2.536612	1.873559	3.891391	5
1.155282	0.720076	1.978406	2.550957	1.676011	2.227286	1.931072	5
1.344237	1.329165	2.176408	2.522749	2.36858	1.113254	1.862452	5
1.884397	0.811162	2.366897	3.193561	1.903167	0.529586	3.039549	5
0.857138	1.991846	4.143588	3.203741	2.567467	1.723389	2.662205	5
0.316037	0.913369	3.265191	3.908459	2.02769	2.805904	3.226179	5
0.941557	1.611534	3.550319	2.397795	2.465604	1.637112	2.268425	5
1.001373	0.053415	2.59386	3.243315	2.765545	1.745535	1.070277	5
0.503857	0.731232	2.859462	3.221411	1.999709	0.617281	0.785101	4
0.606582	1.644987	2.617478	3.87998	1.79895	0.52075	1.931541	5
0.028959	0.051636	2.679662	3.743596	1.258786	0.796158	2.684655	5
1.346641	0.874823	2.367707	3.081821	1.922213	0.204586	1.535142	5
1.860828	2.605349	3.667323	4.365784	-0.09249	1.265363	1.238416	2
3.841476	0.719424	2.257701	4.478491	1.331765	0.100831	1.896058	5
1.661837	1.572432	2.894384	4.184757	1.296394	0.92299	2.19499	5

1.639518	1.463103	2.652642	1.584517	2.156156	1.371609	1.96164	5
0.422721	1.235118	2.915662	1.806378	1.774961	1.461898	1.782514	5
1.706561	2.255214	2.013119	3.335592	1.432492	1.106246	0.37835	2
1.400759	1.11035	3.176518	2.727226	1.683432	1.484354	2.072159	5
0.261743	1.846856	2.95069	1.604365	1.313196	2.201688	2.045153	4
0.589363	1.63248	2.607093	3.117401	1.985862	1.962965	2.226981	5
-0.25198	1.221123	3.025169	3.361783	1.767464	1.630335	2.390124	5
2.291071	0.293838	3.270165	3.243712	2.442306	-0.00452	2.387481	5
1.537487	0.068818	3.108614	1.546074	2.023246	1.696579	2.706242	5
0.582496	1.908653	2.366867	2.51433	1.475041	0.41553	1.263473	4
2.181457	1.917974	2.429864	2.922081	1.514385	-0.21779	1.973444	3
2.263951	0.29547	3.331314	1.415383	2.346612	1.031364	2.892756	5
2.009356	1.113335	3.138889	3.341652	1.883817	0.109166	1.958678	5
0.172439	1.489999	3.292475	2.720522	1.176231	1.605558	2.641559	5
-0.17314	1.356652	4.442061	3.10633	2.049317	0.791991	1.912506	4
1.388335	1.095188	3.220865	1.628662	1.732311	1.352052	2.405447	5
1.205138	2.024409	3.791492	2.398941	3.006668	1.787416	2.920256	5
0.464397	1.684218	3.40262	2.726862	3.013933	1.189662	3.61535	5
1.628768	1.308049	2.95217	2.745054	1.327077	2.028925	3.357957	5
0.586597	2.536766	2.916748	3.252801	2.392646	2.207333	3.37449	5
0.668672	0.21496	3.401807	3.499059	2.747658	2.264928	3.708938	5
1.85842	1.032293	3.81473	3.017692	2.560804	1.060393	2.687179	5
0.421477	1.193203	3.072718	3.197042	2.410182	2.327653	3.342285	5
0.705007	2.094874	1.758942	2.993589	1.631168	1.769052	2.175233	1
1.341319	2.511154	2.487053	0.737579	1.309727	1.172314	2.21039	3
-0.10475	3.201991	2.494132	3.312053	0.911785	2.561984	0.543735	2
1.26418	1.34083	2.50963	3.164473	0.66512	1.883488	1.486237	2
2.135516	2.140969	2.155306	4.111724	2.433874	1.272746	2.910099	5
0.11181	3.029033	2.241817	4.074078	2.229162	1.485626	1.801666	1
0.57075	4.309476	3.042631	3.640668	1.121444	1.676763	0.985236	2
2.368828	2.078152	1.757995	3.68918	2.238158	0.832056	3.202517	5
0.460592	3.343601	1.369653	3.591892	3.052149	1.590111	1.853283	1
1.039519	2.73413	2.797452	4.794559	3.188477	1.32171	2.069804	1
-0.10856	3.283553	2.221476	2.861392	2.916771	1.670176	1.495856	1
1.635721	1.670994	2.776531	3.481021	3.648923	1.09168	3.517521	5
-0.28728	1.550428	3.027047	1.569179	3.495302	1.675143	3.72542	5
0.629977	1.356138	4.076404	1.705047	2.22813	1.423955	2.063269	4
2.307646	2.236448	2.680489	0.969736	2.569013	-0.08536	2.277701	3
2.477069	3.263651	2.163565	2.139497	1.721061	-0.00358	0.65799	3
1.243638	2.913075	4.107979	2.66461	0.995093	-0.14437	1.22687	4
0.527388	1.958446	1.279965	3.081775	0.643036	1.853639	2.172642	1
0.424628	2.137735	2.088917	1.156878	1.766872	1.219234	1.53977	1
2.527044	0.76957	4.013747	2.360512	3.03441	-0.3789	4.007144	5
-0.19304	1.261063	2.340497	2.776243	2.052291	1.922053	3.962693	5
0.533501	1.87061	4.417346	2.075672	3.323951	-0.27006	4.225107	5
2.411661	1.882853	4.355587	1.036112	1.98607	0.055844	1.311082	3
-0.48578	1.752793	4.45535	3.947321	1.094441	2.902358	2.033406	4
0.464869	3.413253	2.635796	2.121825	2.8906	1.996746	3.22642	1
4.132441	0.401081	2.381923	3.456109	0.953315	3.096096	0.555434	2
0.218247	3.435941	1.849422	1.196065	2.511003	1.363478	0.35237	1
-0.32981	4.544489	1.360392	3.024887	1.106194	2.727317	0.572736	1
0.544813	4.282196	2.116876	2.290366	2.541964	1.369559	1.818978	1
-0.47234	4.088985	0.577244	2.967936	2.63388	2.877609	2.381399	1
-0.55527	4.84008	1.960686	2.982342	2.094423	1.626178	1.184506	1
0.263513	3.736018	1.959549	1.758239	1.640343	1.004376	1.472666	1
0.705893	3.718196	2.301378	0.926439	1.774488	0.994932	1.79793	1
0.069405	3.026261	2.43983	3.17107	3.19792	2.883761	1.97275	1

-0.32695	0.330879	2.510527	3.441654	2.057765	2.304866	2.878307	5
2.690017	0.693133	1.730133	3.88509	2.562458	1.455035	1.213344	5
0.46547	1.287936	2.939181	1.394492	3.396399	2.015295	2.080734	5
1.394982	1.559578	2.471032	3.161232	2.57522	0.992441	2.406263	5
0.672309	2.393359	1.896502	2.598218	0.993053	3.154678	1.696235	1
1.693716	1.325886	0.880014	5.37448	1.164323	3.653433	2.895248	5
1.356159	2.406733	2.037301	2.919935	1.869511	3.465406	1.13788	2
1.027015	1.062603	0.659294	4.357499	2.82001	3.266347	4.132878	5
1.436698	-0.58649	1.964863	3.95011	3.191804	0.377813	4.488555	5
4.058956	-0.66886	1.317517	4.606702	1.160914	2.731827	3.099033	5
1.416783	1.490505	2.933091	1.730763	3.560499	0.430518	2.821162	5
0.824231	-0.19387	4.748215	0.202208	2.896445	0.69977	4.873985	5
-0.36924	2.678109	3.163096	1.596358	0.59506	3.346233	1.61617	4
2.327808	1.715927	3.390249	3.327197	-0.07099	1.647033	1.876406	2
1.146957	1.732186	2.467294	4.312694	0.967439	3.606223	2.364763	2
-0.08434	2.371234	1.923559	2.551661	2.780099	-0.41496	2.607441	5
2.330935	1.249285	1.977942	-0.29365	1.750854	1.887952	3.34313	5
-0.29097	2.579936	4.03501	2.453226	1.223345	1.756084	1.578965	4
2.433418	1.586402	2.744031	2.943148	2.595221	-0.15045	4.456784	5
1.686219	2.133575	3.063004	2.625084	1.837615	0.138859	2.505072	5
2.182811	2.480894	3.512331	2.528045	3.359501	1.174893	2.358992	5
1.726701	2.611469	3.08875	2.914048	3.581237	1.05601	1.522262	1
0.604793	3.12306	2.124151	2.637198	2.7244	2.472494	1.200589	1
3.236433	3.290153	2.702033	2.314023	3.316992	0.3816	1.895082	3
1.425043	3.692046	3.472158	4.057196	2.405972	0.434079	2.869765	1
2.201707	3.084578	2.151076	4.021647	2.182574	2.301893	1.407549	2
1.815693	2.134869	4.303099	4.369005	1.882038	0.949098	1.847457	4
1.20209	3.064755	4.217095	3.649783	2.915971	0.357701	1.225159	4
0.046373	2.916968	4.455808	2.885248	3.107358	0.426352	2.008252	4
-0.01844	3.893585	3.026784	1.817709	0.913144	3.254477	2.670709	1
0.15412	3.328443	1.620771	1.879719	2.673819	2.668971	2.431268	1
-0.07332	4.359244	3.52468	1.723178	0.553973	1.862672	0.970363	4
0.708979	3.65687	2.295132	2.084227	1.178033	3.673556	0.603624	2
1.454947	3.430231	2.232895	2.447069	2.309456	2.631151	2.32591	1
0.583852	3.473869	2.416568	2.141427	0.479351	2.977283	1.947473	2
0.284904	3.74932	2.086627	3.204144	-0.07831	2.28367	1.519997	2
0.882449	3.863615	3.044836	2.195771	-0.10572	1.730727	0.181928	2
0.180445	1.883516	1.562047	2.663036	2.63216	2.250718	2.436309	1
0.378782	2.931791	1.708711	2.980852	2.771396	2.111069	0.610343	1
0.352732	1.89972	2.265854	3.230448	1.11399	1.21381	2.019503	5
-0.07905	1.7187	0.81324	3.213864	2.58132	2.072825	1.596053	1
-0.04268	2.161476	1.854841	2.9067	2.572292	2.05655	3.250114	1
0.532978	3.478254	2.049047	1.952408	2.807302	1.696268	1.824182	1
0.155656	3.999629	3.146047	1.349007	2.792547	1.478153	1.4613	1
0.796148	2.634837	3.132603	3.222581	2.680883	1.854805	2.030157	1
0.86594	2.609557	2.546813	1.751367	1.740951	1.533923	2.228512	1
1.01185	2.816307	2.912837	1.669116	2.542537	1.330716	1.168323	1
1.350645	1.989788	1.74757	3.198019	2.213117	0.804664	1.34773	1
0.349145	2.756305	1.716076	2.68973	2.739907	1.656974	1.623306	1
0.342705	1.679803	1.833402	2.032994	2.960676	1.663841	2.120364	1
1.484201	1.539412	1.50688	2.924464	2.475359	1.705127	1.683536	5
1.562951	3.030532	1.644437	2.014339	1.595521	1.644179	1.164406	1
3.029619	2.819386	1.874296	2.742982	1.788343	2.269874	1.542436	2
0.78352	1.877238	2.074483	2.627216	2.240644	2.194709	2.377748	5
0.710665	2.849776	2.364681	1.919057	2.747839	1.648826	1.233827	1
0.798178	2.933791	3.35471	2.705446	0.796685	3.192393	0.488374	2
1.905889	4.839237	3.456346	0.724097	2.164524	0.999083	1.83366	3

-0.42893	2.354318	2.48451	3.358162	0.714569	2.794577	2.607276	1
2.197681	2.953134	3.844426	1.086876	0.80736	-0.01227	2.050991	3
1.175299	4.850591	4.181569	1.539452	1.490182	0.734061	1.239397	4
-0.50935	3.131051	2.46547	2.550862	1.514948	3.740844	1.942203	1
-0.47872	2.432521	2.670089	3.345092	1.896522	3.066479	3.392814	1
1.647404	2.212889	0.922094	2.565279	2.766181	2.737955	1.599062	1
2.466112	2.010557	3.626749	3.847344	2.514457	1.560699	3.442844	5
3.004502	2.637176	2.798804	3.711184	2.463544	1.57843	2.123784	3
1.241437	2.778655	1.589605	2.563038	2.012834	1.91169	3.491985	1
2.391924	2.637746	2.374582	0.755083	2.629425	2.330716	2.941087	3
1.486578	3.128626	2.487837	1.743571	2.003073	1.737516	1.329548	1
2.586535	2.877124	2.287801	2.632841	1.387282	2.363598	2.453764	2
1.66655	2.838318	2.35911	1.973314	1.859279	2.225311	2.915387	1
1.589938	3.65255	2.956482	2.565466	0.975133	1.615948	0.499501	2
1.945618	3.050839	2.514292	3.234862	2.203473	1.822279	1.99805	1
1.755469	2.075945	3.480556	2.94479	1.519334	1.681199	0.758004	4
2.935053	2.718756	3.31552	2.504717	1.889886	1.201849	1.460136	3
2.119775	3.394806	2.506338	2.120552	2.614302	0.679575	0.89525	3
2.458961	2.329016	2.154788	3.310596	1.474675	2.59347	1.591725	2
1.244654	1.73021	1.827923	2.489334	1.383575	2.073081	1.360675	1
-0.20744	1.946772	4.276268	1.584494	1.25229	0.51958	1.276463	4
1.074974	1.973074	1.265671	1.897755	2.948865	0.870864	1.737043	1
-0.14189	-0.04374	3.164932	3.531256	1.980725	0.632499	3.87712	5
3.376984	0.831567	2.275181	2.779673	1.98059	1.308505	1.968036	5
0.410408	1.295473	3.211679	2.991182	2.99265	1.394861	2.979216	5
0.412831	0.728305	2.774347	3.476108	2.485126	0.143779	1.325316	5
0.395383	1.266636	3.547077	3.848593	2.41841	0.233631	1.330153	4
0.303011	0.68115	3.431149	2.896138	2.845076	0.290205	2.987518	5
0.623263	2.844467	2.011102	3.13837	1.748296	2.03984	2.51607	1
0.430849	2.024006	2.387261	2.938496	1.830338	1.725661	1.602135	1
0.302646	3.078668	1.809565	2.02404	2.874748	0.986561	3.022366	1
0.217969	2.234125	3.086551	2.801215	2.881359	1.925122	2.6483	1
1.148024	4.715529	1.712537	1.143191	1.448075	0.735696	1.255713	1
0.17321	2.714301	3.093773	2.731845	3.555077	0.30472	1.964692	1
1.628505	1.333563	2.279517	3.023174	2.166503	1.909445	2.062154	5
1.460183	2.173385	1.803192	2.793002	2.444099	0.941715	2.221664	5
0.443037	2.964066	1.915887	2.678915	1.792021	2.577074	1.45575	1
0.462123	1.136766	3.163593	3.69979	3.024302	-0.067	2.09806	5
-0.00933	2.530804	3.25533	3.315988	1.517136	0.677362	2.642933	4
1.040869	1.969233	2.705048	4.084591	2.318205	0.820581	2.483245	5
0.146118	1.409769	2.792843	2.852647	2.966719	0.792185	2.797111	5
0.957539	1.814681	2.711	3.043293	1.665616	0.197362	2.822844	5
1.552961	2.008691	3.036311	3.633731	2.497589	-0.00887	1.003566	4
1.250273	3.122429	2.403355	3.189958	1.795676	0.107745	0.924363	1
1.322036	1.215882	3.921602	3.003509	2.284119	-0.24933	1.806291	5
0.251952	2.113829	2.664782	3.034502	1.648737	0.259419	2.65026	5
0.59895	3.329155	2.836852	2.202842	1.497784	1.607472	2.583754	1
0.565399	5.191211	2.58232	2.271006	2.778369	1.798438	0.76725	1
1.891514	1.030671	2.378489	2.521739	2.470474	1.713408	1.830049	5
2.251343	1.964833	2.782653	2.173102	2.552897	0.928943	2.420509	5
0.827273	1.676045	1.79413	2.599383	2.936736	2.290989	1.069859	1
0.933062	4.872175	1.858903	3.41357	1.483246	3.481183	0.717352	2
1.319798	3.170397	2.467164	3.559172	3.259405	2.329196	0.779611	1
1.159981	2.887268	2.048998	1.864787	1.714485	1.964015	0.851252	1
2.594349	4.47202	1.935226	2.39397	0.807125	1.443819	1.010001	2
2.259674	2.817409	2.241478	3.232779	1.265977	2.904775	1.005764	2
3.853234	3.442007	3.483622	1.254111	2.035139	0.95848	2.220828	3

0.107242	2.316128	1.787862	2.913061	2.647041	1.852659	1.796499	1
4.540121	2.034294	1.273216	4.195778	0.812797	3.901634	2.414239	2
1.940409	1.744759	2.334533	3.048773	2.032325	1.673573	2.156116	5
1.771326	1.136763	2.607683	3.880771	1.931054	1.665451	2.462573	5
2.056638	0.596344	2.676342	3.652917	1.954028	1.575281	2.359132	5
1.998099	1.080433	2.593327	4.200915	1.916664	1.49471	2.380617	5
1.973644	0.455134	3.08072	4.16708	1.829094	1.683288	2.447056	5
1.836602	0.707831	2.460104	4.184537	1.830863	1.615467	2.488581	5
1.970747	1.071085	2.266924	3.64906	3.038635	1.177264	2.83891	5
2.048913	1.390075	2.210913	3.567033	2.003754	1.363302	2.075113	5
1.017331	2.182473	3.564923	0.448758	2.352833	2.376049	3.255035	5
1.725945	3.009119	2.694312	0.112874	3.046849	1.046677	2.597689	3
0.631709	2.429373	2.904648	1.845756	1.753777	3.513261	1.93335	1
-0.23163	3.002049	3.345794	2.547498	3.554414	1.593511	3.265845	1
-0.21477	2.923092	2.388016	3.395137	2.936315	2.417217	2.608649	1
2.292153	2.412309	2.891003	2.297742	1.884942	0.821511	1.938632	3
1.826434	3.195578	1.861429	3.285702	2.60437	0.337541	1.982752	1
1.081747	2.024036	3.051124	2.759296	2.689623	2.411139	3.523435	5
1.726368	2.23849	3.132346	2.316369	2.459357	2.194413	2.921579	5
0.273047	2.916457	1.761402	3.342903	1.357142	2.447486	1.642088	1
2.061364	2.246574	2.274476	2.84223	2.513461	1.435599	1.663619	5
-0.44394	1.990884	2.120804	2.786634	1.973897	3.156599	3.453843	1
0.965206	1.901004	1.431642	3.042105	2.183742	2.33692	2.365446	1
1.658993	1.392341	3.179016	2.725544	1.270456	1.609023	2.18851	5
1.841815	2.190828	2.24286	3.811443	2.195616	0.758591	2.922796	5
1.22653	1.421029	2.261803	2.765931	2.425561	1.732311	3.372288	5
-0.23487	2.062772	2.559663	2.79011	1.445805	2.657801	2.760422	1
0.245227	2.689176	1.443797	1.973458	2.887213	1.25989	2.374189	1
2.215864	1.754762	2.859705	4.169328	2.445922	1.18503	2.197257	5
2.827656	1.672037	1.272949	2.704282	2.616846	2.725432	3.720687	5
3.199189	1.422016	2.654105	4.302128	3.544407	1.718565	4.051834	5
2.403098	2.968469	4.036389	2.438671	1.294979	0.563823	1.703829	3
2.45239	3.234068	2.759748	1.024698	1.562684	1.112423	2.375853	3
1.502019	2.281229	1.340381	1.610793	2.423306	1.047639	1.624365	1
1.77479	1.921922	3.237566	1.352774	2.492678	1.049467	2.512043	5
1.663432	3.019771	1.897049	0.759906	3.501306	1.569326	1.914466	1
2.94352	2.35016	2.281449	0.951598	2.511059	1.019162	1.526363	3
1.68009	2.045579	1.887194	2.357748	1.978092	1.635593	2.811834	5
0.808124	-0.13738	2.953735	3.906694	1.947323	1.380431	2.901026	5
1.209549	-0.67634	4.084019	3.428157	1.289318	1.264035	2.480664	5
1.733745	-0.34144	2.996359	2.729753	1.784482	-0.03631	2.462543	5
1.619052	0.150902	4.359022	2.334887	2.914195	-0.11285	1.33825	5
-0.13043	0.923062	2.34262	2.347549	0.138352	3.16152	1.597485	4
1.32315	0.012205	4.865486	0.779994	1.714469	0.367159	2.011743	4
2.650652	1.224055	2.722871	2.274911	1.37163	1.630707	1.845764	3
1.607415	2.287416	2.580634	1.22177	2.238811	1.518263	0.841124	3
0.407971	0.974984	2.534841	2.228252	3.585527	2.013955	3.485656	5
1.576527	1.697772	2.575915	3.470199	2.282271	1.37511	2.962369	5
1.956178	-0.46028	4.546977	2.448721	1.334782	1.148109	3.918205	5
0.18701	2.273386	4.282304	2.119968	2.185045	2.674903	1.84133	4
0.354561	1.314933	4.056158	2.91016	1.719733	1.791516	-0.16259	4
0.797993	0.857493	3.688851	3.229713	3.474734	2.372434	1.533996	5
1.856804	2.053879	1.920647	2.220341	2.898173	0.918768	1.764507	5
-0.13872	3.299856	3.489781	2.220536	1.711955	1.704413	3.085852	1
0.72802	2.655034	3.106166	2.872185	1.647015	1.176479	0.846061	4
0.225626	1.874406	1.825989	3.058365	2.868861	3.509008	2.042135	1
2.051621	1.818373	4.017949	2.104391	1.201151	0.575975	1.724579	3

0.59504	1.95428	5.204595	1.783968	1.497278	1.731733	1.678559	4
1.584827	0.935282	3.327166	1.94125	2.179968	0.358369	3.245291	5
0.928618	0.658035	3.076131	3.113168	2.172916	1.004145	3.430131	5
2.201803	1.135876	4.001561	1.791912	1.757235	0.255488	2.840382	5
3.807773	3.594538	1.889844	0.931891	1.714179	-0.22761	0.176671	3
0.242025	1.84378	3.468098	2.711658	2.422419	0.129613	1.804384	4
2.001564	1.682021	3.01414	2.000518	1.811704	0.298292	1.451765	3
1.563126	0.95651	2.505286	2.57955	1.915208	0.43884	3.595415	5
0.166357	2.392899	3.069375	2.770552	1.708797	3.004771	0.534774	1
0.537015	2.481759	5.567584	0.735376	1.212872	0.596699	1.804847	4
1.419943	3.311596	2.146657	1.1977	1.445532	1.588575	0.49374	3
1.6282	2.717846	3.449848	2.08389	0.548107	3.320778	3.109258	2
0.74564	4.329717	3.465316	2.586558	0.874382	2.331343	0.952736	2
-0.53777	2.184301	1.465823	2.443865	3.215783	3.614718	3.522195	1
0.517961	4.639776	1.693983	2.760274	1.535191	2.33917	2.777603	1
3.464622	3.305747	3.148404	1.874921	1.356197	0.483571	0.587682	3
1.831054	3.21794	1.980434	1.148194	2.693122	0.351515	2.311651	3
1.334201	2.45268	3.196957	1.766991	1.617076	0.218062	2.178214	4
1.925363	1.20103	1.434322	1.670427	2.831532	1.924301	2.443715	5
2.379776	1.265335	2.872741	2.090623	3.297923	2.679207	2.677931	5
-0.50069	3.784005	2.725673	3.553338	0.042037	2.158042	2.048815	2
0.315685	2.035559	1.810852	3.164387	0.491681	3.110445	2.98571	1
1.791176	1.005473	2.139767	2.53269	1.78994	2.214137	2.723798	5
1.979567	1.748545	1.776153	2.846214	2.002051	1.003302	2.429969	5
1.853418	3.53585	3.835734	0.856978	1.400599	3.712702	2.91704	1
1.63315	1.316722	2.619318	2.937318	1.916679	1.496701	3.180816	5
1.884768	1.551881	2.123122	4.401792	3.459827	1.945	2.269949	5
3.020426	2.411129	2.633178	2.075542	1.667037	2.194526	2.91346	3
1.449371	3.431235	3.018328	1.125531	3.259058	1.10168	1.764484	3
0.84953	1.932868	3.02034	1.862252	3.688928	2.444511	1.698493	1
2.228413	1.91244	2.305406	2.513044	2.202764	1.670849	3.270545	5
1.208468	2.707595	4.269007	2.566786	2.451727	1.520423	1.423032	4
2.061931	1.903822	2.856964	2.327123	1.620568	0.117391	1.840711	3
0.262233	3.43046	3.196516	2.788729	2.266742	1.759309	-0.00986	1
1.357973	0.780838	2.722596	2.246043	2.321431	1.691787	2.072079	5
0.114807	2.509803	2.692398	3.128366	1.181392	2.545597	1.148067	1
1.28309	0.90347	3.001318	4.109714	0.083325	2.33898	1.950549	2
0.506534	1.782591	2.399148	2.907124	2.313644	1.898565	1.305203	1
1.213072	0.529087	4.048949	2.688219	1.612988	2.403943	1.783422	5
1.313982	1.203218	2.354178	3.867624	1.752954	2.803632	0.720678	2
1.872386	0.357258	3.278948	2.103521	0.673257	2.418421	2.767138	5
0.721409	1.36012	2.099485	2.777914	1.511871	1.263105	3.078166	5
1.803057	1.579713	2.093822	2.916097	2.61537	2.381333	1.975054	5
1.511414	2.714801	2.477878	2.356489	1.608225	2.422306	1.576296	1
3.784065	1.862054	1.713389	0.213838	2.933285	1.556042	1.609158	3
1.205779	3.309772	2.478432	0.880979	1.048996	1.852513	1.572679	1
3.810057	2.116697	2.3975	-0.04406	3.077084	1.416204	1.145462	3
2.507306	2.291566	2.189901	3.038778	1.571151	1.557165	1.056906	3
0.103926	2.725501	3.826067	2.194335	1.86495	2.26395	1.177269	4
0.809178	1.040189	1.730576	2.894496	3.211068	2.478951	1.698509	5
0.838928	1.784799	2.841608	0.794042	1.844635	1.75334	1.732254	4
2.569555	0.4746	3.345086	1.136888	2.120048	1.299826	1.999741	5
1.322061	-0.11907	2.775271	1.95979	2.899401	1.783886	3.379287	5
-0.76506	4.724631	2.893808	2.774245	2.50157	3.237441	2.484975	1
2.804131	1.719649	1.570869	1.93659	2.742195	1.139427	2.036416	3
1.205436	1.512286	3.53046	1.379409	2.993918	0.657272	2.418126	5
0.051672	0.879804	2.650317	2.384895	3.283675	1.39516	3.257062	5

-0.39607	1.190186	2.649046	2.575062	2.076664	2.576419	3.426286	5
-0.40315	0.425886	3.815744	3.942569	2.3952	1.989152	2.833274	5
-0.07924	2.622817	4.052617	1.266456	1.17043	1.867025	1.448149	4
-0.13567	2.362155	4.004661	2.462405	1.297833	2.140488	0.681625	4
0.477195	1.17295	2.913251	2.483704	2.848027	2.056686	1.758322	5
0.56271	1.616479	1.830526	2.923669	3.684984	0.849889	3.423473	5
1.579464	2.173769	2.527411	3.219991	1.767273	2.623521	2.888911	5
2.700568	1.320227	1.239929	2.207632	2.038575	1.646896	1.555653	3
2.151782	1.974439	4.213681	2.612496	2.459162	0.91177	1.399608	3
1.576249	1.452704	4.058938	2.575511	2.394314	1.063594	2.603736	5
3.780426	1.734454	3.849178	2.897637	2.083926	1.825276	1.092608	3
1.390327	2.075764	4.243	3.125061	1.273445	2.840671	1.859468	4
1.607157	2.968483	3.24849	2.076404	2.62992	2.696016	2.195731	1
2.569179	2.272447	4.441177	2.249513	1.372362	2.432124	0.511077	3
3.757162	1.90669	4.023394	2.056548	2.092316	0.702579	2.357687	3
3.200396	1.822515	4.443242	2.109396	2.22672	1.391675	1.539029	3
2.250052	3.01667	3.066849	1.523405	2.086696	1.93857	1.362553	3
3.564286	1.622048	4.393762	2.323449	1.023309	0.742946	1.799375	3
1.820917	1.750117	4.53634	2.28264	1.228009	2.070476	1.366165	4
3.837824	3.469015	3.399461	1.508111	2.106133	0.646965	1.877185	3
3.086287	3.311494	3.384577	1.007094	2.34214	0.704304	1.716368	3
0.735348	2.431545	4.265286	3.135617	1.18764	1.246144	1.800427	4
1.061379	3.511977	3.233219	1.598488	1.538965	1.701663	1.133595	4
1.481552	3.995962	3.090677	1.705871	2.747919	0.002467	1.188856	3
-0.00182	3.260239	3.669034	1.489115	1.660088	3.071547	1.895616	1
2.364332	3.423769	3.730801	0.464028	1.449773	0.034636	0.491184	3
1.790911	3.020807	2.397504	2.504064	3.159573	2.110374	2.839354	1
1.845525	2.336941	3.108308	2.925869	1.398286	1.004538	1.277946	3
3.774452	3.283662	2.601613	1.319941	3.095036	0.246845	0.737773	3
1.505742	3.82593	3.401152	2.344606	1.070413	1.189597	1.387092	4
1.612573	2.40045	3.297188	2.902049	2.074842	2.284885	2.024605	1
1.088512	2.784298	3.62959	2.500349	2.343832	3.113105	2.404938	1
1.42413	2.253803	3.343379	2.051898	2.425804	0.579324	1.473222	3
0.905829	3.986124	2.764364	2.658993	1.428778	2.003098	0.431219	2
1.778831	2.523333	3.375314	2.030899	0.692378	2.061231	0.704335	2
1.765234	2.818131	2.887796	3.433211	1.183735	2.435894	2.171128	2
1.960731	4.06999	4.008457	3.39411	0.026767	1.542573	1.270132	2
0.764445	3.897983	3.379027	3.055913	0.426009	3.234069	0.929019	2
3.687367	1.522458	4.258232	2.500019	0.945134	1.624383	0.883844	3
2.64934	2.323337	3.874644	2.744603	1.575332	0.305109	0.525865	3
1.789778	3.038155	3.024023	3.769444	0.323103	2.528426	1.142301	2
4.672162	3.069382	3.688413	2.440952	1.405466	0.020889	1.708298	3
2.340334	2.50208	3.653272	2.672299	1.360596	1.219283	1.643292	3
1.89812	3.145009	2.649546	3.571723	1.739567	2.162005	2.432012	1
2.405691	2.557828	2.234228	3.77717	0.918691	2.055871	1.870516	2
1.991084	3.045781	3.097603	3.246524	0.560414	3.354772	2.362809	2
2.652284	2.692073	2.782371	1.637233	2.017997	0.278823	1.12878	3
2.078746	2.558682	3.375823	2.666212	0.672835	2.323415	1.714464	2
2.272887	3.299781	2.934946	3.415632	1.601629	2.553767	1.538921	2
2.174742	2.020834	3.200357	3.304615	1.962247	1.781806	1.57773	5
1.554845	3.411567	3.696475	1.814908	2.144365	0.424043	1.026569	3
2.601653	2.277123	4.083702	3.772831	-0.42827	1.541241	1.480311	2
1.853866	4.368635	2.087155	1.677374	1.142678	1.287609	1.80835	3
2.681699	3.558978	3.406055	1.417839	1.343321	0.426572	0.474613	3
2.24989	0.822324	3.131529	2.802165	1.135157	0.648374	2.308554	5
2.111609	1.90889	2.584371	2.77702	1.595925	0.485008	2.907262	5
0.173858	1.347144	2.399445	2.292993	2.871639	2.099188	3.231836	5

1.546568	2.585044	3.272659	0.477661	1.807298	0.726058	1.899376	3
1.156342	1.765744	2.866667	1.718082	2.954764	1.113488	2.110821	5
1.494649	1.806517	2.856774	1.354115	2.009178	1.117367	2.192055	5
1.364551	1.615682	2.777178	1.997047	1.850187	1.154867	1.975221	5
1.412895	1.93883	2.560225	1.571869	1.177979	1.037155	1.555193	3
2.205521	1.692739	2.633795	2.812203	1.770763	1.12824	3.014037	5
0.745193	1.490097	3.379798	2.22975	2.245205	1.51202	1.55745	4
1.378298	2.662703	1.85831	1.981788	1.283554	1.282433	1.512774	1
1.884125	2.075508	2.16487	1.55485	2.294037	1.421776	2.021908	3
0.985738	2.323031	3.344249	2.186234	1.046613	1.139703	2.08681	4
1.339493	2.1716	2.640416	1.643363	1.890265	0.862075	2.452216	5
1.411204	1.768375	2.509155	2.071366	1.069819	1.270294	2.138543	5
1.603957	2.393124	4.600104	1.479665	0.3686	1.257599	1.671143	4
1.593894	1.808995	1.276598	2.542793	2.668689	1.234447	3.011351	5
0.437205	2.05325	2.233585	2.342777	2.863301	0.989024	3.132892	5
1.796248	1.921808	4.253712	0.987076	2.703099	0.264328	0.99685	3
1.637491	2.60536	2.78299	3.176663	3.185908	0.945942	1.681183	1
2.397302	1.887024	1.91816	2.197268	2.581808	1.771002	2.369984	5
2.328269	2.27798	2.125474	3.005204	0.099046	1.713398	1.026657	2
0.11416	2.396599	2.853036	3.178833	1.031306	1.899937	0.55292	4
0.646272	2.409414	3.949841	1.627033	1.13211	1.385222	1.246331	4
1.819873	2.572002	1.843449	1.60919	3.013846	0.301808	1.919204	3
2.893933	1.199162	2.164442	2.545358	2.839459	1.856562	2.979892	5
1.657387	-0.04104	2.817115	2.885721	2.252117	2.258384	3.244889	5
3.223918	1.104266	2.818893	1.829432	1.385741	2.348728	3.350843	5
1.567883	1.69097	2.678636	3.576635	1.69927	2.373808	1.665361	5
1.444466	2.164448	3.129106	2.105301	1.025459	3.286115	2.679373	5
0.789237	2.751414	4.503448	2.279741	0.594937	1.47052	1.258745	4
1.32103	1.739759	2.91269	1.970637	1.670966	2.325363	1.734543	5
1.417863	1.565313	2.942052	2.716931	2.031696	2.665588	1.504992	5
0.105744	2.701506	3.935611	3.081274	0.140042	2.612532	1.21387	4
0.093926	1.328851	3.657152	2.021215	2.748042	1.799659	2.503177	5
2.058253	1.409092	3.385514	1.720862	1.359984	2.940476	2.368557	5
0.610951	2.617612	2.618744	2.959006	1.079474	1.703607	0.602328	2
1.620419	1.452286	3.220025	2.04852	1.620619	2.70717	2.011157	5
1.26425	2.492492	2.254208	3.149003	0.20461	2.680442	0.963521	2
0.931603	0.778784	3.816232	2.411449	1.588901	1.749691	2.903384	5
1.883671	1.958262	2.662179	2.06722	1.593241	2.260557	1.932458	5
1.616866	1.148898	3.165864	2.700711	2.133769	2.779107	2.060409	5
1.96896	1.173538	3.408077	1.916709	1.627131	2.562472	2.227437	5
0.775019	3.539821	1.948109	1.474039	1.512137	2.192336	0.356982	1
-0.48434	2.801792	3.341801	1.253899	2.23096	2.792869	3.211511	1
1.735924	3.692729	4.176931	0.871424	2.20432	-0.09871	1.803309	3
2.436967	2.242692	2.95653	2.42781	1.861757	1.764807	2.614867	5
1.658166	2.250213	2.272366	3.709927	2.741535	2.928559	1.376769	1
1.333809	3.28714	1.923658	2.704404	1.874826	2.942094	1.95615	1
0.304445	2.431619	3.242846	1.164343	2.616041	2.179615	2.512263	1
1.093769	2.70846	3.188444	1.452049	2.704276	2.837869	3.558715	1
0.979075	2.932777	2.236762	1.834613	3.024493	1.92344	3.156133	1
1.504879	2.118966	1.74156	1.487179	3.392883	2.680421	2.117358	1
0.235742	1.514871	2.640203	4.244476	1.9561	1.274938	3.144923	5
0.721346	2.624908	2.503404	1.783081	2.070988	2.354757	2.050832	1
1.511873	1.611845	2.686757	2.24819	2.398428	0.857729	2.340673	5
1.483817	1.742122	2.38017	2.115277	2.46686	0.885315	2.411145	5
1.412824	2.023799	2.394205	2.244071	2.566338	1.066282	1.957895	5
0.96656	1.956889	2.503954	1.889427	2.584678	0.635303	2.486109	5
1.445583	1.659629	2.820313	2.291001	1.995405	1.615854	2.326673	5

1.264227	1.559251	2.530892	2.351941	2.005204	1.908408	2.08316	5
1.300572	1.506208	2.456656	2.476265	1.930084	1.826288	2.238183	5
1.395494	2.681821	2.399638	1.861954	1.670527	2.336857	1.348026	1
1.071372	1.64587	2.335144	2.049403	2.134302	1.103433	2.192995	5
0.972549	2.213103	2.453235	1.965736	1.820293	1.210596	1.269824	1
1.492335	1.795098	2.306659	1.928596	2.03471	1.206811	2.336041	5
0.290952	2.170553	2.27139	3.121171	1.858355	1.795948	1.144805	1
1.575429	2.032213	2.465815	3.19347	1.550548	2.006904	0.837601	2
-0.28365	2.768528	2.892846	2.010788	3.199715	1.111858	1.784	1
1.699107	1.726334	2.98967	2.659644	1.172693	1.45147	1.176434	4
2.310326	1.084356	3.212852	0.991361	2.383933	1.0178	3.223335	5
0.538985	0.684544	2.87213	3.319863	0.471048	1.146485	3.037455	5
1.320483	0.370392	2.959414	2.893502	3.208969	0.487022	2.159851	5
0.632746	0.962392	3.786251	3.674781	1.636723	0.976119	0.43589	4
1.260572	1.114517	3.471529	3.147704	2.509499	0.784426	0.739571	4
1.81431	0.908937	3.437827	3.115334	1.089183	0.8543	1.536967	5
0.480491	1.603937	3.497161	3.171849	2.858567	1.045461	0.796103	4
2.448276	0.9507	3.11357	2.242604	2.513886	1.092078	1.001218	3
1.667621	0.720564	3.065787	2.789554	2.601914	1.00463	1.646084	5
1.36549	0.471031	3.670106	2.32908	2.812428	0.692981	2.377931	5
1.782831	0.668699	4.303075	2.950578	1.196954	1.473613	2.410163	5
1.779422	1.804898	2.372978	2.236031	1.796164	1.101095	2.408556	5
0.752197	1.221928	3.601867	1.913002	2.917384	0.485048	2.184378	5
1.090207	0.371767	3.657906	3.103313	2.695586	1.088557	2.130409	5
1.449626	1.446819	4.565353	2.201232	1.589811	1.28579	1.45593	4
1.538993	0.432944	3.880188	2.973588	2.369882	1.22025	3.079243	5
1.267368	0.956728	3.771335	2.573059	2.060642	1.354038	2.111837	5
0.812903	2.100727	2.003404	2.841437	1.176845	4.042103	2.308406	1
-0.12421	2.607063	2.9329	2.202843	1.640928	2.10373	2.387402	1
0.542068	2.551937	3.744826	2.376175	0.753738	3.505419	2.13489	4
0.372456	3.354352	3.712648	1.479283	0.715589	1.445332	0.635211	4
0.305215	2.289783	4.46517	2.340381	1.999469	2.164077	1.869376	4
2.755486	3.573517	3.853695	1.941299	2.051228	1.450862	2.118203	3
1.626729	2.778755	1.826495	3.451388	1.873129	3.158793	0.826211	2
0.076946	1.646119	2.222775	2.737351	1.203729	2.5871	4.468302	5
1.013232	2.162299	3.088201	2.495127	1.321445	0.938687	1.910282	4
1.20519	-0.07545	2.885382	1.956822	2.266986	2.416183	3.019212	5
1.39817	1.852987	3.197305	2.136321	1.394049	0.442642	2.051922	4
0.873249	2.555248	2.54208	2.041056	2.167741	0.808359	1.213751	1
0.806786	1.256641	3.512638	2.772089	1.439192	2.428634	3.160887	5
0.026556	1.299047	2.254734	2.758667	2.102032	2.059072	2.925602	5
-0.37456	1.577272	2.356102	3.532591	1.521418	2.161338	1.712706	1
0.294225	1.883966	2.915752	2.171537	1.986679	0.595522	1.150333	4
1.332085	0.698822	2.722347	3.810148	1.240012	1.953593	2.289551	5
1.531207	1.639334	2.208954	2.580159	1.424991	1.388167	2.864206	5
0.649526	1.983378	3.004372	2.763197	0.644957	1.465754	1.641154	4
1.062165	1.703427	4.137153	3.523577	-0.25471	0.274785	2.414101	4
1.613615	1.567968	2.01006	2.909649	1.084012	1.64672	3.082602	5
2.611317	1.360381	2.572052	3.842697	2.318571	1.267588	1.442266	5
0.244814	0.983054	2.619721	3.328562	3.670014	1.220171	3.959349	5
0.212633	1.470245	3.736618	2.26854	3.534922	1.163535	2.752749	5
0.210494	2.000189	3.356024	2.1878	2.134824	1.09907	3.104368	5
1.926494	2.720868	1.743791	1.398287	2.173038	3.352568	2.561924	1
1.072198	3.31218	4.423606	0.480775	1.247225	1.562622	3.173473	4
1.357499	2.189561	2.255633	3.35382	1.874947	3.258765	3.437023	5
1.497423	1.962183	2.210324	1.454927	2.617754	2.249815	2.748368	5
1.704547	1.358564	2.589937	2.18018	2.343222	1.467078	3.609101	5

1.339563	2.526236	2.490679	1.016699	2.780961	2.661584	2.361953	1
2.328581	2.394616	2.552002	1.14282	2.842293	0.484683	4.308226	5
1.85317	1.934251	3.869415	0.499016	2.363052	1.674276	1.029997	3
1.45469	2.190708	3.760847	1.722148	1.768372	3.116628	3.478788	5
3.470967	3.439438	3.360445	0.721942	-0.20575	-0.06164	0.009922	3
1.296298	2.090994	1.963986	3.324418	1.359161	1.950194	4.18974	5
0.814951	2.698575	2.986318	0.932067	2.782515	1.42676	0.998865	1
0.701812	2.816236	4.503632	3.118434	1.809571	2.136325	1.220668	4
-0.10962	4.748057	1.311358	3.02705	1.085849	3.705541	2.662043	1
1.458165	3.619007	2.461477	1.602822	1.411744	2.264779	2.547659	1
0.800917	4.262438	2.544643	2.894222	0.613533	3.956862	1.671726	2
0.717591	4.02109	1.879332	2.441721	1.49057	2.877834	0.429284	2
0.643691	3.855714	1.005858	3.175629	0.103246	3.558945	0.795806	2
0.460533	3.698006	2.572437	2.387381	2.850441	2.808884	3.094858	1
4.04329	2.578201	0.799226	1.244423	1.632081	1.311067	1.735986	3
1.774165	4.058947	4.405546	1.785724	2.283782	0.758058	0.79129	3
2.724334	4.789961	1.917886	3.663023	0.860011	2.905804	-0.22034	2
1.890045	3.070056	2.121002	2.630324	1.471761	1.45338	1.399154	2
1.179053	2.241616	2.464325	1.743874	2.39835	0.483349	2.739105	5
0.910327	1.109921	3.392557	1.840023	3.649984	0.230089	2.727363	5
-0.76467	2.630535	4.08284	1.372603	1.512798	2.614801	1.87896	4
0.018361	2.910309	2.608297	1.602254	2.228515	-0.1038	2.327382	4
2.31223	2.140411	3.730239	2.46278	1.824992	1.428426	2.476548	3
2.000375	2.189982	3.724534	2.161509	1.635054	1.57342	0.200782	3
3.566437	0.913912	4.240227	1.9238	2.017575	2.399885	0.391107	3
1.62852	1.018615	3.425307	2.069394	2.752738	2.893608	1.471069	5
2.456128	1.924375	4.611679	1.543373	2.675139	1.215867	0.819487	3
2.955322	1.138264	3.747873	1.707216	2.573102	0.483788	0.805569	3
2.62885	1.755127	3.044607	2.3257	3.162495	2.415337	1.155672	3
2.310367	1.524535	3.543808	2.150572	2.369389	2.057397	0.899822	3
2.827557	1.951977	3.069947	1.919696	2.682531	1.73087	1.301477	3
2.354338	1.852527	4.186875	2.762147	2.727398	1.526546	1.348267	3
3.133866	1.126868	3.578091	2.250377	2.22218	0.989612	2.052883	3
3.902417	1.344091	2.9635	2.392058	2.238225	1.139263	1.925944	3
4.044799	2.560889	2.663006	2.169593	0.901192	1.77012	1.96679	3
4.155056	3.609037	2.424906	2.437343	0.670008	2.751403	1.023351	2
3.229569	3.060956	1.07279	2.674057	0.661189	2.715768	2.115442	2
2.921269	3.279488	2.066332	2.23657	1.842327	2.123827	1.809801	3
3.044779	4.07456	3.89887	1.460329	1.288036	0.384507	1.178261	3
2.740083	1.644629	2.55435	3.62446	1.955832	2.066756	0.815177	2
3.672096	3.42332	1.365735	3.932623	0.190274	3.855517	0.758265	2
3.179953	3.568001	2.620359	2.696917	-0.87467	3.369777	0.541363	2
2.519518	3.268074	3.607177	2.930387	1.07823	3.237732	2.437606	2
2.225039	3.775535	1.123748	3.689868	1.819697	3.939923	2.586388	2
3.709609	3.536046	2.146801	3.13129	1.525033	3.051844	1.077151	2
3.922836	3.537094	2.352621	3.817752	0.344085	3.99746	1.601192	2
2.559641	4.363924	3.081225	3.940225	1.04974	4.147581	1.955423	2
2.506535	3.511332	2.686218	2.671171	0.351229	3.135231	1.534423	2
3.611068	4.140873	2.759899	3.567679	0.327898	3.496142	1.915584	2
5.041109	4.030347	2.811553	1.898102	0.623562	2.481326	0.318056	3
3.987555	3.862457	2.73161	2.815862	0.253199	2.530565	0.116675	2
3.206587	3.376827	1.547706	3.04708	0.941526	3.026795	1.442369	2
2.687183	3.33638	2.737193	3.16023	0.407868	1.803257	1.018576	2
4.22479	4.024705	2.715407	2.974781	0.622469	2.100873	0.07855	2
3.485571	4.124516	1.799485	1.550554	0.865302	2.835845	0.512219	2
3.689093	2.992012	2.750544	2.126705	0.951029	1.841686	1.154485	3
1.507022	1.700048	3.643006	1.920586	1.721019	1.670477	0.88364	4

2.276998	1.872161	3.071937	1.551547	1.758093	1.456656	3.036033	5
1.722543	1.742988	3.195897	1.77644	1.623838	1.707611	1.691541	3
2.065441	1.855082	2.560649	1.429018	1.677676	1.63554	1.462513	3
1.74568	2.356083	3.455882	1.940336	1.498636	1.462326	1.919923	3
0.158772	2.513544	4.247838	2.551583	1.045512	1.299605	1.587535	4
1.80119	2.071641	4.041234	1.902576	1.296598	1.057213	0.731661	4
2.215429	2.553712	3.092798	1.870086	2.016486	1.713556	1.211197	3
2.561767	1.359762	3.215666	1.723347	2.649111	1.506876	1.212116	3
2.008407	2.326931	2.699744	1.797094	2.059043	1.621615	1.595778	3
2.063938	2.29876	3.576087	1.683763	1.536197	1.5092	1.604547	3
1.870314	3.05033	2.832324	1.120539	1.534361	0.937647	1.53327	3
1.545386	2.699153	2.90158	1.987278	1.572393	0.979358	2.326712	3
1.459833	2.793298	2.536495	1.525111	1.671519	1.382715	1.130589	3
2.883239	1.229672	3.978406	2.649253	1.311891	0.28695	1.875801	3
3.555512	0.756289	4.859439	2.591224	-0.00136	1.007842	1.233879	3
0.508175	3.178791	4.788698	1.290105	-0.27008	1.16648	1.256636	4
-0.43375	2.490532	4.749263	2.352686	-0.37615	2.187117	0.105813	4
3.964904	4.089137	4.415442	3.244999	-1.16908	1.236213	-0.05455	2
2.359152	2.995853	2.391476	2.378635	0.185879	0.813561	0.190325	2
1.015333	3.244709	3.91884	1.170988	-0.83935	0.70902	1.389022	4
-0.1317	3.371376	2.410057	3.437201	0.297436	2.487018	0.199548	2
1.47955	1.064245	4.922544	1.301369	0.974274	2.158269	1.332632	4
1.137828	1.970334	4.54537	1.77048	0.962424	1.676055	0.879076	4
1.978596	2.050605	4.222893	1.545038	2.620691	1.180971	2.380491	3
1.621695	1.681869	2.94142	2.467838	-0.34802	1.869441	0.368981	2
1.218523	1.811689	4.994002	2.11	-0.69899	2.880036	1.550563	4
2.064395	1.173791	3.932134	2.708803	1.250605	1.115845	0.557882	4
0.532071	1.356335	3.948873	2.254287	2.468433	1.466865	1.992075	4
1.429912	3.253482	2.093267	3.097008	2.026439	2.325492	1.059837	1
1.462999	2.915668	2.516664	3.674496	3.004662	1.589824	0.748062	1
0.733537	2.892451	2.643295	3.09355	3.151582	1.65196	1.337782	1
0.791875	2.884693	2.779237	3.413417	2.44907	2.601256	1.424172	1
-0.10517	3.040316	3.360112	2.855718	2.873678	1.188593	0.322964	1
0.875719	2.924053	3.610616	2.741726	2.132826	1.585964	0.493479	4
2.176518	4.067647	1.934115	2.559868	2.254118	2.083677	1.380008	1
-0.17358	3.503438	2.423085	3.051185	2.147663	1.953754	2.706169	1
1.679471	2.53749	2.705387	2.011349	3.219434	1.704823	2.592947	5
-0.62134	3.307752	3.073545	2.275577	1.186566	2.329074	1.121935	1
-0.58953	4.10793	2.459029	3.07827	1.627415	1.960017	0.474559	1
-0.4566	3.748106	2.48163	1.703436	2.031344	2.439934	2.085523	1
-0.40305	4.629888	1.803605	2.719529	0.109098	2.449213	0.376085	2
-0.13362	3.298538	2.094871	2.657361	2.068097	2.119957	1.46328	1
1.051681	3.044125	1.860595	2.414682	1.750706	2.127842	0.624443	1
-0.46756	3.672684	2.609306	2.798242	2.727397	2.08414	1.927971	1
-0.22257	3.403974	3.992026	1.594233	0.951226	1.79945	1.564202	4
0.879599	2.559537	2.682985	2.436528	1.732751	1.685048	0.478358	1
2.068797	4.083433	2.641366	3.421411	2.299622	2.077696	0.331541	2
3.216228	3.0991	2.141928	3.095791	1.858518	2.550298	0.088065	2
3.29187	3.301854	1.867055	2.807832	2.601268	1.726811	0.402809	3
3.144054	3.6932	1.424622	1.494059	2.486708	2.370872	0.574533	3
2.457114	2.686718	2.077536	2.537355	2.735416	1.764817	0.329161	3
1.390182	3.449505	1.922259	2.738923	2.591671	0.9854	1.00846	1
2.120156	2.579095	2.882224	2.725341	2.006488	1.055209	0.117931	3
1.970891	3.700663	1.468186	1.396667	1.40279	2.8171	2.009906	1
2.336216	3.764322	2.473572	2.329863	2.576363	1.084098	1.365232	3
-0.10381	3.389959	2.547536	3.543453	2.283116	2.61914	1.589867	1
1.530012	3.427078	3.194501	2.701941	1.67882	0.968439	1.025129	4

0.857718	3.392356	0.472536	3.279675	2.230862	2.233642	1.218844	1
1.505968	2.621823	1.743091	2.215408	1.95822	2.639966	2.912557	1
0.725015	3.984839	1.182635	3.701695	1.594431	2.084002	1.741048	1
1.473229	3.459439	1.638031	3.406329	1.333691	1.702277	0.560334	2
1.060838	4.181436	2.247993	3.323963	1.172574	1.898132	0.339313	2
2.990401	2.281804	3.070215	3.687298	-0.31184	1.27937	0.285347	2
0.769166	3.840194	2.731756	3.841705	1.747542	2.137993	1.252245	1
0.75415	3.558579	3.263125	2.647108	1.429326	2.333785	1.492619	1
1.303379	3.795161	1.530871	3.377136	2.072449	1.99248	1.083788	1
0.524407	3.859915	0.853766	3.074975	2.435645	3.317072	2.826819	1
0.12645	3.785307	2.629406	3.674972	1.265829	3.524083	1.271341	2
0.343963	3.983414	2.502811	1.906588	1.645706	0.417935	0.845107	1
1.710316	3.076969	2.060937	1.610017	1.059669	2.128205	0.703361	2
0.417446	3.648473	1.424328	3.711073	2.197958	3.114104	3.181453	1
2.04927	3.750571	1.462268	2.262071	2.189925	2.108657	0.792803	1
0.69803	2.205002	2.111445	2.568238	1.649992	2.488567	2.237445	1
0.951935	2.583197	3.095091	1.735256	2.707042	2.199157	0.645377	1
1.068594	2.818606	1.152625	2.573538	1.774493	3.034217	1.334008	1
1.308397	2.569901	3.080408	2.525086	2.007064	1.700561	0.976378	1
1.712708	2.433669	2.691373	2.580652	1.52399	1.378826	1.194658	3
0.91916	2.37196	2.775352	2.330603	1.599222	2.702074	0.89072	1
0.817149	3.12306	2.784622	2.661203	1.768797	1.560057	1.036902	1
0.791967	2.595179	1.847499	3.263682	2.414274	2.375985	1.818882	1
0.849967	2.071186	2.320527	2.101878	1.589166	3.016033	2.319835	1
1.60647	1.993996	2.891402	2.562998	2.438122	2.625546	1.083263	1
0.942826	2.975032	2.008094	2.730432	1.613834	2.493358	0.169133	2
1.07511	2.919006	2.379194	3.328983	1.773508	2.139629	0.766729	2
1.325045	2.690406	2.595724	1.726559	2.106144	2.474342	0.974182	1
1.411178	2.448139	2.713626	1.825376	2.091093	2.512333	0.987373	1
1.433908	3.131516	2.788815	2.250392	0.990708	2.570261	0.605752	2
0.880346	2.425598	2.678058	1.88785	2.024216	2.640519	1.366953	1
0.260364	2.906487	2.683074	2.969851	2.87145	1.602331	0.491496	1
0.423654	3.974504	2.400218	2.156817	1.89691	1.267873	0.473422	1
0.427651	3.447316	3.1171	2.700789	0.708482	1.333679	0.149171	4
0.579635	3.585689	2.21721	2.667774	2.940801	2.46273	0.537045	1
-0.02029	3.840243	2.522009	2.530284	1.500204	2.86294	0.081363	1
-0.06372	4.230166	3.597157	1.843047	0.983072	1.515249	-0.07676	4
-0.26029	3.873231	3.083164	2.437457	1.954143	1.404252	0.414916	1
-0.09942	2.776442	2.750918	2.707537	3.145203	1.570567	0.377695	1
0.275255	2.768954	4.02854	3.181462	2.991128	2.109993	1.402953	1
0.113402	2.605435	3.763227	2.119889	2.826393	0.865589	0.907433	4
0.149213	2.508363	3.846134	2.298856	2.899768	0.618085	1.543748	4
0.340557	2.541882	3.976928	2.681444	2.89268	1.145417	2.776941	5
-0.22202	2.844312	3.663467	3.049983	2.78542	0.617824	1.919961	4
-0.42178	2.192275	3.690923	2.891726	2.728776	1.202586	1.759638	4
0.457553	2.492178	3.576297	2.309842	2.744103	1.488316	0.765272	4
-0.07661	2.609934	2.688168	3.119072	3.314492	1.011728	2.009197	1
-0.30624	2.770384	3.647785	2.925661	2.651414	1.323014	1.751405	4
0.140752	2.594201	3.258795	3.069871	3.47017	0.903461	0.651931	1
1.494952	2.999964	2.300849	1.995311	1.425531	2.775196	1.773108	1
1.41039	2.949323	2.387595	1.69254	2.185164	2.487053	1.731274	1
1.118924	2.488969	3.415318	2.801899	2.178712	2.20894	1.709332	1
0.680572	3.258869	2.936039	1.918446	2.464094	2.07186	1.309618	1
1.141929	3.06936	2.624611	2.402971	2.363638	2.640456	1.426466	1
0.746483	3.534708	3.054122	2.286824	2.79205	2.205442	1.267024	1
1.011091	3.031657	2.571288	2.223547	2.575557	2.478644	1.656454	1
1.40917	2.33553	2.061849	1.689985	1.99935	1.701782	1.404149	1

0.768691	3.058953	2.917657	1.717871	2.803346	1.933463	1.826406	1
0.623259	3.10424	3.355942	1.998985	2.639103	2.307023	1.329493	1
1.357966	3.236041	1.628006	1.779124	2.009948	2.126546	2.923375	1
2.07341	2.95349	2.752977	0.969581	1.431418	1.74605	0.802422	3
0.792031	2.649246	3.21402	2.835091	2.391127	1.799076	1.483771	1
0.858457	3.130532	3.015193	2.654074	2.640759	1.527418	0.322885	1
0.80738	2.732501	1.65259	2.665072	1.627335	2.728416	2.013305	1
2.121461	3.110723	1.16904	2.698361	2.430201	1.879455	2.229385	1
1.359222	3.174655	1.435069	2.530789	2.244504	2.450394	2.122023	1
0.801118	3.074178	2.997585	3.838252	1.685823	1.335476	0.356832	2
0.080879	2.361793	4.274073	3.686526	2.221517	1.268115	0.479096	4
-0.17235	2.88178	4.48302	3.728202	1.719875	1.135475	0.350021	4
1.761006	2.297744	2.459649	3.053792	1.618949	1.878463	0.104232	2
0.216599	2.173008	3.770535	2.930397	2.304761	1.358994	0.372433	4
0.269085	2.048156	4.424645	2.43455	2.333657	0.970885	0.469465	4
0.065369	2.640117	2.597345	2.581476	2.209659	2.753815	1.558239	1
0.345163	2.569093	3.249664	3.07534	2.493951	1.078831	0.499263	4
0.052513	2.518404	3.110811	3.134081	3.319594	0.871954	0.68042	1
0.30771	3.104776	3.560694	3.132041	2.383767	0.800719	0.482138	4
1.154284	3.557102	1.593781	2.129454	2.591031	2.608611	1.732789	1
3.548581	3.065902	3.364989	2.870269	-0.19792	0.576981	0.807048	3
1.265666	2.865337	3.30641	1.610438	0.737536	0.923749	1.090937	4
1.399631	3.450565	3.602698	2.993068	1.321121	3.436824	2.859307	2
2.071889	4.124985	2.273219	3.721401	1.332661	2.351524	0.687626	2
0.876012	3.10726	5.157052	2.502289	1.431415	0.674595	1.330972	4
2.349308	2.583863	1.776008	3.662912	2.041628	1.749898	2.531925	5
2.636519	2.334488	2.925445	2.995422	2.243155	2.308253	1.318905	3
2.987487	2.852596	2.434173	2.467237	1.838249	2.755136	1.358205	2
0.81905	1.825397	3.348165	4.522798	1.350309	1.59561	1.848665	5
1.774038	2.862877	2.685874	2.435596	2.107649	1.280506	0.910797	3
2.471096	2.604342	2.691034	2.817636	1.91936	2.006992	1.160133	3
3.060003	2.389687	3.987338	3.677606	1.309749	0.365417	0.614433	3
3.262966	3.396536	4.41932	0.726091	2.244941	0.726714	0.128801	3
2.494411	3.012345	4.550361	1.22457	1.950454	1.090167	0.322092	3
2.079433	2.14239	3.469334	1.070271	2.489137	1.932302	0.438562	3
2.268403	1.873654	4.282994	1.313821	1.418581	2.464574	0.276199	3
3.08802	1.748826	4.565023	-0.33519	2.055988	2.092309	0.217988	3
2.777448	1.078595	4.10723	2.455113	1.397793	2.134951	0.741937	3
3.102757	1.592921	3.055213	1.054164	2.005069	1.878598	0.214148	3
3.479759	1.33687	3.174094	1.2196	2.175686	2.51985	-0.06827	3
0.623457	2.841408	1.295385	3.855206	2.838636	3.356909	2.354045	1
1.847572	3.354191	3.861348	3.103105	0.405502	2.467452	1.557334	2
2.32006	2.266582	2.220428	2.264085	0.940936	1.327739	1.041959	3
2.959903	2.952272	3.331057	3.012319	0.19202	1.653348	0.098445	2
1.703666	4.825642	2.81377	-0.18771	1.279538	0.122421	0.405711	3
0.475181	2.03538	3.124756	3.793217	2.522743	3.14862	3.03574	5
2.204704	4.680761	3.398592	-0.06387	1.459862	0.056371	0.729264	3
2.002607	2.755353	3.376209	0.036351	1.407113	0.555023	2.247859	3
0.907119	1.708706	4.912416	2.140988	1.922985	2.28953	1.116472	4
1.825809	2.128214	4.741464	0.159796	1.636236	2.063124	0.352333	3
0.153648	2.889437	2.800667	0.352795	2.08095	2.082555	1.234468	1
0.587994	3.861874	2.269366	1.68284	1.605637	1.89417	0.802835	1
1.024508	3.664618	2.874202	0.661802	1.556209	1.204374	0.130695	3
0.283041	3.817617	2.288075	1.913851	1.877978	1.808863	1.815715	1
0.311823	3.273917	2.51415	3.816218	1.458316	2.762033	2.043699	1
0.718942	4.25634	4.459668	2.072599	1.638075	0.100716	1.716839	4
0.008545	2.195237	3.234108	2.99666	2.548574	1.681762	2.171549	1

-0.47133	4.246083	1.528641	2.336485	0.732913	3.646783	-0.41321	2
1.077048	4.530622	3.141172	1.851634	0.845131	1.322201	-0.08585	2
1.705065	3.239689	4.050878	1.401745	0.04819	0.238856	0.758254	4
2.025447	3.033307	2.675933	2.113983	1.52901	0.942658	2.129124	3
0.244751	4.092002	3.424906	1.330836	2.236125	0.876376	0.474374	4
0.151119	2.98758	3.568751	1.451563	1.656526	1.805595	1.468168	4
-0.24368	2.750309	3.5265	1.860395	1.715834	0.987104	1.895436	4
2.648074	3.621529	3.486606	2.933279	0.373718	2.709986	-0.22809	2
2.066586	3.066316	3.580333	2.246909	1.180946	1.055538	0.656804	3
1.944425	1.998555	3.567294	2.594938	1.536046	2.975502	0.613735	2
1.121274	2.724664	2.638417	2.486761	2.431015	2.384841	1.565011	1
2.850815	1.654452	3.992092	2.263066	2.418238	1.276869	1.221492	3
0.684173	2.59755	4.093945	1.046064	3.083327	0.362483	1.38296	4
0.174206	3.493588	3.316332	1.816635	2.951768	0.969128	0.733653	1
1.860815	1.680196	2.476973	1.941281	1.753742	1.344025	1.426395	3
1.752092	2.024168	2.66644	1.898802	1.6596	1.209577	1.477241	3
1.321311	2.063387	2.163432	2.908879	1.330973	1.88362	2.361532	5
1.647948	2.270076	1.86041	1.867999	1.454386	1.969179	2.568774	5
1.325019	2.361829	1.478412	2.266887	1.764518	2.642484	1.702186	1
1.088055	2.85659	2.246922	2.880238	1.555623	1.051089	1.817443	1
1.062752	2.864692	2.06805	2.854408	1.648133	1.414439	1.940907	1
1.898748	2.937805	2.14582	2.108399	1.533958	0.926171	1.734107	3
1.164505	3.039528	2.132053	2.855484	1.416871	1.0435	2.152127	1
1.217726	2.459069	2.369937	2.894859	1.596448	1.29165	1.294127	1
1.205169	2.99523	2.238958	2.69529	1.1099	1.645469	0.920897	2
2.247636	1.559871	2.359851	2.345988	0.75245	2.326831	2.011774	2
0.515809	3.209018	2.974778	0.088037	0.354395	2.184264	0.377669	4
2.664913	2.258446	2.453266	2.835131	0.94236	1.093029	1.450462	3
2.332702	2.904314	2.102263	3.80914	4.423846	2.545838	2.19781	1
0.858277	2.789032	2.675953	3.975471	2.940192	3.199923	1.756495	1
0.135326	3.130819	1.787072	3.322858	3.569177	3.067827	1.901571	1
0.210271	2.715819	3.337833	3.945324	2.118081	3.089931	2.290278	1
-0.10692	3.305084	3.883783	3.738765	2.271649	1.095572	2.372052	4
2.940514	2.045527	1.655645	3.337987	2.325931	1.995342	2.523698	5
0.017031	3.471114	2.781549	3.449273	3.063424	1.982684	2.810396	1
0.217045	3.102494	2.257095	3.712236	3.227408	2.424947	2.706707	1
1.168394	3.158382	2.397039	2.875788	3.195214	1.667232	2.237079	1
2.166365	2.328856	3.406558	3.882285	2.341709	1.610299	1.985158	5
1.207266	3.701287	3.536277	2.471503	2.445392	1.455107	1.94385	1
0.350961	3.216452	3.756608	3.369897	2.633468	1.71541	1.968044	1
2.142924	3.021736	4.265552	2.12064	0.265916	2.962148	1.455148	2
0.33667	1.944071	2.455792	1.119593	2.806737	2.954146	1.19752	1
-0.37456	4.684672	1.857995	2.673432	2.43409	1.675507	0.615034	1
-0.45765	2.951242	3.57413	2.673064	2.310049	1.494068	1.204785	4
2.241543	3.295219	1.761795	-0.46674	2.062207	0.658954	3.085202	3
2.274352	3.904877	0.965383	1.090103	2.177539	1.008027	1.615303	3
0.542086	1.246405	4.771957	2.932708	1.626256	0.35913	2.19558	4
1.405164	4.017422	2.502021	2.645762	2.199201	0.974838	1.105484	1
1.596445	2.820486	2.350912	1.453811	3.042025	1.647329	1.921859	1
-0.10552	2.818759	2.971996	3.080708	1.907297	0.083147	0.823936	4
-0.32487	3.260904	3.534991	2.253789	0.849691	0.516675	1.967281	4
-0.1682	2.358753	3.087227	0.986124	3.435746	2.779199	2.729604	1
2.247645	4.286214	0.019446	3.584856	2.068911	1.866873	0.807345	2
0.47302	1.446077	0.663542	3.750715	1.414859	3.605458	1.93925	1
-0.59701	1.675585	3.925224	1.716529	2.459564	3.219338	0.880136	4
0.861698	3.040857	2.553108	1.336346	1.43595	1.136466	0.604058	4
0.957117	2.787028	3.658154	0.801289	-0.61602	1.330431	0.835537	4

0.124301	2.421105	2.705534	2.460809	1.797187	2.180488	1.753949	1
1.006473	1.997175	1.029746	2.796541	2.776268	0.984417	2.779216	5
0.366053	2.322168	4.060788	1.559525	1.519204	0.253499	2.169938	4
1.583427	3.27796	2.562148	1.507864	2.014645	0.852825	2.43981	3
0.751172	3.492416	4.487172	2.507872	1.848005	0.476099	2.176782	4
0.859564	2.121968	3.57061	2.07186	1.694885	2.381739	1.771004	4
1.150281	2.229375	3.993247	1.538726	1.713609	1.263208	2.984529	4
1.009329	2.523104	3.632711	1.751953	2.49709	0.747835	1.973844	4
0.800092	2.313618	1.947549	2.129778	2.779523	2.736547	1.287074	1
0.507842	2.126182	3.709382	2.025182	2.014483	2.499448	1.949562	4
1.707627	1.784648	3.412401	2.081609	1.543876	1.982379	2.252024	5
1.520279	2.053032	3.102355	2.341057	1.547812	1.045763	2.045449	5
2.051176	1.709775	3.481137	1.391418	1.709236	1.635493	3.759327	5
0.911119	1.734922	3.484695	1.986006	2.121027	3.065789	1.925379	1
1.401215	1.524107	2.979994	1.938822	2.037472	0.806494	2.666591	5
1.082589	1.594227	3.461005	1.861188	2.047426	1.824083	2.205309	5
0.782273	1.504928	3.980124	1.198786	2.167906	1.904642	2.458123	4
1.130089	1.618194	3.558431	1.84232	1.224004	2.513945	1.961609	4
0.777959	2.330444	4.134831	2.302482	1.573921	1.895572	1.789862	4
1.708766	1.298943	2.563442	2.053514	2.096883	1.721538	2.927518	5
1.154063	2.688875	2.425242	2.718147	2.253345	1.159137	1.198447	1
0.809999	1.599301	2.619081	2.243507	1.198234	2.379065	3.111126	5
1.98482	1.356919	3.401547	2.87027	2.888688	0.917695	1.559026	5
2.623055	0.067936	2.551413	1.795425	2.420002	0.685113	3.023309	5
0.104503	0.941991	2.736113	4.900371	2.223849	2.112671	1.511158	5
1.397307	0.341324	2.840602	2.29184	2.505188	0.169115	3.259495	5
1.270621	0.496461	2.746452	2.312243	3.044293	0.303743	3.174375	5
2.274565	0.005369	2.76484	2.662452	2.414838	0.887809	2.310469	5
0.086942	2.180963	2.659627	3.723745	-0.4808	2.794365	2.358254	2
2.554201	2.382038	2.613128	2.197507	2.622773	0.417857	2.937588	5
0.665437	-0.15309	3.013491	3.591409	2.397752	0.910813	3.196063	5
0.219131	0.988948	2.949241	2.832939	2.812933	1.931909	2.337423	5
0.08191	1.904748	2.697057	2.395814	2.909281	0.849056	1.816543	1
-0.5757	2.364009	3.812397	1.903619	2.952605	1.246934	2.699965	4
0.281395	2.412998	4.491506	1.717264	1.527465	0.20048	1.743169	4
-0.37792	0.853802	3.500635	4.447944	1.770293	2.376319	2.945239	5
1.43101	1.729342	2.285234	3.594539	2.158406	1.41163	2.35083	5
2.242448	0.452776	2.03011	2.175292	2.960922	0.892266	3.490946	5
0.772287	1.044562	4.099495	2.099755	2.303216	-0.07957	3.408013	5
1.687683	0.705034	3.483106	3.50241	0.084663	1.296573	1.360677	4
0.08152	2.497989	2.633608	2.102286	1.992036	2.405288	2.854927	1
0.564148	0.290457	1.858481	3.457962	2.040157	2.621054	4.093532	5
1.432265	2.214134	2.28557	2.447828	3.114609	1.697488	0.560871	1
1.22986	4.209676	4.152368	1.648818	2.4148	1.380472	3.982964	1
1.798733	2.321707	1.944999	2.484884	2.09713	2.497045	3.945049	5
1.548915	2.98621	2.419907	4.166224	1.884883	3.007174	1.354243	2
1.736698	2.102224	2.781879	2.624937	1.287076	1.154947	2.066471	5
1.841468	2.779364	2.014616	1.952026	1.864021	0.832871	2.831117	5
1.850788	3.557185	1.247119	2.762191	2.367131	2.073187	2.334656	1
1.988117	1.848378	1.617975	3.235807	3.561746	0.849005	3.282251	5
2.963195	1.875433	2.294584	2.090209	1.373802	0.773446	1.733781	3
1.280458	3.577684	3.18186	2.344035	3.374431	2.15427	2.751256	1
0.884161	5.784644	3.534264	1.819497	2.386301	3.77747	0.141682	1
0.074259	3.574523	1.619785	2.533091	0.988846	2.903029	2.823716	1
3.04004	2.314318	2.13163	1.6602	1.868691	0.651936	2.527277	3
2.717961	1.981777	1.938336	2.53088	2.20996	0.227048	1.92194	3
1.469363	2.818761	1.884582	2.648021	2.089939	2.410461	1.996118	1

2.709623	2.493832	1.025723	2.408424	3.062117	3.46406	1.106719	1
2.161146	1.174376	2.314965	2.254531	3.234909	1.291243	2.520153	5
2.287607	1.838934	1.818019	2.927362	2.361122	0.866097	2.034928	5
3.353594	3.559703	2.04658	2.406643	-0.54042	0.195315	0.023831	3
1.392493	2.078828	2.6005	1.897844	2.84124	0.383242	0.947499	3
1.725897	3.336555	1.507295	1.7479	3.54761	2.859758	2.606246	1
1.2252	3.287465	2.245327	2.208732	1.496208	2.975495	2.753529	1
1.518102	2.010543	2.173446	2.299928	2.45509	2.839368	2.859943	5
1.289588	3.386302	4.211413	2.154531	1.303094	0.481756	2.964039	4
1.012439	4.384014	3.35423	2.879892	0.911968	4.236695	1.938896	2
-0.18313	2.332953	2.817455	2.991674	1.413407	2.469997	1.751645	1
-0.50824	2.851968	3.078299	3.017893	1.511157	3.204069	1.452336	1
2.015306	1.892684	3.122085	2.005002	1.28295	1.431305	2.252795	3
1.810405	2.313179	2.719985	2.289299	1.433045	1.995691	2.279748	5
-0.36417	2.441534	4.741204	2.029903	2.179041	1.560313	1.344052	4
1.612228	3.39865	3.771511	2.523235	1.798751	1.338797	1.638589	4
0.498329	2.028352	3.80679	2.242893	1.021459	2.388737	1.175935	4
-0.18434	2.373169	3.690509	2.559589	2.106675	1.890076	2.149593	4
1.521238	2.119707	2.963294	1.800389	1.566119	1.958181	0.758386	3
3.747659	1.227065	2.861703	2.434098	1.443798	2.781314	2.597393	5
-0.4823	1.90793	3.373967	2.878178	2.004723	3.40478	2.332985	1
0.899904	4.377078	2.276759	2.487403	0.184471	1.761139	0.685288	2
1.801516	3.019131	3.060307	2.431625	1.409738	1.490599	0.428911	2
0.524149	2.633798	3.796815	1.644169	0.667038	1.265146	1.836087	4
2.832446	3.170785	1.759903	1.961723	1.444286	1.823112	1.105778	3
-0.07634	2.224685	3.774898	3.031975	-0.1915	1.917331	1.714644	4
-0.00896	3.683818	3.356392	2.308612	1.307789	3.677818	0.323892	2
1.756645	2.94947	3.107809	2.888338	0.822709	3.959166	1.271949	2
2.132132	2.038671	2.938456	2.077305	1.016538	1.692268	1.867374	3
2.027801	2.090666	3.044967	2.391921	1.466157	2.999378	1.451428	2
2.365434	0.881948	2.909211	2.874983	1.970898	2.364969	2.719813	5
1.951106	1.417047	3.499015	3.274452	1.057297	1.360355	2.54604	5
1.155816	1.648827	3.136144	3.231095	1.479935	2.61277	2.369647	5
1.771195	1.978266	2.468392	2.849778	1.952468	2.637186	2.539566	5
2.175577	0.957878	1.749733	4.318935	2.408992	2.347051	3.083741	5
1.730574	1.460436	2.355927	2.801036	2.458172	2.805657	3.037723	5
1.625811	1.123879	2.555173	2.98834	1.932035	2.598875	3.107223	5
1.300338	1.27347	2.863889	2.670251	2.788495	2.009867	4.144211	5
1.058618	1.640886	3.14455	3.155436	1.597802	1.754571	2.858831	5
1.714292	1.198592	2.361832	3.655121	2.911294	2.190251	2.968629	5
1.240011	1.509991	2.984057	1.286569	2.708608	1.855332	3.967645	5
1.152672	1.764461	2.576472	2.889279	2.721701	1.695326	2.606245	5
1.255709	1.355849	2.521385	2.856854	2.597104	1.876426	3.207666	5
0.74156	1.575887	3.573962	3.438606	3.075308	2.406598	2.848083	5
1.487389	2.083264	1.877643	2.610233	2.580977	2.734694	3.221042	5
1.02402	0.666849	3.200515	3.967067	2.679366	2.374665	3.865079	5
0.904672	0.738232	2.490656	2.403095	2.3109	1.981781	2.503543	5
1.97023	1.764496	2.422681	3.936467	1.939548	2.512576	3.901476	5
2.676331	1.08356	3.41355	3.33541	0.698102	2.519931	3.287986	5
2.614462	4.775062	3.793557	-0.19917	-0.981	0.09312	1.252973	3
0.092529	2.213861	1.666891	3.141264	2.591698	3.012315	1.884515	1
0.62021	3.504931	2.630801	1.965301	1.737083	2.335864	1.035281	1
-0.10889	2.970387	2.077207	2.483217	2.67454	2.810844	2.125511	1
-0.28494	2.862408	4.948831	1.475156	1.273039	0.024325	2.188301	4
0.141229	1.826175	2.57906	3.825405	2.331338	2.178282	3.733651	5
-0.27393	1.798164	2.281096	1.096077	3.405163	2.22112	2.368599	1
1.889118	2.197416	2.662556	0.938291	1.45778	1.768633	1.850104	3

2.026809	1.43333	2.852578	2.062381	2.494402	2.510134	1.003418	3
0.4547	1.822873	1.642994	1.648994	2.465097	2.307406	2.260072	1
1.180574	1.979456	2.190599	0.638097	1.822171	1.684538	1.976499	1
-0.15376	2.113963	2.755861	2.31101	2.417009	2.151042	2.155638	1
2.937327	0.559019	3.293035	1.705683	1.755515	1.537882	2.362831	5
0.356661	2.212595	2.084012	1.942391	2.012923	1.77337	1.492639	1
1.257337	1.708001	1.806124	1.843787	2.280795	1.967791	2.486759	5
1.302175	2.292117	3.27532	2.309357	0.828285	1.952833	1.783675	4
1.714566	2.866174	2.614927	1.165569	2.346443	-0.46207	1.580056	3
2.336772	1.820066	2.107818	2.778122	2.028988	1.729201	2.644071	5
-0.531	1.905626	2.663749	4.288357	2.308736	3.089625	4.707173	5
1.955097	2.75595	1.720104	1.485425	2.439215	0.383829	2.150109	3
0.424371	2.775628	2.618747	3.105367	1.291942	1.385739	1.814535	1
2.682818	1.975018	3.091693	2.359624	2.077224	1.058987	2.189526	3
1.640291	2.201269	3.686279	2.493968	3.027828	0.383334	1.950114	5
1.962298	2.543239	1.478078	2.839681	0.880412	1.964117	2.524755	2
1.518659	3.192809	2.697412	1.905137	2.597932	-0.15954	2.23207	3
1.834275	1.687792	3.803747	2.399916	1.433644	0.562578	1.025609	4
1.540272	1.983626	2.956717	3.394021	1.800051	1.677738	0.662117	2
1.509981	2.642669	3.116794	1.549859	1.938711	1.855646	1.954819	3
2.134296	1.907773	2.690553	3.23495	1.495158	0.775124	1.619342	3
0.427512	2.987253	2.561937	2.27099	1.3845	2.114721	0.565118	1
1.466702	2.301835	2.37308	2.599048	2.254712	1.407731	1.813743	1
1.027552	1.923318	3.15668	3.298839	1.721175	1.344687	1.461926	4
2.925279	2.151205	3.252401	2.148987	1.787043	1.139834	1.406604	3
1.803615	0.897055	2.381724	4.027319	0.612286	2.102622	0.497539	2
0.501035	1.594727	3.748318	3.202126	2.717837	1.217422	2.0056	5
1.135913	2.46013	2.699918	2.040346	1.05604	2.40855	1.437545	2
1.47729	1.576555	2.766053	2.486893	3.088382	0.238345	2.288514	5
2.322109	1.8903	1.856853	3.043669	1.448824	1.854425	2.292022	5
0.943979	2.865445	2.334755	2.361299	1.84453	1.57974	1.455633	1
1.09441	2.61972	2.570202	2.266813	0.822919	1.006511	1.137528	4
1.446558	2.894173	3.720822	2.312959	2.573729	1.242164	1.410237	4
0.736881	2.07327	3.906554	3.063998	1.881051	1.369881	0.160261	4
0.665234	2.183043	2.941374	2.995214	1.14126	3.139709	0.670783	2
1.431209	2.102447	2.877089	3.272383	1.528063	1.667444	0.597345	2
0.48805	2.199462	2.791748	3.053477	1.218693	3.241743	0.81835	2
1.729035	2.60887	2.382874	2.946179	1.154216	2.539631	0.705188	2
0.923982	2.09841	3.134973	3.049035	1.577602	2.226752	0.562968	2
0.473393	1.823634	2.603832	3.244876	2.472785	2.388323	0.70335	1
0.643718	3.162341	2.628687	3.124583	0.697315	3.489079	0.444281	2
1.231598	1.489925	2.575601	2.956323	1.393692	3.056498	2.419777	5
0.885313	3.604693	2.334157	2.907145	1.783189	2.383189	0.473879	2
1.486663	2.382557	2.521454	3.405304	0.122165	2.458242	1.897779	2
1.305746	2.536706	2.503103	2.726279	1.370371	2.271897	0.760181	2
-0.12128	2.931554	2.985789	3.448854	2.373757	3.0748	0.750214	1
-0.3651	3.29011	2.870149	3.014172	0.790517	3.231845	1.216384	1
1.310901	2.905656	3.206514	2.745517	2.308938	2.328841	1.60868	1
0.8192	2.058696	3.311621	2.910875	2.063997	2.20247	1.529922	1
1.579844	2.31691	1.764519	2.700399	1.475303	3.338388	1.799588	2
1.650651	1.172353	2.25335	2.336537	1.40992	2.091142	1.840565	5
2.400323	0.610945	2.145213	1.814261	2.156261	2.594137	1.989301	5
1.337072	1.787411	2.435036	2.180727	1.476423	1.703351	2.390161	5
1.334314	3.493188	3.203095	0.739232	2.752471	1.577154	1.506409	3
2.395664	1.784892	2.990832	1.597801	3.454405	1.431834	2.221238	5
2.834376	1.372208	2.467716	1.487558	2.422688	2.178153	2.292664	5
1.271013	2.190323	2.02582	1.854061	2.466391	2.423069	2.725961	1

0.129491	1.944993	3.627968	1.689957	1.382203	2.063105	2.376668	4
0.915972	2.036587	2.390177	2.812893	1.865705	1.996444	1.482858	1
-0.29183	2.254987	2.829684	2.300647	0.747438	3.259114	1.744497	1
0.234823	3.984334	2.709338	3.583035	0.06296	3.288988	0.717452	2
-0.03279	1.956234	3.73337	2.42477	1.51287	1.496175	2.24365	4
-0.22374	3.954465	4.147648	3.000342	2.095893	1.375367	0.174058	4
4.446452	3.112146	3.834213	-0.56448	2.322335	0.081094	0.815274	3
0.254195	2.219487	2.347961	1.5985	2.939996	1.619148	2.003347	1
0.722066	1.84351	3.439109	3.028911	0.858413	2.820346	2.055325	4
-0.27786	1.621398	3.810628	3.493549	1.61931	2.388291	1.959439	4
1.95763	2.243665	2.419941	1.550256	2.339185	1.526504	0.87867	3
-0.17712	3.679931	2.027275	3.438949	1.227549	4.346655	0.565953	2
-0.52016	2.644474	4.985067	2.777575	2.129857	1.603163	1.322	4
0.139093	3.077551	3.155317	1.84699	1.544916	0.909727	2.255974	4
-0.29745	3.924371	3.427086	2.814315	-0.34252	2.52275	-0.12371	2
1.197751	1.139765	2.959802	3.724448	2.00368	1.870335	3.248781	5
-0.55263	2.850451	3.603637	2.159742	1.61182	3.131141	2.21753	1
-0.09923	3.147932	3.515215	1.300025	2.023952	0.341102	1.147187	4
1.482171	0.598118	4.524763	2.495524	1.920755	1.016522	1.752847	4
0.435803	0.030049	2.99525	5.212456	3.600696	2.278578	3.051625	5
0.896986	2.123555	1.956048	3.483763	3.273525	1.450855	1.995661	1
1.727307	1.314198	3.995778	4.880579	3.018966	2.337371	2.479633	5
1.007479	1.779471	4.011855	3.485044	1.019926	0.992437	0.427342	4
1.133501	3.612282	3.371249	4.166631	0.783912	2.980189	0.390786	2
0.447813	1.584168	4.595198	4.146647	1.49147	1.118816	2.154007	4
1.36141	0.164857	4.184602	4.615451	0.680796	2.828915	2.215485	5
0.237311	1.661926	4.718851	3.915297	1.538351	2.461316	0.972878	4
1.675214	2.703634	3.664126	1.781546	1.381758	1.584137	2.177306	4
-0.0933	4.003946	3.094488	2.609247	-0.45808	3.497689	1.265117	2
1.115991	1.93992	2.449696	2.209266	1.989389	2.600533	1.638723	1
0.565087	1.267156	1.971504	1.821961	2.941994	2.362466	1.948297	5
0.2899	2.425688	2.527741	1.688038	2.859624	1.102273	1.363903	1
0.012578	2.713523	2.772004	1.695502	2.556442	1.490683	1.172728	1
0.457526	2.242863	2.640553	1.38489	2.9747	1.112302	1.723175	1
0.269487	1.856392	2.378915	2.310383	2.23644	1.466357	2.292227	5
-0.30298	2.039958	2.487779	2.484312	2.889577	1.778061	2.620527	1
-0.059	2.329745	2.661882	1.800231	2.943895	0.849261	2.4205	1
3.234036	3.172942	2.152633	1.247851	1.830191	0.741028	1.367281	3
-0.14962	3.212166	2.838131	2.052148	0.76686	2.904901	0.926416	1
1.008297	3.605593	1.552424	2.545575	1.459873	2.458237	1.063863	1
0.069645	3.442147	2.503456	2.854764	2.551114	2.401892	1.840573	1
-0.19621	2.856654	2.546963	3.078251	1.409379	1.312913	2.43579	1
0.922144	3.392091	3.413087	1.786973	0.876997	1.979531	0.815435	4
0.439565	3.695894	3.233887	3.19461	-0.65113	2.981872	0.096498	2
0.463794	3.118323	2.945531	2.132446	0.692042	1.676786	1.832364	4
2.046115	1.860467	4.503206	1.44212	0.944814	0.960159	1.702708	4
0.822082	1.752166	3.96031	3.670542	0.432142	2.094926	1.835506	4
1.384499	1.676338	3.335121	2.344334	1.708029	1.973757	3.015226	5
2.913171	2.251743	3.828942	2.862465	3.506109	2.288636	0.682411	3
2.838667	1.587802	3.139398	2.455651	1.986433	1.559845	2.010168	3
1.984939	1.226032	3.974135	2.871381	1.764569	2.52817	2.269736	5
1.882535	0.965832	3.62802	2.424984	3.088003	2.571588	1.442444	5
2.834767	2.291731	2.914424	1.828595	2.676055	2.190016	0.904297	3
2.406044	2.421871	3.677239	1.100186	2.528083	1.850513	0.909268	3
3.333304	1.738452	3.145411	1.694157	2.436078	0.861111	2.058184	3
2.809199	2.201564	3.268227	2.439596	2.217548	2.20399	0.443276	3
3.232019	2.695417	3.21763	1.39774	1.641224	1.386497	0.029767	3

2.562955	1.649742	4.191257	1.75234	3.416616	0.008248	0.947485	3
2.653311	2.213077	2.654112	1.964367	0.998636	3.271016	3.047206	5
4.088227	3.519633	1.458443	1.578193	0.700923	2.177483	3.025567	3
1.621409	1.437943	3.781382	2.457539	0.583088	1.380606	1.395895	4
2.902669	2.219219	2.532083	1.780608	1.705037	1.497211	1.210752	3
3.005859	2.263617	5.64921	1.245774	-0.42109	0.680305	0.244186	3
2.362506	1.144091	2.361297	2.453162	2.143155	1.79232	2.288028	5
1.667598	2.06235	2.689261	2.022982	2.280881	1.219565	1.887121	5
1.808149	1.78866	4.051322	1.885426	2.158398	0.817292	1.620497	3
0.687603	3.206993	4.011132	3.315963	-0.20797	1.946517	1.362868	4
2.862084	2.377349	2.555443	3.876989	0.702746	2.024126	1.165072	2
0.710643	1.936612	2.900109	3.781125	2.51583	1.740071	2.016443	5
2.057296	3.589327	2.526465	2.853584	-0.28298	1.54849	0.178033	2
1.717724	3.312208	3.219567	3.832021	0.433151	1.332947	0.398813	2
1.784393	3.483958	1.901055	2.434483	0.562683	3.044089	0.828156	2
2.365971	2.201863	3.519977	1.583483	1.150986	1.335765	0.655795	3
4.319165	1.590442	3.087611	1.69606	0.770118	0.599462	1.282893	3
3.346217	1.09885	4.812988	1.455227	0.212139	1.128825	1.865715	3
3.530807	1.567584	4.504891	1.8653	0.940612	0.82131	0.77248	3
2.891285	1.89644	4.433179	2.19465	1.006817	1.09154	0.498398	3
1.928594	2.236547	4.683135	1.988054	0.544993	1.246763	0.558855	4
2.285322	2.125545	4.559235	2.288247	0.666203	1.084367	0.472938	4
1.89005	1.011516	5.266577	2.797959	0.412246	0.880222	0.483154	4
0.418664	1.731204	5.061108	3.2518	0.698308	3.020168	0.715598	4
1.367057	2.925187	4.655244	3.350586	-0.01201	3.470676	0.821254	2
2.309585	1.804595	2.978303	3.676435	0.676995	2.935604	1.066488	2
1.8683	1.609789	3.585674	3.410347	1.090116	2.76966	0.538212	2
1.582343	1.893786	4.194117	3.161633	1.008141	2.783293	0.669849	2
2.150257	2.572329	2.223382	1.867505	2.895349	1.994313	3.149671	5
2.438346	4.148842	2.612882	3.155902	0.171949	1.607915	2.041156	2
2.643976	3.492028	2.734121	3.093574	0.779863	2.711358	1.925412	2
2.855769	2.880836	1.739848	1.828785	2.194659	2.847119	1.926847	3
3.399597	3.245786	2.023543	2.512159	1.595768	2.089901	1.455838	3
2.737046	3.037004	0.67967	3.566229	1.882432	3.613259	1.022656	2
2.989004	3.050118	1.218374	2.338301	1.72523	2.930881	2.004095	2
3.730418	3.135985	1.6401	2.053811	1.028681	2.857294	2.173015	2
2.463663	0.859639	5.162668	0.886539	1.554102	0.509594	2.314751	3
2.946992	0.400476	4.639125	3.18962	1.353431	1.528145	2.900802	5
3.042424	4.105682	3.575925	0.706032	-0.75609	-0.13641	0.230446	3
2.253494	0.88575	4.05183	1.474706	3.073917	0.406476	3.763321	5
1.675898	2.724666	4.647242	2.097785	0.23467	0.574127	0.663669	4
2.582725	2.741702	4.9941	1.059533	1.35462	1.077715	1.16564	3
1.050035	2.210001	5.021932	3.464061	1.364692	0.340931	1.686686	4
1.561219	0.545155	4.069079	1.690497	3.179686	0.016492	3.553318	5
1.265462	3.092702	3.594905	2.829159	0.750077	3.152979	1.644279	2
1.074474	3.037171	4.680648	3.823089	0.788346	0.936433	0.868559	4
1.091429	3.677598	3.423406	2.745653	1.001984	2.498806	1.66485	2
2.720772	2.102133	3.405409	2.797069	0.364539	1.46441	1.087318	3
3.226577	1.922205	2.953435	1.647369	0.593546	2.083638	0.851123	3
2.96997	2.214062	3.505646	2.499191	0.846053	0.964966	1.384221	3
3.651752	1.742185	4.164508	2.691835	0.553888	1.162542	1.663439	3
1.774319	2.621301	3.839708	2.941738	1.179815	1.918955	1.74463	4
3.320918	1.48185	3.289602	2.379944	0.653762	1.801415	1.466398	3
2.604631	2.198748	3.566384	3.787496	0.095679	1.115488	1.241199	2
3.833065	2.359699	3.028004	2.96456	0.979526	1.33778	1.312105	3
3.004658	1.994467	3.340586	3.123453	0.168374	1.183954	1.303827	3
3.557233	1.908423	3.907425	3.378859	0.393898	1.68292	1.077381	3

2.411464	2.16817	3.985166	2.790466	1.111273	1.797105	1.584131	3
1.491612	2.692824	3.446391	1.610859	2.136308	1.597012	0.673667	3
1.570925	1.579912	3.93983	2.736112	1.868873	0.511005	2.476103	5
1.74664	1.266399	2.752911	3.290547	2.346396	2.387008	4.022284	5
1.154398	2.149252	1.965355	2.992882	1.978235	3.127639	0.860784	1
0.688774	2.974488	1.694827	3.193321	2.122084	3.338055	1.028929	1
1.131356	2.409504	3.316011	4.297027	-0.46325	1.780486	0.505052	2
2.478426	4.047283	2.050103	4.226233	-0.2782	3.394542	-0.23253	2
2.083689	3.657652	2.921747	3.583169	-0.01864	2.614121	-0.05174	2
0.436883	4.775917	2.633991	3.694657	-0.60229	3.109147	0.170619	2
4.010344	4.141069	2.630313	3.047465	-0.95245	2.075121	-0.17676	2
-0.12992	3.393718	5.397824	0.854292	2.35004	0.100554	2.472098	4
1.590358	2.277793	1.279885	3.553163	2.987285	1.843279	1.926848	1
0.723736	3.291846	0.950193	3.990674	0.001098	3.059685	0.568444	2
2.182197	3.841742	3.585516	1.894945	-0.17265	1.744152	0.364155	2
3.352942	2.882326	3.866515	1.546324	0.773397	0.696639	1.2335	3
2.389582	2.199895	5.216224	1.660491	0.991467	0.364649	1.546675	4
1.212857	3.882324	5.050131	1.263146	-0.44613	1.522973	1.118274	4
0.472468	3.753695	4.995122	2.815492	0.027114	1.436463	0.056062	4
0.938919	3.164955	5.159946	0.67008	1.569086	0.043587	1.313561	4
1.298786	3.083568	1.830169	2.236362	2.000518	3.179449	1.594717	1
0.366913	2.044937	2.617066	3.038203	3.593626	1.970333	0.407605	1
-0.20437	3.531738	2.182952	2.036282	1.892294	2.801329	1.66814	1
0.28563	2.587021	2.643787	2.445734	3.925445	0.792276	0.350427	1
0.996504	3.106436	2.692807	1.902592	3.575833	1.568171	-0.2585	1
2.260508	3.017908	2.137207	1.674803	1.196457	2.873861	1.848838	2
-0.03506	3.609465	2.625299	2.368762	1.671222	3.0121	1.916716	1
0.854331	1.998625	3.000042	3.004479	3.726537	1.246325	0.524352	1
0.262891	2.741493	2.465511	3.593546	2.739738	1.530374	0.298851	1
2.270781	2.561758	2.539467	0.271137	3.602786	0.407443	0.328955	3
1.318672	2.621613	2.430487	2.202098	3.112685	0.926337	0.382588	1
1.473336	3.617204	2.026884	3.569903	3.190754	1.528451	0.754648	1
3.029609	3.419414	0.786625	4.327039	3.598551	1.734834	0.51481	1
1.792849	2.884772	2.081495	3.645535	2.82959	1.953796	0.623779	1
1.334464	2.874837	2.544076	3.153225	2.856396	1.395013	0.581578	1
1.368727	3.383985	2.730762	3.125914	3.853141	1.181855	0.793415	1
1.158614	2.646456	2.146818	2.3928	2.766568	2.142429	1.291993	1
0.880486	3.031536	2.821478	1.423451	0.733423	2.545687	1.142586	2
1.174285	2.721081	2.441791	2.207948	1.827167	2.157325	0.964771	1
0.870188	3.398999	2.271434	2.450359	2.154208	1.686502	0.205592	1
1.653495	3.671909	1.899133	3.211423	3.15191	1.735527	0.69995	1
0.682774	4.503063	1.489453	2.222444	1.302957	2.698368	1.259985	1
2.663757	3.054066	3.250958	2.184488	2.114672	1.565751	0.71493	3
-0.03549	2.627792	3.353033	2.490402	1.333189	3.449527	2.01461	1
0.176902	3.363572	1.788922	2.632445	2.046902	1.661218	1.862941	1
1.665005	3.096207	1.841999	2.76653	2.242893	2.006812	0.692106	1
0.434799	3.054804	2.514313	1.468836	0.715913	1.864575	0.778837	4
2.414456	2.360334	2.306623	2.052518	1.905444	2.084339	1.41141	3
1.548719	2.645218	2.647588	3.017119	1.307344	2.603688	1.402963	2
1.043513	2.563992	0.768526	3.563116	1.338746	4.07294	0.737781	2
2.75563	2.346252	3.231356	2.059784	2.305691	0.999648	2.35069	3
1.618229	1.55903	2.663824	2.071062	1.269606	2.184555	2.946364	5
1.927056	2.062933	2.708249	2.422282	0.670938	1.652872	0.78742	2
1.888032	1.739451	3.022219	0.731892	0.901051	1.484288	2.493283	3
1.373058	3.726288	2.173993	1.611522	1.419764	1.355206	1.332446	1
1.587711	4.845681	1.633788	2.276364	0.613327	2.951609	0.774923	2
1.107882	4.1896	0.662106	3.017648	2.54298	3.18947	1.811624	1

0.80748	4.128602	3.05368	0.753182	1.523971	2.218486	1.551826	1
1.792069	5.297029	-1.4584	4.517665	0.420555	3.75568	-0.2235	2
0.29681	2.154562	4.291881	-0.71309	3.192156	4.1492	2.884095	1
2.641933	4.808604	1.697382	3.192166	0.262471	2.395388	1.412021	2
1.862043	3.096722	2.942964	1.87311	2.463407	1.027912	2.61095	3
2.842538	4.881212	0.084864	3.656311	1.139249	2.492176	1.855205	2
-0.56891	4.003578	3.196236	3.384194	0.419863	2.238542	0.05731	2
2.881629	2.605602	4.146121	2.6831	-0.69501	1.296744	1.351407	2
1.066547	2.269026	3.176295	3.933355	0.905649	3.788415	2.012815	2
-0.27702	5.214505	3.964305	-0.42548	3.649732	1.399817	2.064414	1
3.247233	1.250798	1.933796	3.519258	1.290077	3.216229	3.350252	5
5.269156	3.595336	1.57854	4.563517	3.322321	2.0089	2.253221	3
0.402385	3.988677	1.888783	3.045963	2.415748	2.16155	2.283636	1
1.305141	3.669467	2.596833	3.356985	1.244654	1.832795	2.358681	1
1.198453	3.482618	2.315618	2.959246	0.01394	2.162574	0.785387	2
2.34431	4.126819	2.223733	1.390981	1.353677	1.772295	1.929	3
1.125582	2.252314	3.475507	3.005104	1.493761	0.598888	1.6825	4
0.540524	2.337962	4.474714	1.180037	1.137322	1.401177	1.350397	4
0.605022	2.493479	3.007678	3.416692	1.835619	3.153643	1.208213	1
1.70579	2.90063	2.763136	3.22817	2.736035	1.453346	1.065606	1
1.774505	2.964929	4.050098	0.483415	1.620176	2.106961	1.469905	3
0.37949	3.798105	3.253912	2.618223	2.893426	1.931221	1.662662	1
4.088323	4.086708	1.203542	3.401486	1.006494	1.889707	1.626608	2
1.119508	1.699654	3.586956	2.997562	1.258626	1.989826	0.903255	4
0.613604	3.759827	3.856952	2.125737	1.154775	0.907478	1.761888	4
0.907833	2.530289	2.395073	2.958473	0.736132	1.751963	0.549846	2
3.173489	3.591836	4.33018	2.384611	3.189142	3.388148	1.267663	3
0.198984	2.664969	2.869373	4.610011	0.313022	2.824204	0.625394	2
0.630253	2.095562	4.612635	3.10251	0.403171	0.586135	1.524354	4
1.172078	3.404195	2.258	4.688623	0.018005	3.749981	0.113934	2
4.007734	4.416939	3.65958	2.156696	1.668164	2.136666	-0.46751	3
1.868898	3.149336	2.275342	3.520585	0.30994	2.832434	1.386088	2
0.780472	3.074664	2.209664	2.923805	1.234535	3.130313	0.715847	2
4.848926	2.952455	3.823995	0.591641	1.587537	2.18594	-0.83412	3
1.211911	3.276599	1.160352	3.7608	0.172588	3.302692	0.900316	2
1.345695	4.407982	2.247066	3.577123	1.592001	1.564087	2.094433	1
1.224475	3.147634	2.941942	3.798999	1.535248	2.344394	1.478652	2
3.814597	3.334847	3.097241	4.383301	1.594088	3.575003	2.193627	2
2.618453	3.317255	1.941214	3.630248	2.69847	3.52205	2.648051	1
1.294275	1.56371	3.043611	2.412047	2.498057	1.647309	1.693621	5
0.789672	3.383044	3.337881	3.451955	2.680502	1.791768	-0.33461	1
5.565368	3.181652	3.711348	1.365467	3.165442	0.633596	1.577293	3
0.669129	2.118351	2.117884	2.709941	1.785749	2.353919	1.396308	1
2.122874	2.370528	4.039168	0.044906	1.404239	0.054061	1.210217	3
-0.31367	1.429249	3.608487	3.153238	3.435385	2.595252	1.562	1
2.998431	3.071495	3.935008	-0.03663	1.493068	-0.0469	0.969036	3
1.208636	1.198679	3.797957	1.94229	3.154749	1.181498	1.587801	5
1.238483	2.984314	4.102558	1.020331	1.746735	0.210602	0.596202	4
0.721211	2.570974	4.789879	1.510915	0.470652	0.495575	0.773934	4
2.182478	2.318548	4.180739	2.217635	1.400813	1.181345	1.366411	3
4.973196	1.25845	3.181555	1.930606	1.754247	0.502145	0.808431	3
1.299859	3.358898	2.963783	2.996693	1.210242	2.837687	2.661287	1
1.721604	4.747844	2.938984	3.246941	0.280358	1.577821	-0.18553	2
2.151246	2.475189	2.327683	1.99312	0.50071	1.478181	2.367488	3
-0.52803	2.946022	3.74577	3.453622	1.366665	1.530891	2.898386	4
2.520474	2.840891	4.605005	2.492233	1.505935	0.933693	1.547949	3
1.953568	4.710961	2.059415	3.21843	0.404182	2.072298	-0.48158	2

0.67322	2.059827	3.378463	3.263051	1.593942	1.411997	3.478853	5
0.482849	1.669846	5.337114	3.92286	0.857681	2.098765	1.276031	4
1.436908	3.006341	2.111445	3.63576	1.17833	2.696489	-0.03468	2
-0.16469	3.037464	2.593747	2.19126	1.150814	1.183965	2.885273	1
3.098244	2.591925	4.55368	2.771836	0.409717	4.100465	1.1617	2
0.287138	2.638836	3.863141	2.410391	1.952481	0.480413	3.121472	4
0.88184	3.625722	4.892386	0.792852	-0.38779	0.599907	0.319505	4
2.150267	2.531001	1.798742	1.734505	2.569138	1.474977	1.943503	3
0.080232	1.944229	2.89941	3.091852	1.297553	1.130481	1.479588	4
1.307558	3.242025	3.928579	0.550179	0.489302	-0.2167	1.569607	4
-0.23345	2.508582	4.13559	3.019692	1.012514	0.803014	2.163831	4
0.452287	4.095796	2.938024	2.755959	1.197267	1.736364	1.48946	1
0.333146	3.491975	2.998474	2.348185	2.863105	2.005441	1.99996	1
-0.2021	2.38004	4.119341	2.26864	1.40722	0.247862	1.495971	4
1.27648	2.71056	3.416199	3.573639	1.124956	2.475951	1.110492	2
1.071622	0.058392	4.1753	3.035761	3.147516	0.463041	3.434267	5
0.767058	2.902141	2.81539	1.046366	3.481824	2.314722	3.456745	1
3.199205	1.794078	3.094138	0.666184	2.680831	0.969656	3.012809	3
0.381606	1.855712	2.180899	2.28543	2.69681	2.129198	3.061778	5
1.199252	1.771864	3.210781	2.048203	2.117378	1.37389	2.377955	5
0.91132	1.981741	2.199601	2.419341	2.215353	2.0596	2.989397	5
1.465285	2.997421	3.137443	1.03661	2.101259	0.412757	0.556006	3
1.445957	2.331573	1.916218	2.899514	1.818489	2.843057	2.654736	1
2.190434	2.781964	2.697725	2.215768	1.935821	3.086303	2.382583	1
3.060515	2.893715	3.843192	1.274351	2.77693	1.999967	1.625444	3
3.43918	4.685975	2.511207	0.606142	2.48964	0.899216	2.126643	3
2.248858	3.078349	2.536622	1.289691	2.240462	3.084218	2.519339	1
3.37998	3.32946	4.457823	2.144631	1.21309	0.40427	0.75011	3
1.485575	0.653133	3.573337	1.804786	2.614735	1.700206	2.294768	5
-0.11639	1.697496	3.894954	1.163997	2.803677	1.62084	3.170209	5
0.265337	0.794674	3.483188	3.196532	2.270673	0.733305	3.105335	5
0.487467	2.134018	3.509739	2.158815	1.670326	3.086941	1.766996	1
1.785974	2.325783	3.97547	1.09789	1.533602	0.00662	0.661087	3
2.199662	1.043731	3.230455	1.471481	1.594108	0.196087	1.699968	3
0.432774	0.473242	3.749216	2.000787	2.260527	2.0028	2.936089	5
-0.03225	1.823518	3.460935	2.026709	2.073493	1.822957	2.199521	4
2.922641	1.912792	2.869191	1.92473	2.23171	1.463312	1.771086	3
1.95851	2.620691	3.209711	2.40885	2.167502	1.410435	0.780651	3
1.673373	3.1535	3.384783	2.665686	2.386609	3.045046	1.306632	1
2.052142	2.801713	3.616672	2.376778	2.198514	2.571284	2.109671	1
2.398755	2.656117	3.599123	2.113145	1.85368	1.955369	1.029531	3
1.600749	2.772373	2.97559	2.356207	2.179088	2.727056	2.963031	1
2.407436	2.876793	3.588069	2.349736	2.603454	1.472847	1.481762	3
1.477092	2.367975	3.279323	3.706314	2.496294	1.970748	2.027569	5
2.117032	3.129461	3.33882	2.353723	1.303854	3.213898	2.046513	2
0.862852	1.787891	4.693773	3.920364	1.536504	1.598562	0.812846	4
2.124976	2.522997	2.142115	2.017715	1.329319	1.353485	2.01721	3
2.053942	1.282666	2.60817	2.173067	1.883355	1.446771	1.932743	5
1.051968	1.351924	2.743535	2.133289	2.15663	1.277404	1.947453	5
1.711215	1.470019	2.419263	1.720749	1.882597	1.273467	2.368535	5
2.929092	1.337477	2.249875	2.137536	0.784348	1.365049	2.001452	3
1.158983	1.4628	2.915975	1.823459	1.509886	0.551248	2.793893	5
2.091268	1.750324	3.37735	1.24898	0.459163	1.414763	2.315137	3
2.076045	1.774582	2.512304	2.256736	1.866886	1.14936	2.611307	5
0.888772	2.398703	2.96251	3.053851	0.409217	0.752585	2.749108	4
1.385868	2.726663	4.786969	1.926702	-0.29151	1.447619	0.300511	4
1.573504	1.385677	2.765509	1.797339	2.803497	0.70662	1.886113	5

1.36709	2.250416	2.120969	3.156059	0.953453	0.834286	0.332707	2
1.83963	1.020248	2.261243	3.005754	1.931713	0.376005	1.855818	5
1.601561	1.25261	2.891928	2.486944	1.195034	1.634183	1.888287	5
-0.02354	3.287441	3.06615	1.477316	0.788567	1.769741	0.388055	4
1.218747	0.968508	2.310128	1.840931	3.599996	2.546517	2.353331	5
2.273433	1.691484	4.048696	2.607554	3.589263	1.255111	0.435131	3
2.088968	1.147388	2.211211	2.663832	2.513624	1.159295	2.510907	5
1.671819	1.377036	3.442522	3.119088	2.535569	0.140997	2.209565	5
0.655599	2.044898	3.029	2.970167	1.316146	2.118602	2.10233	4
1.85728	0.119835	2.531109	2.346743	1.542376	2.049295	3.632266	5
0.810013	0.519835	2.208672	2.690966	1.793883	2.252788	3.340709	5
-0.53672	1.90413	3.751989	2.896342	2.684364	0.736452	2.240227	4
0.912099	0.843401	3.863282	1.466242	1.900905	1.511621	3.068371	5
0.717642	1.816272	2.257425	3.060543	1.17801	1.755652	3.457668	5
-0.58683	3.081178	4.155074	3.340262	-0.52844	2.870146	1.44833	4
0.948814	1.329927	2.309509	2.638619	2.425392	2.050609	2.055008	5
1.405381	2.577678	4.286141	1.980834	2.432689	-0.09613	1.148452	4
1.567328	2.933253	3.513708	2.585126	1.043179	-0.13341	2.420696	4
0.654842	2.497284	3.603089	3.237035	1.70472	1.099211	1.797649	4
1.512999	0.611854	2.683634	2.169291	2.81694	1.732635	3.711279	5
1.750541	0.9083	3.874494	4.076287	-0.0004	3.253308	1.558526	2
3.554138	3.798572	3.92936	3.171349	1.134508	-0.27824	2.674967	3
1.843493	2.035074	1.975868	1.991719	2.417606	0.563503	2.469965	5
1.717436	2.392262	3.051026	2.060343	2.753362	1.495397	3.641729	5
-0.42161	4.174919	2.381554	3.388356	0.438055	3.444924	1.033751	2
1.763247	1.821026	3.455334	0.63166	3.032002	1.410237	2.909767	5
1.676444	2.552671	2.604784	0.875316	1.878914	-0.17302	2.688803	3
2.421358	0.897852	1.757336	1.945325	2.978777	0.589719	2.963783	5
1.091983	1.664438	3.094837	2.810642	2.668531	3.176472	3.365537	5
0.95825	2.322112	2.79394	1.357469	2.849933	1.464401	1.685897	1
1.686879	1.209325	2.357908	1.591704	2.3949	2.815835	3.473977	5
0.679991	0.490045	3.649338	3.121814	3.233997	1.803668	3.433076	5
0.576465	1.683357	3.679851	3.021204	2.972976	2.905107	2.180476	5
0.136986	3.709519	2.895228	2.006352	2.08725	0.559701	0.559701	4
1.992158	1.887124	2.751854	4.05701	2.787676	3.611463	1.616108	1
2.188311	1.67236	3.624552	2.120629	2.385157	-0.40732	2.290743	3
1.103505	3.213246	3.56517	1.335934	2.322979	2.073316	2.533389	1
1.172266	1.179647	3.3055	0.938081	2.639	3.333973	2.398904	5
0.946777	1.12983	3.224024	2.29541	2.958102	2.775739	1.638153	5
1.180773	2.20079	3.909757	0.784649	2.537993	1.654572	2.353767	4
-0.29837	2.708103	4.010237	3.212327	2.782713	2.544077	2.617483	1
0.999984	1.601736	3.175787	1.809006	2.008332	2.584361	2.924514	5
1.191219	1.61463	2.640179	2.097072	2.463071	2.923712	2.126753	5
0.81584	1.766591	1.901241	3.201082	3.089132	1.507481	2.906519	5
-0.52005	-0.21152	3.877069	3.117811	2.445868	1.942376	3.528102	5
0.698561	1.581811	3.206016	2.966686	2.174549	2.628289	3.4346	5
0.294319	1.243359	3.264264	2.504067	2.125595	1.764063	2.399821	5
0.552522	1.94189	3.663707	2.656138	1.682984	1.361744	2.218496	4
3.133129	-0.27546	2.912236	2.424335	1.345903	0.670599	2.517861	5
-0.24638	0.480544	3.246561	3.188092	2.920533	2.712854	0.739785	5
1.14412	0.149335	2.163497	1.884293	2.33313	3.013641	3.065498	5
1.106268	1.42373	4.030908	3.058467	1.784729	1.151248	3.145549	5
1.747898	2.289926	3.193032	2.342344	1.836667	2.341647	2.572253	5
1.249783	1.366357	1.891003	3.500575	2.873969	2.428008	3.977269	5
1.369205	1.426718	3.489257	2.725576	2.382661	1.919912	3.088201	5
2.047065	0.823226	2.345861	3.062785	1.533924	2.751118	4.369498	5
1.665568	1.758852	2.102023	2.36764	1.985868	2.164683	2.997736	5

1.235974	1.308576	2.981051	2.429463	1.928441	2.464002	2.952178	5
1.8261	1.512971	3.123711	2.497745	2.373443	2.094497	3.044643	5
2.84051	1.175393	2.586929	3.28986	2.33567	2.090763	3.742619	5
0.279548	1.895825	5.388341	2.120073	2.247174	0.868701	1.081032	4
0.99619	1.012696	1.960564	3.89922	2.166986	3.011827	2.011537	5
0.40928	3.185794	2.623647	1.940549	1.825407	1.698621	1.568015	1
0.215144	2.091797	4.171211	2.320654	3.369494	3.191467	1.64836	1
2.510542	2.017149	2.234838	3.722974	3.594265	1.538423	4.527227	5
2.191789	2.27999	0.75166	3.750002	2.901422	1.686636	2.481703	5
3.326313	2.528328	3.928792	3.121216	1.453615	1.682897	1.617506	3
1.664394	3.09397	1.78878	1.884236	2.924941	1.515557	2.520133	1
3.639972	2.296478	1.151978	4.058536	3.114612	3.240043	1.390437	2
0.449924	1.48284	0.97592	2.929817	3.717695	4.493118	4.460917	5
2.003783	1.617244	1.483172	3.165291	2.814826	1.544825	3.40854	5
1.642709	2.599317	2.743092	2.478182	1.216038	1.569686	2.955092	5
2.020474	3.031131	1.458374	1.963512	2.002057	0.863468	1.791431	3
1.588088	1.83981	1.621011	2.296312	2.576374	1.595488	3.050562	5
-0.03704	2.618573	2.73468	3.523944	1.728803	3.092423	1.011341	1
1.507168	2.289949	2.907394	2.494175	0.342619	2.955806	2.238876	2
0.65722	1.948092	3.384632	3.591149	1.093019	1.948022	2.226399	4
0.906972	2.341611	3.474023	3.766265	1.319244	2.054854	0.849818	2
1.099988	2.333797	3.238913	2.937232	0.493977	1.700426	1.402933	4
1.280015	2.513557	2.225763	1.868445	1.739776	1.374607	1.782267	1
-0.11139	2.095035	2.947376	3.142256	3.032293	1.639643	0.480099	1
1.551912	1.887402	2.344782	3.686308	2.768613	2.681956	1.157552	1
-0.08866	3.745314	2.220336	3.071661	2.849671	1.862011	1.695552	1
-0.14035	2.459132	2.989569	2.991661	2.682929	2.55258	1.272708	1
0.863472	1.802155	2.07836	2.793182	3.686965	2.535373	3.223135	5
1.939982	1.028043	2.661535	3.283031	2.849478	1.791159	2.935827	5
0.202088	2.772472	3.860564	2.418321	1.221271	2.686473	3.045804	4
1.536423	3.963189	3.539271	3.213546	2.934773	0.878772	1.750439	1
0.716654	3.769872	2.337558	3.21909	3.257411	3.09655	1.200753	1
0.002053	2.579149	1.708619	1.826842	2.902119	2.69227	1.846354	1
1.878384	1.367029	2.529927	2.219242	3.170144	1.372932	2.595525	5
1.113165	4.083788	2.197008	2.347144	2.640993	3.571014	1.565829	1
-0.55411	3.677333	2.607452	2.868568	1.895632	1.742989	1.350166	1
0.728818	5.38512	1.999552	1.995521	1.688124	1.794364	1.567654	1
2.000957	2.156025	2.529648	2.916682	2.007876	1.796838	1.507756	3
1.464876	4.794305	2.399407	2.661065	2.77422	2.379961	2.595127	1
1.639087	2.011963	1.930406	2.611254	3.568298	2.516589	2.812242	5
1.446411	3.638014	2.57226	2.162072	2.791145	2.57307	1.488721	1
1.167265	2.626558	2.203502	2.296486	1.842762	2.90644	1.855448	1
2.792874	1.787912	2.792314	2.672087	2.421138	2.292698	1.817582	3
1.661313	1.518343	3.330552	2.900845	1.686547	3.210328	0.977498	2
1.818558	1.962483	3.011182	2.984796	2.464553	2.212576	2.227476	5
2.368946	1.765466	2.807844	3.021599	1.988137	2.766653	1.264226	2
1.519612	1.349884	2.745033	2.585421	1.414565	2.762992	0.696093	2
2.525452	1.940259	3.229155	2.42824	1.51069	1.699371	0.8384	3
1.470027	2.213906	2.174315	2.641719	2.62319	2.124632	1.701656	1
1.40074	1.014476	4.221012	2.082268	2.397258	1.566852	2.246523	5
3.364591	1.251376	3.290845	2.500423	2.222562	2.499598	1.64981	3
2.129269	2.710131	2.313439	3.013249	3.038706	2.468915	1.469671	1
3.640786	2.112478	2.740796	2.354109	1.865754	1.397937	0.737311	3
1.421128	1.717524	3.14217	3.412806	1.643833	2.767619	1.014461	2
3.634259	3.829661	2.455371	1.544377	1.340034	3.256891	2.485461	3
2.697317	2.840325	2.636191	2.10339	1.209549	2.466469	1.862657	3
2.125605	1.718318	2.887255	2.48321	2.397532	1.066204	2.379777	5

3.792892	2.650793	2.764114	1.400925	1.851319	2.681576	2.986922	3
2.072001	3.045846	3.962105	2.177186	2.573999	0.25015	0.832666	3
3.47285	2.593043	2.890262	3.791422	0.974418	0.107865	1.905316	3
3.442853	2.49001	3.917911	2.182262	1.331236	0.624292	0.56678	3
2.219969	2.735774	2.653031	1.323758	1.209602	2.197175	1.866327	3
3.544702	2.323891	2.279193	1.803041	1.570909	2.167078	2.118647	3
3.420414	1.926201	3.185597	0.632802	0.632656	1.50262	1.384866	3
3.209916	2.705199	3.627112	1.981629	2.297275	1.142996	1.049544	3
3.048556	2.6651	3.121058	2.043578	1.409733	1.083988	0.612292	3
2.713898	2.765805	2.622923	3.012792	2.375676	2.068843	1.575362	3
2.443942	2.666966	2.428546	0.891082	0.771637	2.603498	1.684131	3
2.905297	3.397697	2.938849	1.225181	1.163792	1.690736	1.431206	3
3.593219	4.593676	2.85064	2.031216	0.486013	2.463427	1.85159	2
2.102827	2.396113	2.513477	3.23259	0.053848	0.624753	1.872851	2
1.064304	1.898978	2.016754	3.140289	0.964322	2.533744	1.1192	2
2.444071	2.783835	4.013843	2.538264	-0.99133	1.913701	1.514094	2
0.597051	2.841435	3.260321	2.331223	2.770425	1.762876	1.657292	1
1.277791	1.224479	4.027602	2.223094	1.528438	1.553553	1.985067	4
2.544969	1.139785	3.265251	2.26823	-0.46458	2.591822	0.882637	2
1.825547	1.669443	3.223452	3.179786	-0.42529	1.875906	1.452051	2
2.962217	3.600508	5.143498	1.353762	0.671814	0.235175	0.560646	3
1.456116	2.008452	4.33278	2.854759	0.605656	0.405156	2.166573	4
0.626556	3.945301	3.324774	2.371494	-0.03127	1.118954	0.265501	4
-0.31383	2.113856	2.59672	1.908942	1.667484	2.524643	2.408832	1
1.228335	1.387955	5.154633	1.452413	1.155377	0.786883	1.862063	4
1.25387	2.254079	4.47892	1.999785	1.359129	0.771985	2.204713	4
2.077432	1.663845	5.072246	2.79507	-0.51169	0.56814	0.610627	4
0.599443	1.280542	4.815207	2.746904	1.803925	0.649366	2.415114	4
0.598819	1.589002	4.750287	3.058779	1.458149	1.533219	1.688224	4
0.931227	2.847927	4.160636	2.13367	0.982232	1.452196	1.729529	4
0.316014	1.483445	5.063682	1.620782	1.363688	0.744981	2.184789	4
1.805851	0.751263	4.905275	2.126935	0.927103	0.411213	1.870546	4
1.817658	1.874295	3.402797	2.738788	0.632739	3.089684	0.283125	2
2.080507	1.479588	3.698097	2.018675	1.102444	3.123037	0.499457	2
2.155577	1.737956	3.83843	2.286946	1.14978	2.696318	0.43201	2
1.608477	1.801606	3.90294	2.616016	0.307342	3.013917	0.867098	2
2.281242	0.685045	2.986646	2.985925	1.546753	3.087632	0.720522	2
2.214117	0.65798	3.986178	2.320973	1.01724	3.012481	0.405324	2
0.781439	0.915361	4.091384	2.741706	1.203266	2.853794	0.715125	4
1.727043	2.106237	3.150811	3.001749	0.701208	2.788492	0.486409	2
1.728331	1.779813	3.270322	2.618096	0.884794	3.065053	0.971797	2
1.749562	1.403262	3.229064	3.006373	1.472604	2.900566	0.640564	2
0.679291	1.950655	4.747832	2.835375	0.382722	2.499583	0.591783	4
1.147152	1.826271	4.035526	2.320126	-0.02238	3.159645	0.731292	2
1.941818	2.082537	2.989712	2.260192	-0.00818	2.787371	1.151937	2
1.249031	1.527114	4.299129	2.535885	-0.5818	2.879486	0.525447	2
1.19344	1.077144	4.43854	2.214834	1.010501	3.005332	0.498575	4
1.38946	2.086965	3.925157	2.506738	0.61587	2.518739	0.56424	4
1.877671	2.377552	3.591046	2.443115	-0.60871	2.798473	0.648804	2
2.957277	2.94879	2.629078	2.712291	2.437214	2.745738	2.306572	3
2.992108	2.599115	2.293851	3.124804	2.015908	3.133204	2.268303	2
3.921003	3.011791	1.363058	2.752717	2.051352	2.988232	2.550854	2
1.728135	3.382881	2.602387	3.073562	1.122538	2.970503	0.769473	2
0.89866	3.708311	3.08077	2.230172	1.323137	1.21315	0.775188	4
0.108157	3.703654	4.751098	2.833147	1.226326	1.494066	0.657168	4
0.949288	3.908633	4.21671	2.584499	1.12431	2.357137	1.324043	4
1.685074	3.335918	4.22883	2.169423	1.972558	2.209607	1.534274	4

2.355394	2.924333	3.329398	1.851904	1.452708	1.768292	1.320825	3
1.392201	2.646019	3.262224	3.078521	1.380314	2.171287	1.551109	2
1.872292	2.807496	3.365211	2.991789	1.430271	1.604211	1.31471	2
4.06007	1.952389	4.366534	2.666384	0.004945	2.058869	1.022499	3
2.515136	3.582175	3.164015	2.511792	0.303662	2.456513	1.106662	2
2.353872	2.84456	3.277328	3.030188	0.686356	1.732787	1.083689	2
3.092874	2.935414	3.090189	3.004494	0.234085	1.989451	0.991129	2
2.985002	3.046288	3.149261	2.913923	0.221522	2.037312	0.911563	2
2.991006	3.1423	3.128822	2.930944	0.71372	1.97819	0.9461	2
2.498692	3.030364	3.712698	3.228355	0.051874	2.453515	0.868749	2
2.932435	3.234334	3.266269	3.874878	1.708321	0.299856	2.488879	3
3.732834	3.443928	4.925664	2.483556	-0.84478	1.269878	-0.24187	2
2.764755	1.765644	4.289369	5.662817	1.16513	2.814028	1.745695	2
3.089919	3.356786	4.52097	0.52877	1.356926	0.340221	0.917349	3
2.476432	2.565019	4.555364	2.821781	-0.36831	1.590714	0.438113	2
2.910139	4.087892	3.980479	1.786325	-0.66089	0.481637	0.032882	3
3.135612	4.630961	3.628399	3.051233	-1.17422	0.352569	0.381981	2
2.872695	3.720954	4.51504	3.199279	-0.98896	1.381106	0.015064	2
2.089671	2.377447	6.417695	0.828802	1.741449	0.852393	0.681979	4
1.288354	2.713286	5.504821	0.619534	1.160781	1.224874	0.05934	4
2.068221	2.422813	6.131995	0.715511	2.167848	1.25567	0.822885	4
1.624061	3.815175	6.237579	2.066145	-1.00305	2.208537	0.277069	4
2.445324	3.714635	5.837543	0.946298	-0.31739	1.034344	0.393447	4
1.445021	2.958948	2.395126	3.098661	2.870223	0.928077	0.090669	1
2.375642	2.68096	2.183977	3.157854	2.235614	1.306861	0.393268	3
1.505374	2.723895	3.330147	2.767737	3.015288	0.696092	0.640706	3
1.567687	2.888448	2.295104	3.176463	3.193394	1.005992	0.495985	1
2.912557	2.523757	1.949625	3.107942	2.987511	1.188252	0.531214	3
1.851181	3.069879	2.227234	3.15	2.626483	1.087311	0.423944	1
2.377584	2.854885	1.961183	2.925096	3.283892	1.388586	1.156093	3
1.467044	2.694963	3.178889	2.979329	2.500077	1.289893	1.388323	1
1.415615	2.35197	2.874528	3.014931	2.432711	1.772328	0.987868	1
2.030281	2.431548	2.221421	3.091684	2.478228	1.352556	0.871416	3
2.553599	4.262361	1.874516	2.474586	2.511507	2.529192	0.508671	2
3.185728	3.696322	1.49651	3.046902	2.934443	2.880074	0.135186	2
2.850695	3.55922	2.511403	2.548477	2.859269	2.493715	0.459517	3
3.577836	3.580969	1.643502	2.802134	2.574489	1.719936	0.253408	3
2.958074	3.415299	2.264899	2.677293	2.42812	2.083265	0.589096	3
3.087259	3.61867	2.115313	3.326557	3.243235	1.954775	0.300382	3
2.751739	3.585996	2.497658	3.382737	2.407784	1.805826	0.848883	2
3.0043	3.158151	2.642835	2.811435	3.556004	2.073591	0.192526	3
2.70127	3.29477	2.061836	3.531687	2.321305	2.139039	0.260408	2
2.866981	3.461092	2.503888	3.076605	2.320136	2.322889	0.164261	2
3.02909	3.796378	1.622972	3.100696	2.428454	2.112373	0.302758	2
1.832561	3.035723	2.92606	3.152572	1.969182	1.66836	2.027277	1
0.391172	3.724756	1.959737	2.563242	2.126821	1.498965	0.513307	1
0.537508	3.205037	1.664459	3.411925	1.951163	2.136093	1.881294	1
-0.03323	3.496502	1.921167	2.296864	2.092613	1.947697	1.894757	1
-0.28869	3.535061	3.032781	1.687279	2.179816	1.986136	3.189025	1
0.043266	3.098997	2.935675	2.583162	0.79795	1.274482	1.279583	4
0.111472	3.729742	3.438625	3.315709	1.270037	1.351169	0.323621	4
1.824843	2.878876	2.439134	3.205687	2.056859	1.26008	0.245724	2
-0.34372	3.260611	1.669527	2.611259	2.802661	1.975953	1.996848	1
0.929042	4.229001	0.958476	1.837791	2.345441	0.85991	0.266006	1
0.835028	4.094564	1.624835	3.745215	0.676649	1.596787	0.633265	2
0.518017	3.482631	0.026971	3.232487	2.585949	1.714216	1.247258	1
2.142077	2.763266	1.717985	2.132657	1.981876	1.682524	1.359786	3

1.163136	2.278781	2.040656	1.66038	2.28934	2.245927	2.48422	1
1.773945	1.815762	2.296841	2.241036	2.003111	2.440107	2.329185	5
0.370864	1.828904	3.135938	1.977168	1.213476	1.233708	2.011518	4
1.286832	2.260544	3.247904	2.244789	1.087078	2.409808	1.666524	4
0.665569	2.919365	2.218953	2.267884	1.69468	1.892542	1.390264	1
0.499638	1.950232	2.077153	2.111414	2.362764	2.243769	2.65479	1
1.813017	3.779611	3.381505	1.889955	2.499938	1.561516	0.468737	3
0.397136	4.680782	2.396155	3.188569	3.35778	3.188256	1.316963	1
1.019573	2.844814	3.271878	1.693419	1.576868	2.980728	1.484369	1
-0.12102	2.640397	1.937596	2.509998	2.081944	2.465172	1.921706	1
0.52094	4.365047	0.079631	3.39627	0.649761	3.180026	0.097283	2
2.731117	3.182713	2.077638	3.00734	2.583772	1.26684	0.103849	3
1.771354	3.13086	2.349316	1.061821	2.445899	2.343069	1.002997	1
2.059941	3.055221	2.663597	1.88279	2.215695	1.325664	0.702866	3
1.303168	2.959174	2.820694	2.397158	2.033969	1.579769	2.122712	1
2.429935	2.785714	1.96915	1.688699	2.165227	2.253247	1.325774	3
0.891107	2.804571	3.191638	2.048713	1.508145	1.19412	1.88979	4
1.907596	2.544843	1.657253	2.422589	1.154796	1.183471	1.661215	3
2.385735	3.027558	1.489701	1.884331	0.99354	1.180347	1.127258	3
1.251581	3.68027	2.711777	2.1435	1.619374	1.509578	0.333364	2
0.798065	3.178204	1.337118	2.323722	1.813707	1.180386	0.886322	1
2.252769	3.452674	2.544877	4.622918	-0.07422	2.354946	0.115854	2
0.583991	1.996347	3.522147	2.550794	2.507082	2.036728	2.388671	5
-0.13509	2.898338	2.444281	2.521597	1.825635	2.888208	1.921385	1
-0.36838	2.995744	3.441612	2.97643	1.572292	2.68975	1.238128	1
-0.30352	3.100945	3.418419	1.915066	2.18415	2.148555	2.157188	1
1.244294	3.111563	2.930995	1.059978	0.847236	1.804209	0.909519	4
-0.14236	1.646401	3.496471	1.485099	1.650087	0.930843	2.037234	4
1.19828	2.207907	2.349218	1.552053	1.722359	1.499779	1.598663	1
0.38149	3.928541	1.372957	2.687336	1.838206	2.154214	0.524778	1
2.481611	3.481827	2.197603	2.130881	1.476809	2.260437	1.234254	2
0.481608	2.39286	2.337152	1.8301	3.06498	1.393734	2.654131	1
2.037414	2.085096	1.496653	2.455538	3.879859	1.623686	2.888888	5
1.550216	3.153218	1.742108	1.904519	1.712383	1.807038	1.351736	1
1.648021	2.673175	1.638725	3.046737	1.692765	2.351428	1.857887	1
1.374126	2.435089	2.234815	2.18588	1.898093	2.19479	0.889646	1
1.019342	2.647679	2.648263	2.498198	1.115062	0.804325	2.647109	4
2.736435	0.551078	3.752571	1.417281	1.549031	0.691697	3.033024	5
1.076616	4.06708	2.069281	1.842046	1.935288	1.900541	2.868004	1
1.33195	2.484582	2.416758	2.379112	1.760003	3.692732	0.736447	2
2.77427	3.355737	2.304729	1.78513	0.741504	2.762615	1.853789	2
1.110734	3.632882	3.21394	1.776796	1.612268	0.850391	0.641557	4
2.389185	2.881695	1.795131	3.20699	0.41942	3.494308	1.27316	2
0.730482	2.662928	2.413819	2.880268	1.47977	2.413753	1.470869	1
1.544426	3.943903	2.727814	1.735903	0.3283	1.153388	0.127138	2
1.279774	1.859157	2.630356	2.828011	0.364033	1.515973	1.979112	4
1.793325	3.012943	1.797364	3.337012	0.706964	2.779247	1.325387	2
2.238936	3.999729	2.426756	1.92557	2.32772	3.174616	1.094697	2
1.328915	2.584895	2.436472	2.695512	0.404388	2.423566	0.966932	2
0.949881	2.271697	2.870003	1.331377	3.139382	1.581926	2.831327	5
1.447089	4.561358	2.758321	1.890039	1.155236	2.090646	-0.24765	2
1.559906	3.743831	2.957692	2.926744	0.70788	3.029807	1.492514	2
0.037952	2.623521	2.977699	2.60586	1.7889	1.516554	1.752384	1
0.544136	2.470642	3.054143	1.796674	2.630448	1.995703	1.006744	1
1.103825	2.393463	3.065722	1.774394	2.428612	1.982995	0.895501	1
1.399663	2.370678	3.102827	1.824285	1.496074	2.043118	0.86195	4
0.897121	2.54747	3.141174	1.854219	1.595786	2.011652	0.804589	4

1.201974	2.640957	2.332992	2.627714	2.533396	2.930975	1.314934	1
1.363306	2.722	2.897964	1.712665	1.587274	2.16176	0.545037	2
0.723609	3.782392	3.074652	2.64536	2.840634	1.366008	0.711355	1
0.719305	3.75657	2.379346	3.293745	1.618362	3.079174	0.353328	2
0.328069	3.287281	2.131284	2.691661	1.991577	1.488309	0.506056	1
-0.64046	2.981621	2.625653	2.987986	1.415446	2.682281	2.372283	1
0.787829	3.43195	2.429392	3.333081	1.33786	2.979558	0.795472	2
0.227007	3.521006	2.724771	3.137629	0.03393	2.165901	0.06169	2
-0.40163	3.609939	2.626096	3.870232	-0.36079	2.958831	0.209338	2
1.965187	3.49462	2.311837	3.878262	-0.49392	1.852627	-0.02262	2
1.791554	2.700887	2.96369	2.574842	1.361732	1.22905	0.905313	3
0.592842	2.498902	3.325384	1.998149	2.970382	1.484991	2.433574	1
0.93449	3.04107	3.092865	3.005954	3.044192	1.088331	1.023012	1
0.003281	2.687613	3.929499	2.543304	2.892851	2.191037	3.148313	1
1.068601	3.440496	2.803361	2.066853	2.684096	1.392016	0.972695	1
0.253151	3.366974	3.134181	2.849601	1.98879	1.665742	1.794241	1
0.568625	2.599822	3.489269	2.403426	2.2514	1.457632	1.842686	4
0.00812	2.891183	3.527231	2.837727	2.056235	2.082804	1.521558	1
0.032748	2.470632	2.393383	2.203077	2.552633	2.522461	3.323862	1
0.542252	2.924785	2.188542	1.648248	1.714741	2.188392	2.210163	1
0.489436	2.782794	2.799251	2.348694	2.562243	2.045669	2.597358	1
0.598497	3.537035	2.270759	1.885296	2.640754	1.931446	1.9822	1
2.684479	4.627392	1.323444	2.104489	3.085864	1.524276	4.186668	1
0.655399	2.42486	2.702211	1.692073	2.686051	2.115035	1.992235	1
1.00012	2.63573	1.946578	1.927783	2.474008	2.149825	2.785688	1
0.803679	2.576829	1.90842	2.733659	2.142713	2.062206	2.425543	1
1.362799	2.747179	1.705736	1.951721	2.795911	2.423492	1.966459	1
0.963135	3.36129	1.576244	2.275032	2.391988	1.914535	2.548146	1
0.957478	3.325917	2.675156	2.401962	0.999558	1.423449	0.931414	2
0.847499	2.932603	2.498088	1.810525	2.707284	2.590633	2.0517	1
1.234055	2.177802	2.697905	2.809799	2.466852	1.403281	2.495561	5
2.015017	3.586158	1.209095	0.797506	1.692396	1.815927	1.146375	3
1.555804	2.938869	1.394756	0.825921	2.281687	1.885865	1.503032	1
1.919184	2.652597	2.006072	1.579702	1.47809	1.927411	1.892786	3
1.164025	3.354408	1.683151	2.741454	2.56621	1.453452	2.74602	1
0.86959	2.681597	1.65861	2.77981	2.819379	1.416855	2.724348	1
1.043517	2.337804	1.855299	2.055885	2.697255	1.476669	2.311822	1
2.083676	4.361556	1.724352	2.17223	2.581234	2.50454	1.35888	1
2.615128	3.571862	0.682013	3.528703	2.241834	3.449389	2.821293	1
2.085683	3.602037	1.088369	2.923386	2.205792	2.28507	2.979874	1
1.898764	3.276854	1.77007	2.506758	1.517037	2.607894	1.089812	2
2.5278	2.059308	1.713481	3.124673	1.225085	3.026174	3.025545	5
2.864402	3.013686	1.637174	1.573196	2.441859	1.623372	1.120725	3
2.072019	3.282316	0.870472	2.358488	2.208217	2.802844	1.730093	1
1.63954	3.096221	2.814322	2.561726	2.063223	1.377709	1.451547	1
2.309299	3.454196	1.661915	2.559652	1.830277	1.966368	0.014157	2
0.72982	2.395892	2.585869	2.750007	2.132678	2.026769	1.971763	1
2.549466	3.574283	2.038015	3.583879	1.986217	2.118853	0.140961	2
2.083922	3.433225	1.320953	2.441424	2.589508	2.780382	1.209729	1
1.293829	3.273937	1.462928	2.817106	1.721652	3.104604	2.554968	1
1.195288	3.769418	1.210908	2.98681	1.044027	2.749903	0.60132	2
2.061813	2.704437	2.316068	2.554463	2.553281	3.014762	2.00189	1
2.468648	2.98751	2.060243	3.21991	1.330698	2.781815	2.311667	2
0.936901	2.780699	1.501068	3.119347	1.893182	1.345022	1.445776	1
2.096261	3.729782	2.528279	2.942293	2.272058	1.668373	0.184038	2
-0.06866	2.323305	2.466225	3.008179	2.310103	1.806849	1.758138	1
2.600323	1.57889	2.767321	2.701491	1.678983	0.431804	0.746914	3

1.904414	1.941858	2.790823	1.733361	1.862784	0.627279	1.648438	3
1.596553	2.69657	2.367887	2.664833	1.633339	1.978123	0.121749	2
1.07667	1.205244	2.672278	1.959053	2.384767	1.783993	3.279252	5
1.595228	3.077974	2.380944	2.815531	1.774421	1.243553	0.373183	2
3.05165	1.742192	3.165878	2.403648	1.464842	0.801114	0.72373	3
2.207574	2.570317	1.919201	3.671462	-0.20097	2.181307	0.583058	2
1.136287	2.834087	3.186852	2.882391	1.934227	0.932035	1.06899	4
3.138606	1.675005	3.392111	2.846753	0.800305	1.366669	0.36267	3
3.006056	1.788769	2.430313	2.210938	2.343229	0.8086	1.471998	3
3.301842	2.534269	2.727616	1.645315	2.297743	1.398658	0.504945	3
1.045698	3.34271	2.926759	2.671772	-0.54325	3.05828	1.151877	2
1.474318	3.49987	3.358005	2.668088	-0.34163	0.727697	0.198376	2
1.418577	3.540259	1.859501	1.848117	0.758087	1.62029	1.178268	2
1.792042	3.571176	2.781245	2.623082	2.059251	2.687523	0.663873	2
2.246787	3.973687	2.288619	2.616655	0.964431	2.932953	0.383798	2
2.557149	3.009742	3.015698	2.63141	1.263235	2.701192	0.65265	2
2.406639	2.86216	2.747641	2.887785	2.069158	2.148691	0.371257	2
2.144278	3.008093	3.211825	4.019281	0.030605	2.866497	0.860084	2
2.555363	2.579017	3.075949	2.0346	2.256304	2.102979	0.446911	3
2.53739	3.435742	2.628374	3.319847	1.749244	2.053878	1.172975	2
2.645764	3.632515	2.547884	2.116629	2.961363	2.525557	0.751793	3
2.167688	3.177878	2.822987	2.693744	2.104781	2.348668	0.571723	2
1.225418	2.761464	2.284974	2.906629	1.555919	2.234763	1.344509	1
2.549378	1.883245	4.847159	-0.38613	2.328991	0.399031	0.899669	3
0.835491	3.410214	3.238864	2.174315	1.569618	3.313993	1.048845	1
0.197072	3.720005	3.210243	1.462301	1.715089	3.289458	0.349891	1
0.956348	1.634326	4.496375	2.859105	1.713968	2.541391	0.572134	4
2.710831	2.895985	4.542081	1.117162	1.602833	0.638402	1.605333	3
0.468519	2.775847	4.793864	1.572114	2.577669	2.142251	0.374559	4
0.801185	3.856247	4.476053	1.102946	1.665504	2.180561	1.051688	4
1.396774	2.38184	3.159023	2.272422	1.642917	2.218226	0.494604	2
1.029972	1.815946	3.624451	2.805185	1.766394	1.950249	0.557906	4
2.351785	2.454701	1.492669	4.377274	1.452214	3.421769	1.610619	2
2.32405	3.466859	1.816886	2.125494	2.298043	2.802006	1.772149	1
1.22715	2.873227	2.457041	2.742809	1.886899	1.460491	1.371267	1
1.281567	3.046454	2.498313	1.471574	2.914418	2.038731	1.977465	1
0.288136	1.74727	3.931425	2.686452	2.618377	2.564444	2.479821	5
2.522687	2.759939	1.745555	1.6985	2.060347	0.322064	1.304326	3
0.543637	2.544981	3.348045	1.906861	2.258307	1.031273	1.44175	4
1.620347	3.401088	2.574342	-0.41533	2.252736	0.219513	1.438078	3
1.842942	3.37822	2.328411	1.420737	2.466913	0.174455	2.317012	3
0.948361	3.600731	3.023847	2.142095	2.757594	0.861544	1.1149	1
1.868794	3.629237	1.867504	3.675692	1.405051	3.091689	0.902801	2
0.109365	3.572819	2.384525	2.616362	1.429333	1.794456	1.190442	1
2.186493	1.83317	2.188746	1.631281	2.02835	1.133724	2.584236	5
-0.19669	3.080497	2.427698	1.772721	1.871182	2.58294	1.963527	1
1.045365	3.084264	2.502615	1.233211	2.190984	1.398955	2.304011	1
0.498219	3.184056	3.006726	1.873029	1.272331	2.277158	2.527363	1
0.064184	3.279553	2.142248	1.683496	2.028901	1.967967	2.81393	1
1.294706	3.528197	2.401889	2.620905	1.628489	2.505685	1.915161	1
1.237893	4.214992	3.247795	1.255129	1.727378	1.922664	1.535637	1
0.895371	2.295853	2.195042	3.304022	1.494507	2.228977	1.607169	1
-0.15976	2.294287	3.693329	1.853443	2.346265	2.371389	1.889254	4
0.765196	3.619231	3.406026	2.56884	1.039612	2.176356	1.173186	2
0.040116	2.078193	3.350767	1.54803	2.515734	2.492502	1.961021	1
-0.01981	2.391736	2.677275	2.01822	2.822933	2.111246	2.320911	1
2.137868	3.088558	2.695161	1.66284	2.394352	1.829432	2.164855	3

2.081211	1.547291	3.061405	1.85112	1.647561	2.145304	1.606017	3
2.045868	2.033077	4.076113	2.57444	2.231006	2.358381	2.016695	5
1.758938	3.006452	2.01326	0.699399	3.04425	1.384979	0.665989	3
1.237003	2.523978	2.330382	2.049435	1.997275	1.271707	0.498445	1
0.667497	2.718609	2.958894	1.611983	2.782766	2.031715	2.059987	1
2.0786	2.254637	2.013767	2.860412	1.253703	2.580455	1.367255	2
1.137981	2.2767	2.173088	2.474196	1.543822	2.78904	1.474368	1
0.83508	2.375671	2.923106	2.319775	1.112637	1.568078	1.782344	4
1.532628	2.452578	4.199479	2.184313	1.28271	1.39555	1.30231	4
2.832667	3.229237	2.248558	5.046877	-0.14981	3.168044	0.514728	2
2.804329	3.544024	3.281753	1.443864	0.979548	1.515588	2.244697	3
4.176895	3.853278	3.442913	3.436163	-0.20598	1.787425	0.697663	2
1.447793	1.661014	4.651958	1.638069	0.705343	1.763816	0.192127	4
0.837814	3.230974	2.320599	3.009408	0.461031	2.905844	1.343623	2
1.802944	1.716569	3.558995	2.552908	0.4513	2.238213	-0.50813	2
0.957177	1.475594	3.511604	2.462799	0.950496	1.55846	1.053852	4
1.767879	2.111048	3.558412	1.886744	-0.32273	1.971333	-0.18521	2
0.567263	0.795808	2.30941	2.196065	2.747347	1.982559	2.3133	5
1.47234	2.608456	2.826792	2.398996	1.022706	2.533647	0.7236	2
1.025226	2.719732	2.423171	2.797212	2.343007	2.681939	1.803731	1
1.665459	0.517428	3.510286	1.925527	2.679155	2.339655	2.32634	5
0.626203	3.278759	4.570286	1.802226	1.454045	0.984405	1.873493	4
0.989795	3.025333	2.064807	1.322011	2.195479	2.639946	1.743527	1
0.748755	2.27195	2.717904	3.103542	2.114782	3.677446	1.694106	1
-0.54808	3.454881	2.794786	0.243503	2.598806	2.136147	2.934898	1
1.73608	2.049779	2.363716	2.801236	2.019415	1.639227	1.9725	5
2.540272	3.227549	3.596597	2.319795	1.413479	2.179313	0.192601	2
4.283287	3.240125	2.663105	2.760057	0.818601	1.64212	1.574151	3
1.391141	2.810916	2.450279	2.953166	2.210613	2.323273	1.154374	1

APPENDIX 14. MARDER PANSS NEGATIVE SYMPTOMS (MPNS) HETEROGENEITY INDEX METHOD

Subject-level PANSS item scores between two assessments (e.g., Screening and Baseline) are encoded in a variance-covariance difference (VCD) vector. The VCD vector captures the intra-item variance, between-item covariance, and between-item differences of PANSS items between two assessment time points from a single subject.

Briefly, for each subject h, a variance-covariance matrix of the 30 PANSS items is defined as

$$V = \begin{bmatrix} \sigma^2_{s_1} & \cdots & \sigma_{s_{1,30}} \\ \vdots & \ddots & \vdots \\ \sigma_{s_{30,1}} & \cdots & \sigma^2_{s_{30}} \end{bmatrix},$$

where

$$\sigma^2_{s_j} = \sum_{t=1}^{2} \left(s_t^j - \bar{s^j}\right)^2,$$

is the unbiased estimator of the variance of s^j (score of PANSS item j), $j = 1,2,\ldots,30$, and

$$\sigma_{s_{i,j}} = \sum_{t=1}^{2} (s_t^i - \bar{s^i})(s_t^j - \bar{s^j}),$$

is the unbiased estimator of the covariance of s^i and s^j (scores of PANSS items i and j), and

$$\bar{s^j} = \frac{\sum_{t=1}^{2} s_t^j}{2};\ \bar{s^i} = \frac{\sum_{t=1}^{2} s_t^i}{2}.$$

Note that the denominators of $\sigma^2_{s_j}$ and $\sigma_{s_{i,j}}$ are 2 – 1 = 1, for two time points.

The unique elements of V for subject h are kept in vector u_{cov_h}, consisting of the elements of V on and below the main diagonal.

Separately, for each subject h and each timepoint t, a different matrix for the 30 PANSS items is defined as

$$D = \begin{bmatrix} d_{s_{1,1}} & \cdots & d_{s_{1,30}} \\ \vdots & \ddots & \vdots \\ d_{s_{30,1}} & \cdots & d_{s_{30,30}} \end{bmatrix},$$

where $d_{s_{i,j}} = s^i - s^j$ for scores of items i and j. Note that the diagonal elements of D are 0.

The unique elements of D for subject h at timepoint t are kept in vector $d_{t(h)}$, consisting of elements of D below the main diagonal.

Together, the VCD vector of subject h for 2 timepoints (e.g., Screening and Baseline) is defined as

$$VCDV_{h(t=1,t=2)} = [u_{cov_h} \quad d_{1(h)}, d_{2(h)}] \rightarrow \mathbb{R}^{1,1335},$$

and the VCD vector for N subjects is

$$VCDV_{(t=1,t=2)} = \begin{bmatrix} VCDV_{h_1(t=1,t=2)} \\ VCDV_{h_2(t=1,t=2)} \\ \vdots \\ VCDV_{h_N(t=1,t=2)} \end{bmatrix} \rightarrow \mathbb{R}^{N,1335}.$$

Using the PANSS-defined VCD vector, and the 7 items of the Marder PANSS Negative Symptoms factor, a new vector of 84 elements per subject is used to define a Marder Negative Heterogeneity Index (MNHI). Table 7 lists the parameters used to derive the MNHI.

Table 10: Parameters Used to Derive the Marder Negative Heterogeneity Index (MNHI)

$\sigma^2_{s_i}$	Variance of PANSS item i between Screening and Baseline for subject h
$\Delta\sigma^2_{s_{(i,j)_t}}$	$\sigma^2_{s_i} - \sigma^2_{s_j}$ at visit t for subject h
$\sigma_{s_{i,j}}$	Covariance of PANSS item i and PANSS item j between Screening and Baseline for subject h
$d_{s_{i,j}}$	Difference between PANSS item i and PANSS item j at a given timepoint for subject h
P	Set of combinations of two Marder PANSS Negative Symptoms factor items
$C(x)$	Count of x

The 7 items of the Marder PANSS Negative Symptoms factor are congruent based on the Marder factor model. Therefore, $\sigma^2_{s_i} - \sigma^2_{s_j}$ is expected to be small for all p combinations. Similarly, $\Delta\sigma^2_{s_{(i,j)_t}}$ is expected to be small for all p combinations, at t = Screening and t = Baseline. Furthermore, $C\left(\sigma_{s_{i,j}} | < 0\right)$ is expected to be small for all p combinations. Hence, the raw Marder Negative Heterogeneity Index (rMNHI) of subject h is defined as the sum of L1 norm of variance differences, count of negative covariance, L1 norm of between item differences at Screening and Baseline. It can be expressed as

$$rMNHI = \left\|\Delta\sigma^2_{sp}\right\|_1 + \sum_{p=1}^{21} C\left(\sigma_{s_p} | < 0\right) + \left\|d_{sp,t=1}\right\|_1 + \left\|d_{sp,t=2}\right\|_1.$$

The min-max scaling (min = 0, max = 223) is then applied to rMNHI to derive the MNHI for subject h.

The optimal threshold to classify MPNS enriched subjects is determined by fitting the one-factor Marder Negative model through computing confirmatory factor analysis (CFA) statistics (comparative fit index [CFI], Tucker Lewis index [TLI], and root mean square error of approximation [RMSEA]) iteratively. The first iteration draws samples from the range of MNHI from the lowest to the lowest + 0.01 point. The range expands incrementally by 0.01 point for each iteration until the upper bound of the range is above the observed maximum MNHI. The smallest upper bound MNHI corresponds to the median CFI (>0.95), TFI (>0.95), and/or RMSEA (<0.08) and is identified as 0.113. It is used to classify subjects into MPNS enriched (MNHI ≤ 0.113) or de-enriched (MNHI > 0.113) groups.

APPENDIX 15. SCHEDULE OF EVENTS

Table 2: Schedule of Assessments – Adults Subjects

	Inpatient or Outpatient	Inpatient								Inpatient or Outpatient
Study Visit Number Study Visit Week	Visit 1 Screening[a]	Visit 2 Baseline	Visit 3 Day 4	Visit 4 Week 1	Visit 5 Week 2	Visit 6 Week 3	Visit 7 Week 4	Visit 8 Week 5	Visit 9 Week 6[b] EOT or ET[c]	Visit 10 Week 7[d] Follow-up
Study Visit Day	-14 to -1	1	4	8 ± 1 day	15 ± 1 day	22 ± 1 day	29 ± 1 day	36 ± 1 day	43 ± 1 day	7 ± 2 days after last dose
Obtain informed consent	X									
CCI										
Review inclusion/exclusion criteria	X	X								
Prior/concomitant medication review	X	X	X	X	X	X	X	X	X	X
Randomize (IWRS) to treatment		X								
Dispensation of study drug[e]		X		X	X	X	X	X		
Study drug accountability				X	X	X	X	X	X	
Demography	X									
Medical history	X									
Psychiatric history	X									
Tobacco use information	X								X	
SCID-CT[f]	X									
Physical and neurological examination	X								X	X
Height	X									
Vital signs[g]	X	X	X	X	X	X	X	X	X	X
Weight (including BMI)[h]	X	X				X			X	

Table 2: Schedule of Assessments – Adults Subjects (Continued)

	Inpatient or Outpatient	Inpatient								Inpatient or Outpatient
Study Visit Number Study Visit Week	Visit 1 Screening[a]	Visit 2 Baseline	Visit 3 Day 4	Visit 4 Week 1	Visit 5 Week 2	Visit 6 Week 3	Visit 7 Week 4	Visit 8 Week 5	Visit 9 Week 6[b] EOT or ET[c]	Visit 10 Week 7[d] Follow-up
Study Visit Day	-14 to -1	1	4	8 ± 1 day	15 ± 1 day	22 ± 1 day	29 ± 1 day	36 ± 1 day	43 ± 1 day	7 ± 2 days after last dose
Waist circumference		X				X			X	
12-lead Electrocardiogram (ECG)	X	X		X					X	
Hematology, chemistry, and urinalysis[i]	X	X							X	
Blood sample for hepatitis Screening	X									
Serum follicle stimulating hormone (FSH)[j]	X									
Serum human chorionic gonadotropin (β-hCG), (females)	X									
CCI										
Urine drug screen[m]	X	X							X	
Urine β-hCG (females)[n]		X							X	X
Positive and Negative Syndrome Scale (PANSS)	X	X	X	X	X	X	X	X	X	
Clinical Global Impression – Severity (CGI-S)	X	X	X	X	X	X	X	X	X	
Brief Negative Symptom Scale (BNSS)		X	X	X	X	X	X	X	X	

Table 2: Schedule of Assessments – Adults Subjects (Continued)

	Inpatient or Outpatient	Inpatient								Inpatient or Outpatient
Study Visit Number **Study Visit Week**	**Visit 1** **Screening**[a]	**Visit 2** **Baseline**	**Visit 3** **Day 4**	**Visit 4** **Week 1**	**Visit 5** **Week 2**	**Visit 6** **Week 3**	**Visit 7** **Week 4**	**Visit 8** **Week 5**	**Visit 9** **Week 6**[b] **EOT or ET**[c]	**Visit 10** **Week 7**[d] **Follow-up**
Study Visit Day	**-14 to -1**	**1**	**4**	**8** **± 1 day**	**15** **± 1 day**	**22** **± 1 day**	**29** **± 1 day**	**36** **± 1 day**	**43** **± 1 day**	**7 ± 2 days after last dose**
Montgomery-Asberg Depression Rating Scale (MADRS)		X	X	X	X	X	X	X	X	
Columbia Suicide Severity Rating Scale (C-SSRS)	X	X	X	X	X	X	X	X	X	X
Simpson-Angus Scale (SAS)[o]		X							X	
Barnes Akathisia Rating Scale (BARS)[o]		X							X	
Abnormal Involuntary Movement Scale (AIMS)[o]		X							X	
Pittsburg Sleep Quality Index (PSQI)		X							X	
Brief Assessment of Cognition in Schizophrenia (BACS)		X							X	
University of California San Diego (UCSD) Performance-based Skills Assessment, Brief Version (UPSA-B)		X							X	
Personal and Social Performance Scale (PSP)		X							X	
EuroQol – 5 Dimensions – 5 Levels (EQ-5D-5L)		X							X	
Medication Satisfaction Questionnaire (MSQ)	X[p]								X	

Table 2: Schedule of Assessments – Adults Subjects (Continued)

	Inpatient or Outpatient	Inpatient								Inpatient or Outpatient
Study Visit Number Study Visit Week	Visit 1 Screening[a]	Visit 2 Baseline	Visit 3 Day 4	Visit 4 Week 1	Visit 5 Week 2	Visit 6 Week 3	Visit 7 Week 4	Visit 8 Week 5	Visit 9 Week 6[b] EOT or ET[c]	Visit 10 Week 7[d] Follow-up
Study Visit Day	-14 to -1	1	4	8 ± 1 day	15 ± 1 day	22 ± 1 day	29 ± 1 day	36 ± 1 day	43 ± 1 day	7 ± 2 days after last dose
Healthcare resource utilization		X								
Pretreatment/Adverse events (AE) monitoring[q]	X	X	X	X	X	X	X	X	X	X
Duplicate Subject Check[r]	X								X	

Abbreviations: AE = adverse event; β-hCG = human chorionic gonadotropin; BMI = Body Mass Index; BNNS = Brief Negative Symptom Scale; EOT = end of treatment; ET = early termination; IWRS = interactive web response system; SCID-CT = Structured Clinical Interview for DSM-5, Clinical Trials Version; UPSA-B = University of California San Diego (UCSD) Performance-based Skills Assessment.

[a] Subjects who screen fail may be re-screened up to two times after consultation with the Medical Monitor. Screening assessments may occur over multiple days. Hospitalization during Screening is optional at the Investigator's discretion. The Screening Period may be extended for up to 7 days after approval from the Medical Monitor.

[b] All procedures and assessments scheduled for Week 6 will be utilized as Baseline procedures and assessments for the open-label extension study (SEP361-303).

[c] If a subject discontinues from the study, all Early Termination (ET) procedures should be performed at the ET visit, within 48 hours of last study dose.

[d] Subjects who discontinue early from the study or complete the study and do not enter the extension study (SEP361-303) will have a safety Follow-up Visit (7 [± 2]) days after their last dose of study drug. Upon completion or early discontinuation from the study, hospitalization will be allowed for up to an additional 7 days to stabilize the subject, if necessary. Prior authorization for the hospitalization must be provided by the Medical Monitor.

[e] All study drug will be taken once daily in the evening at bedtime by mouth, with or without food.

[f] The SCID-CT will be used to support the DSM-5 diagnosis and must be administered by a qualified rater listed on Form 1572 with at least 2 years' experience with the population under study.

[g] Vital signs will include respiratory rate, oral body temperature and supine and standing measurements of blood pressure and pulse rate.

[h] BMI will be calculated and recorded in the electronic case report form (eCRF) at the clinical site at screening. For other visits, BMI will be calculated in the eCRF and during statistical analysis.

[i] Subjects must be fasted (no food or drink except water at least 8 hours prior to specified blood tests). Blood samples should be drawn in the morning followed by a snack or meal. Serum prolactin results will be blinded after the Screening visit. A list of clinical laboratory tests is provided in Section 22.

[j] Blood samples for follicle stimulating hormone (FSH) will be collected for post-menopausal women or if menopause is suspected.

[k] Requested, but not required for participation in the study.

CCI

[redacted]

[m] If a subject is issued a day pass, an unscheduled urine drug screen will be performed upon returning to the site. Urine drug screen may be ordered at other visits as deemed clinically appropriate. Positive results should be discussed with the Medical Monitor.
[n] Any positive urine β-hCG test should be confirmed by a serum β-hCG test.
[o] Unscheduled SAS, BARS and AIMS scales should be administered if a subject develops extrapyramidal symptoms (EPS) requiring treatment.
[p] Only those subjects who were currently treated with an antipsychotic medication or had been treated with antipsychotic medications within 30 days of the Screening Visit will be analyzed.
[q] Events occurring prior to first dose of study drug are programmatically identified as pretreatment events. Events occurring after first dose of study drug are programmatically identified as adverse events.
[r] Signed consent collected at screening to perform the Duplicate Subject Check. Following the last contact with a subject, the duplicate enrollment system should be updated, as appropriate (US sites only).

CCI

[redacted]

Table 3: Schedule of Assessments – Adolescent Subjects

Study Visit Number Study Visit Week	Visit 1 Screening[a]	Visit 2 Baseline	Visit 3 Day 4	Visit 4 Week 1	Visit 5 Week 2	Visit 6 Week 3	Visit 7 Week 4	Visit 8 Week 5	Visit 9 Week 6[b] EOT or ET[c]	Visit 10 Week 7[d] Follow-up
Study Visit Day	-14 to -1	1	4±1	8±2	15±2	22±2	29±2	36±2	43±2	7 ± 2 days after last dose
Study Visit Type	Inpatient or Outpatient	Inpatient[f]	Inpatient or Outpatient							
Obtain informed consent/assent	X									
CCI										
Review inclusion/exclusion criteria	X	X								
Prior/concomitant medication review	X	X	X	X	X	X	X	X	X	X
Randomize (IWRS) to treatment		X								
Dispensation of study drug[a]		X		X	X	X	X	X		
Study drug accountability				X	X	X	X	X	X	
Demography	X									
Medical history	X									
Psychiatric history	X									
K-SADS-PL[f]	X									
Physical and neurological examination	X								X	X
Tanner staging		X							X	
Menstrual cyclicity (female subjects)		X							X	
Height as measured by stadiometer	X								X	

Table 3: Schedule of Assessments – Adolescent Subjects (Continued)

Study Visit Number Study Visit Week	Visit 1 Screening[a]	Visit 2 Baseline	Visit 3 Day 4	Visit 4 Week 1	Visit 5 Week 2	Visit 6 Week 3	Visit 7 Week 4	Visit 8 Week 5	Visit 9 Week 6[b] EOT or ET[c]	Visit 10 Week 7[d] Follow-up
Study Visit Day	-14 to -1	1	4±1	8±2	15±2	22±2	29±2	36±2	43±2	7 ± 2 days after last dose
Study Visit Type	Inpatient or Outpatient	Inpatient[f]	Inpatient or Outpatient							
Vital signs[g]	X	X	X	X	X	X	X	X	X	X
Weight[h]	X	X				X			X	X
BMI[h]	X	X							X	
Waist circumference		X				X			X	
12-lead Electrocardiogram (ECG)	X	X		X					X	
Hematology, chemistry, and urinalysis[i]	X	X							X	
Hormonal Parameters: FSH, LH and estradiol (females); Testosterone (males)[j]		X							X	
Blood sample for hepatitis Screening	X									
Serum human chorionic gonadotropin (β-hCG), (females)	X									
CCI [redacted]										
Urine drug screen	X	X			X[s]		X[s]		X	
Urine β-hCG (females)[n]		X				X			X	X
Positive and Negative Syndrome Scale (PANSS)	X	X	X	X	X	X	X	X	X	

Table 3: Schedule of Assessments – Adolescent Subjects (Continued)

Study Visit Number Study Visit Week	Visit 1 Screening[a]	Visit 2 Baseline	Visit 3 Day 4	Visit 4 Week 1	Visit 5 Week 2	Visit 6 Week 3	Visit 7 Week 4	Visit 8 Week 5	Visit 9 Week 6[b] EOT or ET[c]	Visit 10 Week 7[d] Follow-up
Study Visit Day	-14 to -1	1	4±1	8±2	15±2	22±2	29±2	36±2	43±2	7 ± 2 days after last dose
Study Visit Type	Inpatient or Outpatient	Inpatient[f]	Inpatient or Outpatient							
Clinical Global Impression – Severity (CGI-S)	X	X	X	X	X	X	X	X	X	
Columbia Suicide Severity Rating Scale (C-SSRS)	X	X	X	X	X	X	X	X	X	X
Simpson-Angus Scale (SAS)[o]		X							X	
Barnes Akathisia Rating Scale (BARS)[o]		X							X	
Abnormal Involuntary Movement Scale (AIMS)[o]		X							X	
Brief Assessment of Cognition in Schizophrenia (BACS)		X							X	
Personal and Social Performance Scale (PSP)		X							X	
EuroQol – 5 Dimensions – 5 Levels (EQ-5D-5L)		X							X	
Medication Satisfaction Questionnaire (MSQ)	X[p]								X	
Healthcare resource utilization		X							X	

Table 3: Schedule of Assessments – Adolescent Subjects (Continued)

Study Visit Number Study Visit Week	Visit 1 Screening[a]	Visit 2 Baseline	Visit 3 Day 4	Visit 4 Week 1	Visit 5 Week 2	Visit 6 Week 3	Visit 7 Week 4	Visit 8 Week 5	Visit 9 Week 6[b] EOT or ET[c]	Visit 10 Week 7[d] Follow-up
Study Visit Day	-14 to -1	1	4±1	8±2	15±2	22±2	29±2	36±2	43±2	7 ± 2 days after last dose
Study Visit Type	Inpatient or Outpatient	Inpatient[f]	Inpatient or Outpatient							
Pretreatment/Adverse events (AE) monitoring[g]	X	X	X	X	X	X	X	X	X	X
Duplicate Subject Check[z]	X								X	

Abbreviations: AE = adverse event; β-hCG = human chorionic gonadotropin; BMI = Body Mass Index; BNNS = Brief Negative Symptom Scale; EOT = end of treatment; ET = early termination; FSH = Follicle stimulating hormone; IWRS = interactive web response system; K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children; LH = luteinizing hormone.

[a] Subjects who screen fail may be re-screened up to two times after consultation with the Medical Monitor. Screening assessments may occur over multiple days. Hospitalization during Screening is optional at the Investigator's discretion. The Screening Period may be extended for up to 7 days after approval from the Medical Monitor.

[b] All procedures and assessments scheduled for Week 6 will be utilized as Baseline procedures and assessments for the open-label extension study (SEP361-303).

[c] If a subject discontinues from the study, all Early Termination (ET) procedures should be performed at the ET visit, within 48 hours of last study dose.

[d] Subjects who discontinue early from the study or complete the study and do not enter the extension study (SEP361-303) will have a safety Follow-up Visit (7 [± 2]) days after their last dose of study drug. Upon completion or early discontinuation from the study, hospitalization will be allowed for up to an additional 7 days to stabilize the subject, if necessary. Prior authorization for the hospitalization must be provided by the Medical Monitor.

[e] All study drug will be taken once daily in the evening at bedtime by mouth, with or without food.

[f] The K-SADS-PL will be used to support the DSM-5 diagnosis and must be administered by a qualified rater listed on Form 1572 with at least 2 years' experience with the population under study.

[g] Vital signs will include respiratory rate, oral body temperature and supine and standing measurements of blood pressure and pulse rate.

[h] BMI will be calculated and recorded in the electronic case report form (eCRF) at the clinical site at screening. For other visits, BMI will be calculated in the eCRF and during statistical analysis.

[i] Subjects must be fasted (no food or drink except water at least 8 hours prior to specified blood tests). Blood samples should be drawn in the morning followed by a snack or meal. Serum prolactin results will be blinded after the Screening visit. A list of clinical laboratory tests is provided in Section 22.

[j] Blood samples for follicle stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (females); testosterone (males).

[k] Requested, but not required for participation in the study.

CCI

[redacted]

cci