[redacted]GW Research Ltd.

Study Code: GWAP19030

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-GROUP TRIAL TO INVESTIGATE THE SAFETY AND EFFICACY OF GWP42003-P VERSUS PLACEBO AS ADJUNCTIVE THERAPY IN PARTICIPANTS WITH SCHIZOPHRENIA EXPERIENCING INADEQUATE RESPONSE TO ONGOING ANTIPSYCHOTIC TREATMENT

Statistical Analysis Plan

08 April 2022

Approved by:

Signatory	Signature/date
[redacted] Study Statistician GW Pharmaceuticals	
[redacted], Associate Director Biostatistics GW Pharmaceuticals	
[redacted] Clinical Science Lead GW Pharmaceuticals	

CONTENTS

ABBREVIATION

ADR	-	Adverse drug reaction
AE	-	Adverse event
ALQ	-	Above limit of quantification
ALT	-	Alanine aminotransferase
ANCOVA	-	Analysis of covariance
AST	-	Aspartate aminotransferase
ATC	-	Anatomical therapeutic chemical
BACS	-	Brief Assessment of Cognition for Schizophrenia
BDRM	-	Blinded data review meeting
b.i.d.	-	Twice daily
BLQ	-	Below limit of quantification
BMI	-	Body mass index
BP	-	Blood pressure
BSA	-	Body surface area
[redacted]	[redacted]	[redacted]
CGI-I	-	Clinical Global Impression of Improvement
CGI-S	-	Clinical Global Impression of Severity
CI	-	Confidence interval
CrCl	-	Creatinine Clearance
CRF	-	Case report form
C-SSRS	-	Columbia-Suicide Severity Rating Scale
ECG	-	12-lead electrocardiogram
[redacted]	[redacted]	[redacted]
Exp-MPsQ	-	Expectation-Multidimensional Psychological Questionnaire
FAS	-	Full analysis set
GW	-	GW Research Ltd
IMP	-	Investigational medicinal product
INR	-	International normalized ratio
ITT	-	Intention to treat
LOCF	-	Last observation carried forward
LS	-	Least squares
MedDRA	-	Medical Dictionary for Regulatory Activities
MMRM	-	Mixed-effects model repeated measures
[redacted]	[redacted]	[redacted]

PANSS-G	-	Positive and Negative Symptom Scale-General
PANSS-N	-	Positive and Negative Symptom Scale-Negative
PANSS-P	-	Positive and Negative Symptom Scale-Positive
PANSS-T	-	Positive and Negative Symptom Scale total
[redacted]	[redacted]	[redacted]
PK	-	Pharmacokinetics
[redacted]	[redacted]	[redacted]
QTc	-	QT interval corrected for heart rate
SAP	-	Statistical analysis plan
SAS	-	Statistical analysis software
SCI-PANSS	-	Structured Clinical Interview Positive and Negative Symptoms Scale
SOC	-	System organ class
[redacted]	[redacted]	[redacted]
TEAE	-	Treatment-emergent adverse event
ULN	-	Upper limit of normal
US	-	United States

1. INTRODUCTION

This statistical analysis plan (SAP) documents the statistical reporting to be performed for Study GWAP19030.

This SAP has been prepared based on the following study documents:

- Clinical Protocol Global (Version 3, dated 23 Mar 2021).
- Case Report Form (CRF) GWAP19030, (Version 4.0, dated 29 June 2021).

1.1 Rationale

Schizophrenia, a complex neurodevelopmental syndrome, results from gradual alterations in brain connectivity which may begin in utero, and symptoms (distorted thinking that affects language, perception, and sense of self) present and can persist for years before psychosis emerges.

Symptoms are categorized into positive (e.g., hallucinations, delusions, and speech disturbance), negative (e.g., social withdrawal, apathy, and loss of emotional response), and cognitive domains.

Antipsychotic medications, effective in the treatment of psychosis in most cases, act via antagonism of central dopamine receptor D_2 however, numerous longitudinal studies have consistently noted significant heterogeneity and a high frequency of unfavorable outcomes in schizophrenia. Relapse rates reach 80% to 85% during the first 5 years of illness with three quarters of individuals discontinuing antipsychotic treatment in 18 months. A chronic course characterized by residual symptoms and/or relapses occurs in 34% to 57% of individuals. Treatment response is a key determinant of subsequent outcome, as it is an essential precondition for remission and recovery. Sub-optimally controlled psychotic symptoms are associated with a significant reduction in quality of life and functioning. There is therefore a substantial unmet need for new and effective therapies to treat schizophrenia.

In this study the active Investigational Medicinal Product (IMP) is GWP42003-P oral solution.

2. STUDY OBJECTIVES

2.1 Efficacy

- To evaluate the efficacy of GWP42003-P versus placebo after 12 weeks of treatment.

2.2 Safety

- To evaluate the safety and tolerability of GWP42003-P.

[redacted]

3. INVESTIGATIONAL PLAN

3.1 Study Design

This is a randomized, double-blind, placebo-controlled, parallel-group, outpatient trial. The trial will compare the efficacy and safety of 2 dose levels of GWP42003-P (150 mg twice daily [b.i.d.] and 500 mg b.i.d.) versus placebo in participants with schizophrenia who are experiencing an inadequate response to ongoing antipsychotic treatment.

The duration of the trial will be approximately 20 weeks, which includes a screening period (up to 4 weeks), a single-blind placebo run-in period (2 weeks), a double-blind treatment period (12 weeks), and a safety follow-up period (2 weeks).

After signing the informed consent form (ICF), participants will enter the screening period (Visit 1). The investigator will submit participants' eligibility forms for clinical surveillance and training (CST) review. The CST will evaluate the eligibility of participants and provide the outcome of the evaluation to the site. Participants cannot be enrolled until site personnel have received the final CST notification. Additional details for CST will be described in the study manual. At Visit 2 screened participants who continue to meet eligibility criteria will be randomized 1:1 to receive 150 mg b.i.d. or 500 mg b.i.d. dose matched volumes of placebo in a single-blind manner for the placebo run-in period. At Visit 3 (Day 1) participants who continue to meet eligibility criteria will be randomized 2:1 to receive GWP42003-P or placebo of equivalent volume to their placebo run-in allocation in a double-blind manner for the treatment period.

Randomization will be stratified by region (North America, Europe) and by sex (male, female).

A safety follow-up visit will be conducted 2 weeks after the last dose of investigational medicinal product (IMP). If a participant discontinues IMP prematurely (i.e., before the end of the treatment period) they are required to attend an end of treatment (EOT) visit (±3 days) and complete the safety follow-up visit 2 weeks after their last dose. Participants are encouraged to attend any outstanding visits per the trial schema. If a participant prematurely discontinues IMP and withdraws from the trial without continuing trial visits as per the trial schema, they are required to attend an early termination (ET) visit upon withdrawal and complete the safety follow-up visit 2 weeks after their last dose.

Approximately 55 sites are expected to participate in this trial. The number of sites may be reduced or increased depending on recruitment performance.

The study will aim to determine the efficacy, safety and tolerability of 2 dose levels of GWP42003-P compared with placebo.

3.2 Planned Sample Size

Approximately 366 participants were to be randomized following the placebo run-in period to receive 1 of 2 dose levels of GWP42003-P (150 mg b.i.d. or 500 mg b.i.d.) or dose matching volume of placebo (150 mg b.i.d. and 500 mg b.i.d.) on a 2:2:1:1 basis. The placebo groups will be pooled for the analyses of efficacy.

Assuming a common standard deviation of 11.0 and using a 2-sided hypothesis test at a 0.05 α-level, a total sample size of 366 participants (122 participants per active dose group and 61 participants per placebo group) will provide 80% power to detect a significant result assuming a true treatment difference of −4.32 points on the PANSS-T score in change from baseline to end of treatment between 500 mg b.i.d., of GWP42003-P and placebo. This allows for a 15% drop-out rate, with a minimum of 309 participants needed to complete the

trial. Depending on the drop-out rate during the trial, this number may be increased to ensure a minimum of 309 evaluable participants at Week 12.

At least 366 participants were to be randomized to receive dose matching volume of placebo during the placebo run-in period (150 mg b.i.d. and 500 mg b.i.d. in a 1:1 ratio), thereafter randomized to receive GWP42003-P (150 mg b.i.d. or 500 mg b.i.d.) or dose matching volumes of placebo at a 2:1 ratio within each dose level.

However, due to early termination of the study only 80 (22%) subjects were randomized.

3.3 Efficacy, Safety and Exploratory Endpoints

3.3.1 Efficacy Endpoints

The efficacy of GWP42003-P versus placebo after 12 weeks of treatment is jointly measured by the following efficacy endpoints which will be compared between treatment groups:

- Mean change from baseline to Week 12 in the following:
  - Structured Clinical Interview Positive and Negative Symptoms Scale (SCI-PANSS) total (PANSS-T) score (30-210)
  - PANSS positive subscale (PANSS-P) score (7-49)
  - PANSS negative subscale (PANSS-N) score (7-49)
  - PANSS general subscale (PANSS-G) score (16-112)
  - Clinical Global Impression of Severity (CGI-S) score
- Score at Week 12 in the Clinical Global Impression of Improvement (CGI-I)

3.3.2 Safety Endpoints

The safety profile of GWP42003-P compared with placebo will be assessed at each dose level by measuring:

- Changes in body weight, body mass index (BMI), and waist circumference
- Changes in vital sign measurements
- Adverse events (AEs) and adverse drug reactions (ADRs)
- [redacted]
- Clinical laboratory test results
- 12-lead electrocardiogram (ECG) parameters
- [redacted]
- Suicidality as assessed by the Columbia-Suicide Severity Rating Scale (C-SSRS)

[redacted]

[redacted]

4. BLINDED DATA REVIEW MEETING

Prior to breaking the blind, it is anticipated that at least 1 Blinded Data Review Meeting (BDRM) will take place. The objectives of the meeting will include the identification and agreement on major and critical protocol deviations.

The minutes of the BDRM will be documented separately.

5. STATISTICAL METHODS

5.1 General Considerations

In all tables, listings and figures, the treatment arms will be referred to and labelled as per Table 1.

Table 1 Study Treatments

Endpoint	Actual Treatment	Treatment Label
Efficacy and Exploratory	Pooled Placebo	Placebo
Safety	150 mg b.i.d Placebo	Placebo 300 mg
	500 mg b.i.d Placebo	Placebo 1000 mg
	Pooled Placebo	Pooled Placebo
All	150 mg b.i.d GWP42003-P	300 mg
All	500 mg b.i.d GWP42003-P	1000 mg

For safety tables where placebo is split by dose, an additional Pooled Placebo column will be included.

In all tables, listings and figures, the study visits will be referred to and labelled as per Table 2.

Table 2 Study Visits

Actual Visit	Visit Label
Visit 1: Screening	Screening
Visit 2: Placebo Run-in	Day -14
Visit 3: Day 1, baseline visit	Day 1
Visit 4: Day 15	Day 15
Visit 5: Day 29	Day 29
Visit 6: Day 57	Day 57
Visit 7 / Early Termination / End of Treatment*: Day 85	Day 85
Visit 8 Telephone call: Day 99	Safety Follow-Up

*If a participant discontinues IMP prematurely (i.e., after Visit 3 but before Visit 7) they are required to attend an End of Treatment visit and complete the safety follow-up visit 2 weeks after their last dose. The End of Treatment visit will be assigned to the nearest post-baseline visit (for which the assessment is scheduled to be performed), based on the trial day of the visit.

Unless stated otherwise, continuous variables will be summarized showing the number of non-missing values (n), mean, standard deviation, median, minimum and maximum and categorical variables will be summarized showing the number and percentage of participants falling into each category.

Minimum and maximum values will be presented to the same decimal precision as the raw data. Mean and median will be presented to 1 more decimal place than the raw data, and standard deviation to 2 more decimal places than the raw data. Percentages will be presented to 1 decimal place.

All analyses and summaries will be produced using SAS Version 9.4 or higher.

5.1.1 Missing Data

Every effort has been made to minimize missing data for this trial. All questionnaires will be completed on electronic devices. These assessments have been set up in such a way that the participant cannot proceed to the next question if they have not entered a response for the current question. The Cannabis Use Survey is the only exception, where a response to all questions is not required.

[redacted]

5.1.1.1 Handling of Missing Data for the Efficacy Endpoints

Efficacy endpoints will be based on all participants included in the analysis set using all available longitudinal data, either complete or partial. If a participant prematurely discontinues IMP during the treatment period but continues in the study, the data collected after their discontinuation of IMP will be used in the analysis of the efficacy endpoints.

For CGI-S and CGI-I, the score 0 (= not assessed) will be set to missing.

5.1.1.2 Adverse Events

Missing and/or incomplete dates/times for AEs will be imputed in a manner resulting in the earliest onset or the longest duration during the treatment period, taking into account that the start date/time should not be after the stop date/time i.e. missing start dates will be imputed as the first day of the month/first month of the year and missing stop dates will be imputed as the last day of the month/last day of the year, while ensuring that the start date/time is not after the stop date/time. Stop dates/times will not be imputed if the AE is ongoing.

The imputation method will only be used to determine treatment emergence, and imputed dates/times will not be presented in AE outputs.

A worst-case approach will be followed in the event of missing severity or causality data. If the severity is missing, 'Severe' will be imputed. If causality data is missing, 'Yes' will be imputed for the question 'Related to Study Drug?'.

5.1.1.3 Concomitant Medication

Missing concomitant medication dates will be handled in a similar fashion as described for AEs in Section 5.1.1.2.

5.1.2 Day Numbering

The first day of treatment in the treatment period (Day 1) will be taken from 'Date of first dose of IMP in Treatment Period' on the Randomization CRF.

Any days prior to Day 1 will be numbered relative to this day and calculated as:

Date − (Date of Day 1)

to give Day −1, −2, −3 etc.

Any days post Day 1 will be calculated as:

Date - (Date of Day 1) + 1

5.1.3 Definitions

5.1.3.1 Baseline

For clinic visit-based endpoints, baseline is defined as the last non-missing record or measure collected prior to the first dose of IMP in the treatment period.

5.1.3.2 Last Visit

Last visit for LOCF based analyses of efficacy endpoints assessed at clinic visits is defined as the last scheduled visit (not including the safety follow-up visit) at which a participant's last evaluation is performed.

5.1.3.3 Placebo Run-in Period

The placebo run-in period is defined as Day -14 to Day -1

5.1.3.4 Treatment Period

The treatment period is defined as Day 1 to Day 85

5.1.4 Covariates

Region strata will be defined as follows:

- North America: Participants who participate in the United States of America will be pooled together;
- Europe: All participants who participate in European countries (Poland, Serbia and Spain) will be pooled together.

Sex strata will be defined as Stratum 1: Male; Stratum 2: Female.

These covariates will be applied to the efficacy analyses and a number of exploratory analyses as outlined in Sections 5.5.2 and 5.6 respectively.

5.2 Analysis Sets and Protocol Deviations

5.2.1 Full Analysis Set

All participants who were randomized at Visit 3 and received at least 1 dose of IMP in the treatment period will be included and analyzed according to their randomized treatment arm. This analysis set will be the primary analysis set for all efficacy endpoints.

5.2.2 Safety Analysis Set

All participants who received at least one dose of IMP in the treatment period will be included and analyzed according to the treatment received. Only participants for whom it has been confirmed that they did not take any IMP in the treatment period will be excluded from this safety analysis set. This analysis set will be used to report the safety data.

5.3 Listings

All data will be listed and ordered by site, treatment, participant number and, where appropriate, chronological order of assessment. Listings will be created for each of the subsequent sections of the SAP.

Visit date need not be included on all of the listings, but day numbers will be included, where appropriate.

Other derived variables (e.g. changes from baseline values) that are calculated for analysis purposes or to aid interpretation of the data will be added to the listings as appropriate.

5.4 Demographic Data and Participant Characteristics

5.4.1 Participant Disposition

Participant disposition will be summarized using standard summary statistics for all screened participants. The number screened, number of screen failures, reasons for failures, number randomized to the placebo run-in period, number of placebo run-in failures, reasons for failure and number randomized to the treatment period, withdrawals and reasons for withdrawals will be included.

5.4.2 Analysis Sets

Participants included in the safety and full analysis sets and participants excluded together with reasons for exclusion will be summarized by absolute counts (n) and percentages (%).

5.4.3 Demographic Data and Baseline Characteristics

The following demographic data will be summarized by treatment group and overall for the full analysis sets:

- Age (years);
- Sex;
- Race;
- Ethnic origin
- Country;
- Region (United States, Europe);
- Weight at baseline (kg);
- Height at baseline (cm);
- Waist circumference (cm);
- Body mass index at baseline (kg/m^2).

Age will be calculated as:

(Date of screening – date of birth+1) ÷ 365.25.

The following baseline cannabis use data taken from the 'Cannabis Use Survey' CRF page will be summarized by treatment group and overall for the safety analysis sets:

- Age of first use (years).
- Duration since first regular use (years).
- Currently using cannabis (yes/no).
- Regularly using cannabis (yes/no).
- Most common route of current use (smoked, vaped, oral).

5.4.4 Psychiatric History

The following psychiatric history data will be listed only:

- Date of first diagnosis of schizophrenia.
- Date of most recent relapse or acute exacerbation of schizophrenia.

All recorded comorbid psychiatric disorder history will be coded using Version 24.1 of the Medical Dictionary for Regulatory Activities (MedDRA).

The number of participants with comorbid psychiatric disorder history by system organ class, and preferred term, will be summarized by absolute counts (n) and percentages (%) for the safety analysis sets. Percentages will be calculated based on the number of participants in the specific treatment arm. Two tables will be produced, one including any events classified as resolved at screening, and the other including all current conditions.

5.4.5 Medical History

All recorded relevant or significant medical history or current conditions reported other than psychiatric disorders on the 'medical history' CRF page will be coded and summarized using the same method outlined in Section 5.4.4.

5.5 Efficacy Analysis

5.5.1 General Approach

The efficacy analyses will use the FAS. No formal hypothesis test will be performed due to early termination of the study (see Section 3.2). Instead, the point estimates and 95% CI for the effects will be presented for efficacy parameters of interest. However, p-values will be presented for flagging purposes and not to be used for results interpretation.

5.5.2 Efficacy Endpoints

The efficacy of GWP42003-P versus placebo after 12 weeks of treatment is measured by the following efficacy endpoints which will be compared between treatment groups:

- Mean change from baseline to Week 12 in the following:
  - Structured Clinical Interview Positive and Negative Symptoms Scale (SCI-PANSS) total (PANSS-T) score
  - PANSS positive subscale (PANSS-P) score
  - PANSS negative subscale (PANSS-N) score
  - PANSS general subscale (PANSS-G) score
  - Clinical Global Impression of Severity (CGI-S) score
- Score at Week 12 in the Clinical Global Impression of Improvement (CGI-I)

5.5.2.1 PANSS-T

The SCI-PANSS is a medical scale used for measuring symptom severity of participants with schizophrenia or related psychotic disorder. The name refers to the 2 types of symptoms in schizophrenia, as defined by the American Psychiatric Association: positive symptoms, which refer to an excess or distortion of normal functions (e.g., hallucinations and delusions), and negative symptoms, which represent a diminution or loss of normal functions.

It is a 30-item rating instrument that assesses the positive and negative symptoms of schizophrenia as well as symptoms of general psychopathology. Individual items are rated on a 7-point scale, where 1 = absent and 7 = extreme. A PANSS-T score is derived from the sum of the 30 items and the total score ranges from 30 to 210. Missing data will be handled as specified in Section 5.1.1.1. This scale will be measured at each assessment visit, with the primary time point of interest being Day 85.

The change from baseline in PANSS-T score will be analyzed using a mixed-effects repeated measures (MMRM) model. An MMRM model will be fitted to the change in PANSS-T score at each visit and will include stratification factors (sex [male or female] and region [North America or Europe]), associated baseline, visit, treatment arm, visit by treatment arm interaction and visit by associated baseline interaction as fixed effects and

visit repeated within each participant as a repeated effect. For the analysis of the PANSS-T score; baseline PANSS-P, baseline PANSS-N and PANSS-G will be included in the model as fixed effects for the associated baseline instead of baseline PANSS-T.

The PROC MIXED procedure in SAS will be utilized to perform the analysis. An unstructured covariance matrix will be used to estimate the variance-covariance structure within participants across time points. If convergence is not obtained, or model fit is not adequate then other covariance structures will be explored in the following order until the model converges:

- Toeplitz
- First-order autoregressive
- Compound Symmetry

This order is specified according to a decreasing number of covariance parameters in the structure. The primary analysis will use the first covariance structure converging to the best fit. If a structured covariance is used, the sandwich estimator for the covariance estimation will be used by specifying the EMPIRICAL options in the PROC MIXED procedure in SAS with the aim to deal with model misspecification of the covariance matrix.

The least squares (LS) mean estimates for each treatment arm at each visit, along with the standard error and 95% confidence intervals (CIs) will be presented. In addition, the estimate of the treatment difference at each visit will be presented along with standard errors of the difference and associated 95% CIs. The primary comparison is the estimate of the difference at Day 85.

For participants who complete the trial, regardless of whether IMP is prematurely discontinued or not, the visit effect used in the analysis will correspond to the associated score at each trial visit. However, participants who withdraw from the trial are required to complete the procedures for End of Treatment at the time of withdrawal. For these participants, their End of Treatment data will be assigned to the nearest post-baseline visit (for which the assessment is scheduled to be performed), based on the trial day of the visit.

The values including change from baseline for PANSS-T will be summarized using standard summary statistics for the full analysis set.

5.5.2.2 PANSS-P

The PANSS ‘P’ Scale will be calculated as the sum of the items prefixed with an P, 7 items in total, i.e. delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution and hostility. The primary time point of interest will be Day 85.

The change from baseline in PANSS-P score will be analyzed using the same MMRM approach as specified in Section 5.5.2.1. Baseline PANSS-P will be included in the model as a fixed effect for the associated baseline.

The values including change from baseline for PANSS-P will be summarized using standard summary statistics for the full analysis set.

5.5.2.3 PANSS-N

The PANSS ‘N’ Scale will be calculated as the sum of the items prefixed with an N, 7 items in total, i.e. blunted affect, emotional withdrawal, poor rapport, passive/apathetic social

withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation and stereotyped thinking. The primary time point of interest will be Day 85.

The change from baseline in PANSS-N score will be analyzed using the same MMRM approach as specified in Section 5.5.2.1. Baseline PANSS-N will be included in the model as a fixed effect for the associated baseline.

The values including change from baseline for PANSS-N will be summarized using standard summary statistics for the full analysis set.

5.5.2.4 PANSS-G

The PANSS 'G' Scale will be calculated as the sum of the items prefixed with a G, 16 items in total, i.e. somatic concerns, 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 and active social avoidance. The primary time point of interest will be Day 85.

The change from baseline in PANSS-G score will be analyzed using the same MMRM approach as specified in Section 5.5.2.1. Baseline PANSS-G will be included in the model as a fixed effect for the associated baseline.

The values including change from baseline for PANSS-G will be summarized using standard summary statistics for the full analysis set.

5.5.2.5 CGI-S

The CGI-S is a 7-point scale used to rate the severity of participants' illness at the time of assessment. Considering total clinical experience, a participant will be assessed on severity of mental illness at the time of rating 0 = not assessed; 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; or 7 = among the most extremely ill participants. The CGI-S will be assessed at Visits 1, 2, 3, 4, 5, 6 and 7.

The numeric values of CGI-S assessments will be analyzed separately using the same MMRM approach as specified in Section 5.5.2.1. Baseline CGI-S score will be included as a covariate. Both values for the original categorical scale and the converted numerical scale at each visit including change from baseline for the CGI-S numerical scale will be summarized using standard summary statistics for the full analysis set.

5.5.2.6 CGI-I

The CGI-I is a 7-point scale that requires the clinician to assess how much the participant's illness has improved or worsened relative to a baseline state at the beginning of the intervention. This is rated as: 0 = not assessed; 1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; or 7 = very much worse. The CGI-I will be measured at Visits 4, 5, 6 and 7.

The numeric values of CGI-I assessments will be analyzed separately using the same MMRM approach as specified in Section 5.5.2.1. Baseline CGI-S will be included as a covariate. Both values for the original categorical scale and the converted numerical scale at each visit will be summarized using standard summary statistics for the full analysis set.

[redacted]

[redacted]

[redacted]

5.7.2 Adverse Events

All reported AEs will be classified by system organ class (SOC), preferred term and lower level term using Version 24.1 of MedDRA.

Summaries will be presented by treatment group as well as SOC and preferred term.

A treatment period treatment emergent AE (TEAE) is defined as an AE with a start date on or after the first dose of IMP during the treatment period (Day 1), or an AE that was present prior to the first dose of IMP during the treatment period but has increased its intensity during the treatment period.

If an AE has a partial start date and it is unclear from the partial date (or the stop date) whether the AE started prior to or post first dose of IMP then the AE will be considered treatment emergent and if it is unclear which period the event started, it will be assigned to both periods.

An AE will be considered treatment-related if the plausibility relationship to IMP is recorded on the CRF as ‘yes’. If the data on plausibility relationship to IMP is missing then the AE will be considered treatment-related.

An AE will be considered leading to permanent discontinuation of IMP if the action taken with IMP is recorded on the CRF as ‘trial medication stopped’ or the outcome is recorded on the CRF as ‘patient died’.

An AE will be considered leading to IMP dose reduction excluding permanent discontinuation if the action taken with IMP is recorded on the CRF as ‘dose reduced’, ‘dose reduced temporarily’ or ‘trial medication interrupted’.

An AE will be considered leading to temporary IMP dose reduction if the action taken with IMP is recorded on the CRF as ‘dose reduced temporarily’.

An AE will be considered leading to permanent IMP dose reduction excluding permanent discontinuation if the action taken with IMP is recorded on the CRF as ‘dose reduced’.

An AE will be considered fatal if the outcome is recorded on the CRF as ‘patient died’.

For the summary of TEAEs by maximal severity, for each participant, the worst severity recorded by preferred term, SOC and overall will be used for summary purposes. If severity is missing, the worst case (severe) will be assumed.

For summaries by resolution, AEs with an outcome of 'recovered' or 'recovered with sequelae' will be summarized as 'Resolved' and AEs with an outcome of 'continuing', 'patient died' or those with a missing outcome will be summarized as 'Not resolved'.

For the summary of TEAEs by time of first onset of AE, data will be summarized for the treatment period separately under the following categories:

- Weeks 1–2 (Day 1 to 14).
- Weeks 3–4 (Day 15 to 28).
- Weeks 5–8 (Day 29 to 56).
- Weeks 9–12 (Day 57 to 84).
- >12 weeks (> Day 84).

The time to first onset of AE in treatment period will be calculated for TEAEs as:

Start date of AE – Date of first dose of IMP in treatment period + 1

If participants have multiple occurrences of an AE then the AE will be counted once for the first occurrence only. Percentages will be based on the number of participants in the safety analysis set who have a visit or follow-up call within each time period above.

For the summary of TEAEs by time to AE resolution, data will be summarized under the following categories:

- 1 week (≤7 days).
- 2 weeks (8–14 days).
- 3 weeks (15–21 days).
- 4 weeks (22–28 days).
- >4 weeks (>28 days).
- Ongoing (for AEs not resolved).

The time to AE resolution will be calculated for TEAEs as:

Stop date of AE – Start date of AE + 1

If participants have multiple occurrences of an AE then the AE will be counted once for the occurrence with the longest time to AE resolution. However, if any of the AEs are not resolved then the AE will be counted once within the 'Ongoing' category.

The start and stop day of the AE relative to the first dose of IMP will be calculated as per Section 5.1.2. For partial dates, if it is clear from the partial date that the start/stop day was prior to the first dose of IMP, then 'pre' will be listed, similarly if it is clear that the event was post the first dose of IMP then 'post' will be listed as the start/stop day as appropriate.

Listings will include the start and stop day of the AE, a flag for treatment emergence, and limited demographic information about the participant (age, sex, race and weight at screening).

5.7.3 Clinical Laboratory Evaluation

5.7.3.1 Hematology and Chemistry

Hematology and chemistry safety parameters are measured at Visits 1, 3, 5 and 7. Summaries will be presented by treatment group for each laboratory parameter at each visit for the safety analysis set. Change from baseline and percent change from baseline to each post-baseline visit will also be presented.

If values for any of the parameters are below or above the limit of quantification of the assay (BLQ or ALQ), then they will be included in the summary tables at the BLQ or ALQ thresholds. However, for estimated creatinine clearance, results >60 are reported only as '>60'. Hence, estimated creatinine clearance (CrCl) will be calculated using the Cockcroft-Gault equation:

$$\text{CrCl (mL/min)} = [(140 - \text{age}) \times \text{weight} \times k] / \text{serum creatinine}$$

where age is measured in years, weight is measured in kg, k = 1.23 if male, k = 1.04 if female and serum creatinine is measured in µmol/L.

CrCl will be indexed to body surface area (BSA) using the following formula:

$$\text{Corrected CrCl (mL/min/1.73m}^2\text{)} = \text{CrCl (mL/min)} \times 1.73/\text{BSA}$$

where BSA is based on the Du Bois and Du Bois formula:

$$\text{weight}^{0.425} \times \text{height}^{0.725} \times 0.007184$$

where weight is measured in kg and height is measured in cm.

When available, enzymatic serum creatinine will be used. Otherwise, the Jaffe serum creatinine will be used. If height or weight is missing at the collection date, then the closest value to the sample date will be used. If there is more than one height or weight value on the same day or 2 height or weight values equally distant from the collection date, then the mean will be used.

Where laboratory samples are repeated, the baseline value is defined as the final recorded value prior to the first dose of IMP.

Shift tables for hematology and biochemistry parameters will be constructed, based upon normal ranges and GW toxicity limits (See Section 8), to determine the categorical shifts from baseline to each post-baseline visit in the treatment period. Values will be categorized as 'Normal', 'Low' or 'High' based on normal ranges and 'Toxically Low', 'Toxically Normal' or 'Toxically High' based on GW toxicity limits.

For CrCl, results will be assigned to the following grades:

- Normal: >60 ml/min/1.73 m^2
- Grade 1: 60 ml/min/1.73 m^2
- Grade 2: ≥30 and <60 ml/min/1.73 m^2
- Grade 3: ≥15 and <30 ml/min/1.73 m^2
- Grade 4: <15 ml/min/1.73 m^2

A separate shift table will be produced for CrCl based upon the above grades to determine the categorical shifts from baseline to each post-baseline visit.

Table will be produced summarizing the number of participants meeting the following criteria:

- Alanine aminotransferase (ALT) > 1×ULN at baseline
- Aspartate aminotransferase (AST) > 1×ULN at baseline
- AT > 1×ULN at baseline
- Treatment emergent ALT > 3×ULN, > 5×ULN and > 8×ULN
- Treatment emergent AST > 3×ULN, > 5×ULN and > 8×ULN
- Treatment emergent AT > 3×ULN, > 5×ULN and > 8×ULN
- Treatment emergent AT > 3×ULN and either bilirubin > 2×ULN or INR > 1.5

where AT is AST or ALT, and treatment emergent is defined as criteria not met at baseline but met at any time post-baseline. The above will be summarized overall and for sex (male, female).

All laboratory data will be listed; listings will include limited demographic information about the participant (age, sex, race and weight at baseline). Abnormal laboratory values will be listed separately. A further listing will be created for the laboratory reference ranges and toxicity limits. A listing of liver parameters (ALT, AST, bilirubin and INR) will be produced that includes the baseline result, result at the particular visit, change from baseline, upper limit of normal (ULN) value, ratio of result to baseline and ratio of result to ULN.

5.7.3.2 Serology

Serology is assessed at Visit 1 and will be listed only.

5.7.3.3 Urinalysis

Urinalysis is assessed at Visits 1, 3, 4, 6 and 7 and will be listed only.

5.7.3.4 Drug Screen

A drug screen is performed at Visits 1, 3 and 7. Results will be summarized by treatment group for each parameter and visit for the safety analysis set.

5.7.3.5 Pregnancy Test

Pregnancy test results will be summarized by treatment group and visit for the safety analysis set.

5.7.4 Vital Signs, Other Physical Findings and Other Safety Data

5.7.4.1 Vital Signs

Summaries will be presented by treatment group for each vital sign parameter at each visit for the treatment period. Change from baseline to each post-baseline visit will also be presented for the treatment period.

Based on the criteria presented in Section 8, clinically significant changes from baseline in vital signs measurements (except waist circumference) and other defined flagged values will be identified at each visit. The number of participants with a clinically significant change from baseline will be summarized for the treatment period by parameter, visit and treatment group. The number of participants with at least one post-baseline flagged vital sign parameter value will be summarized by parameter, flagged criteria and treatment group.

5.7.4.2 Electrocardiogram

An ECG will be performed at Visits 1, 3, and 7. Summaries will be presented for ventricular rate, PR interval, QRS duration, QT interval and QTcF by treatment group at each visit. Change from baseline to Day 85 will also be presented.

Based on the criteria presented in Section 8, defined flagged values will be identified at each visit. The number of participants with at least one post-baseline flagged ECG parameter value will be summarized for the treatment period by parameter, flagged criteria and treatment group.

5.7.4.3 Physical Examination

A physical examination will be performed at Visits 1, 3, and 7 and will be listed only.

Any relevant findings at screening are included as part of the participant's medical history. Any changes seen after screening that are indicative of an AE are to be recorded as such on the AE form and included as part of the AE summaries.

Additionally, body weight, BMI, waist circumference, and height (collected at Visit 1 only) are recorded as part of the physical examination. Body weight, BMI, waist circumference, and height will be summarized and listed together with the vital signs parameters.

5.7.4.4 Columbia-Suicide Severity Rating Scale (Adult's)

The C-SSRS is completed at Visits 1, 2, 3, 4, 5, 6 and 7, for all participants. Questions are asked on suicidal behavior, suicidal ideation and intensity of ideation. At the screening visit, questions are in relation to lifetime experiences and all subsequent questioning in relation to the last assessment (since last visit).

The following C-SSRS data will be summarized for the treatment period by treatment group at each visit for participants in the safety analysis sets:

- Incidence of the following suicidal ideation:
  - Wish to be dead.
  - Non-specific active suicidal thoughts.
  - Active suicidal ideation with any methods (not plan) without intent to act.
  - Active suicidal ideation with some intent to act, without specific plan.
  - Active suicidal ideation with specific plan and intent.
- Incidence of the following suicidal behavior:
  - Actual attempt.
  - Interrupted attempt.
  - Aborted attempt.
  - Preparatory acts or behavior.
  - Suicidal behavior.
  - Completed suicide.

[redacted]

5.8 Other Measures

5.8.1 Concomitant Medication

Medications will be coded using the World Health Organization Drug Dictionary, Version WHODrug-Global-B3\\202109. A medication will be considered concomitant for each period if it has a start date on or after the first dose of IMP for the corresponding period or if it was started prior to the first dose of IMP and was ongoing. If a medication has a partial or missing start/stop date and it is unclear from the date whether the medication was taken after the first dose of IMP then it will be considered concomitant.

For summaries and listings of medications the following approach will be used to determine the Anatomical Therapeutic Chemical (ATC) term to be presented:

- If coded to level 4 then the level 4 coded term will be presented.
- If coding is not performed at level 4 but level 3 coding is present then level 3 coded term will be presented.

- If coding is not performed at level 3 but level 2 coding is present then the level 2 coded term will be presented.
- If coding is not performed at level 2 but level 1 coding is present then the level 1 coded term will be presented.

Summaries of each of the following by ATC term and preferred term will be summarized by absolute counts (n) and percentages (%) for treatment period (unless stated otherwise):

- History of antipsychotic medications (placebo run-in period only);
- Concomitant antipsychotic medications; and
- Other concomitant medications.

The ATC term, preferred term, reported generic name and reported brand name will be listed.

The start day and stop day will be included in the listing according to Section 5.1.2. If the date is partial and the exact day is unknown then the text ‘pre’ or ‘post’ will replace the start or stop day if it is clear from the partial date that the medication started or stopped prior to or after the first dose of IMP.

[redacted]

6. REFERENCES

7. AMENDMENTS

Notable changes to the SAP that were completed prior to unblinding, are given below. Minor changes, clarifications and corrections are not listed.

Date	Section	Description of Change

8. ATTACHMENTS AND APPENDICES

Appendix 1 Ranges for Clinically Significant Changes and Other Defined Flagged Values in Vital Signs

The range of values that will be used to identify clinically significant changes in vital signs parameters (See Section 5.7.4.1) are presented in Table 4.

Table 4 Ranges for Clinically Significant Changes in Vital Signs

Vital Sign	Range
Sitting Systolic BP	Change: < -20, > 20
Sitting Diastolic BP	Change: < -10, > 10
Heart Rate	Change: < -20, > 20
Weight	Percent Change: ≤ -7, ≥ 7

Defined flagged values that will be used to identify low or high vital signs parameters (See Section 5.7.4.1) are presented in Table 5.

Table 5 Other Defined Flagged Values for Vital Signs

Vital Sign	Flag
Sitting Systolic BP	< 90, > 140, > 160
Sitting Diastolic BP	< 50, > 90, > 100
Heart Rate	< 60, > 100
Temperature	> 38, < 36
Respiratory Rate	< 12, > 20

Appendix 2 Defined Flagged Values in ECG Parameters

Defined flagged values that will be used to identify low or high ECG parameters (See Section 5.7.4.2) are presented in Table 6.

Table 6 Defined Flagged Values for ECG Parameters

ECG Parameter	Flag
QTc	> 450, > 480, > 500

Appendix 3 Toxicity Criteria for Laboratory Parameters

The toxicity criteria that will be used to identify abnormal laboratory parameters are presented in Table 7 and Table 8.

Table 7 Toxicity Criteria for Biochemistry Parameters

Parameter	Toxicity Decrease	Toxicity Increase
Chloride	≤0.96xLL	≥1.04xUL
Calcium	≤0.89xLL	≥1.16xUL
Sodium	≤0.96xLL	≥1.04xUL
Potassium	≤0.90xLL	≥1.10xUL
Glucose (mmol/L)	≤3.2	≥11
Phosphate	≤0.79xLL	
Cholesterol	≤0.85xLL	≥1.6xUL
AST		≥3xUL
ALT		≥3xUL
Lactate Dehydrogenase		≥2.6xUL
Alkaline phosphatase		≥2xUL
Gamma GT		≥3xUL
Bilirubin		>2xUL
Albumin	≤0.84xLL	
Total protein	≤0.84xLL	≥1.16xUL
Urea		≥2.6xUL
Blood urea nitrogen		≥2.6xUL
Creatinine		≥1.5xUL
Uric acid		≥1.16xUL

UL = upper limit of reference range LL = lower limit of reference range

Table 8 Toxicity Criteria for Hematology Parameters

Parameter	Toxicity Decrease	Toxicity Increase
Hemoglobin (g/dL)	≤9.4	
Hematocrit (%)	≤28	
Red cell count	≤0.84xLL	
Mean corpuscular volume	≤0.84xLL	≥1.11xUL
Mean corpuscular hemoglobin	≤0.84xLL	
Mean corpuscular hemoglobin concentration	≤0.84xLL	
Platelets (x10^9/L)	≤74	
Prothrombin time		>1.5xUL
Prothrombin international normalized ratio		>1.5
Total white blood cell count (x10^9/L)	≤2.9	≥21
Total neutrophil count (x10^9/L)	≤1.36	≥14.7
Segmented neutrophil count (x10^9/L)	≤0.75	≥12.3
Eosinophils (x10^9/L)		≥1.5
Basophils (x10^9/L)		≥0.31
Monocytes (x10^9/L)		≥2.1
Lymphocytes (x10^9/L) for participants <18 years (auto hematology)	≤1.0	
Lymphocytes (x10^9/L) for participants <18 years (manual hematology)	≤0.2	
Lymphocytes (x10^9/L) for participants ≥18 years	£0.2	

UL = upper limit of reference range LL = lower limit of reference range

Appendix 4 List of Tables, Listings and Figures

Lists of the tables, listings and figures to be provided are given below in Table 9, Table 10 and **Error! Reference source not found.**, respectively.

Table 9 List of Tables

Table Number	Title	Analysis Set
Table 14.1.1	Summary of Participant Disposition	All Screened subjects
Table 14.1.2	Summary of Demographic Data	Full Analysis Set
Table 14.1.3	Summary of Baseline Characteristics	Full Analysis Set
Table 14.1.4	Summary of Psychiatric History Now Resolved	Safety Analysis Set
Table 14.1.5	Summary of Psychiatric History – Current Conditions	Safety Analysis Set
Table 14.1.6	Summary of Previous Significant Non-Psychiatric History Now Resolved	Safety Analysis Set
Table 14.1.7	Summary of Significant Non-Psychiatric History – Current Conditions	Safety Analysis Set
Table 14.1.8	Summary of Concomitant Antipsychotic Medications	Safety Analysis Set
Table 14.1.9	Summary of Other Concomitant Medications	Safety Analysis Set
Table 14.1.10	Summary of Treatment Compliance	Safety Analysis Set
Table 14.2.1.1	Summary of PANSS-T	Full Analysis Set
Table 14.2.1.2	Analysis of Change from Baseline in PANSS-T During Treatment Period – MMRM	Full Analysis Set
Table 14.2.2.1	Summary of PANSS-P	Full Analysis Set
Table 14.2.2.2	Analysis of Change from Baseline in PANSS-P During Treatment Period – MMRM	Full Analysis Set
Table 14.2.3.1	Summary of PANSS-N	Full Analysis Set
Table 14.2.3.2	Analysis of Change from Baseline in PANSS-N During Treatment Period – MMRM	Full Analysis Set
Table 14.2.4.1	Summary of PANSS-G	Full Analysis Set
Table 14.2.4.2	Analysis of Change from Baseline in PANSS-G During Treatment Period – MMRM	Full Analysis Set
Table 14.2.5.1	Summary of the Caregiver Global Impression of Severity	Full Analysis Set
Table 14.2.5.2	Analysis of the Caregiver Global Impression of Severity	Full Analysis Set
Table 14.2.6.1	Summary of the Caregiver Global Impression of Improvement	Full Analysis Set
Table 14.2.6.2	Analysis of the Caregiver Global Impression of Improvement (MMRM)	Full Analysis Set
Table 14.2.7.1	Summary of PANSS Marders Factors	Full Analysis Set
Table 14.2.7.2	Analysis of Change from Baseline in PANSS Marders Factors During Treatment Period - MMRM	Full Analysis Set
Table 14.2.8	Summary of BACS	Full Analysis Set
Table 14.2.9	Analysis of the Response of Caregiver Global Impression of Improvement	Full Analysis Set
Table 14.3.1	Summary of Exposure	Safety Analysis Set
Table 14.3.2.1	Overall Summary of Treatment Emergent Adverse Events	Safety Analysis Set

Table Number	Title	Analysis Set
Table 14.3.2.2	Summary of Treatment Emergent Adverse Events	Safety Analysis Set
Table 14.3.2.3	Summary of Treatment-Related Treatment Emergent Adverse Events	Safety Analysis Set
Table 14.3.2.4	Summary of Treatment Emergent Adverse Events by Maximal Severity	Safety Analysis Set
Table 14.3.2.5	Summary of Treatment Emergent Adverse Events by Sex	Safety Analysis Set
Table 14.3.2.6	Summary of TEAEs by Time of First Onset of AE	Safety Analysis Set
Table 14.3.2.7	Summary of TEAEs by Time to AE Resolution	Safety Analysis Set
Table 14.3.2.8	Summary of TEAEs Reported in >=2% of Participants in the GWP42003-P Treatment Groups	Safety Analysis Set
Table 14.3.2.9	Summary of Non-Serious Treatment Emergent Adverse Events	Safety Analysis Set
Table 14.3.2.10	Summary of Treatment Emergent Adverse Events by Event	Safety Analysis Set
Table 14.3.2.11	Summary of Treatment-Related Treatment Emergent Adverse Events by Event	Safety Analysis Set
Table 14.3.2.12	Summary of Non-Serious Treatment Emergent Adverse Events by Event	Safety Analysis Set
Table 14.3.3.1	Summary of Fatal Treatment Emergent Adverse Events	Safety Analysis Set
Table 14.3.4.1	Summary of Serious Treatment Emergent Adverse Events	Safety Analysis Set
Table 14.3.3.1	Summary of Serious Treatment Emergent Adverse Events by Event	Safety Analysis Set
Table 14.3.4.2	Summary of Treatment-Related Serious Treatment Emergent Adverse Events	Safety Analysis Set
Table 14.3.4.1	Summary of Treatment-Related Serious Treatment Emergent Adverse Events by Event	Safety Analysis Set
Table 14.3.5.1	Summary of Treatment Emergent Adverse Events Leading to Permanent Discontinuation of IMP	Safety Analysis Set
Table 14.3.5.2	Summary of Treatment-Related Treatment Emergent Adverse Events Leading to Permanent Discontinuation of IMP	Safety Analysis Set
Table 14.3.5.3	Summary of Treatment Emergent Adverse Events Leading to IMP Dose Reduction Excluding Permanent Discontinuation and by Resolution and Overall	Safety Analysis Set
Table 14.3.5.4	Summary of Treatment-Related Treatment Emergent Adverse Events Leading to IMP Dose Reduction Excluding Permanent Discontinuation and by Resolution and Overall	Safety Analysis Set
Table 14.3.5.5	Summary of Treatment Emergent Adverse Events Leading to Temporary IMP Dose Reduction by Resolution and Overall	Safety Analysis Set
Table 14.3.5.6	Summary of Treatment-Related Treatment Emergent Adverse Events Leading to Temporary IMP Dose Reduction by Resolution and Overall	Safety Analysis Set

Table Number	Title	Analysis Set
Table 14.3.5.7	Summary of Treatment Emergent Adverse Events Leading to Permanent IMP Dose Reduction Excluding Permanent Discontinuation and by Resolution and Overall	Safety Analysis Set
Table 14.3.5.8	Summary of Treatment-Related Treatment Emergent Adverse Events Leading to Permanent IMP Dose Reduction Excluding Permanent Discontinuation and by Resolution and Overall	Safety Analysis Set
Table 14.3.6.1	Summary of Columbia-Suicide Severity Rating Scale by Type	Safety Analysis Set
Table 14.3.7.1	Summary of Laboratory Safety Parameters – Hematology	Safety Analysis Set
Table 14.3.7.2	Shift Table for Hematology Laboratory Parameters – Based on Reference Ranges	Safety Analysis Set
Table 14.3.7.3	Shift Table for Hematology Laboratory Parameters – Based on Toxicity Limits	Safety Analysis Set
Table 14.3.7.4	Summary of Laboratory Safety Parameters – Biochemistry	Safety Analysis Set
Table 14.3.7.5	Shift Table for Biochemistry Laboratory Parameters – Based on Reference Ranges	Safety Analysis Set
Table 14.3.7.6	Shift Table for Biochemistry Laboratory Parameters – Based on Toxicity Limits	Safety Analysis Set
Table 14.3.7.7	Shift Table for CrCl – Based on Derived Grades	Safety Analysis Set
Table 14.3.7.8	Summary of Liver Parameter Flags	Safety Analysis Set
Table 14.3.7.9	Summary of Drug Screen	Safety Analysis Set
Table 14.3.7.10	Summary of Pregnancy Test	Safety Analysis Set
Table 14.3.8.1	Summary of Vital Signs	Safety Analysis Set
Table 14.3.8.2	Incidence of Clinically Significant Changes from Baseline for Vital Signs	Safety Analysis Set
Table 14.3.8.3	Incidence of Defined Flagged Vital Signs	Safety Analysis Set
Table 14.3.8.4	Summary of ECG Parameters	Safety Analysis Set
Table 14.3.8.5	Incidence of Defined Flagged ECG Parameter Values	Safety Analysis Set

Table 10 List of Listings

Listing Number	Title	Analysis Set
Listing 16.2.1.1	Screen Failures	All Screen Failure Participants
Listing 16.2.1.2	Participant Disposition – End of Treatment Period	Safety Analysis Set
Listing 16.2.1.3	Inclusion/Exclusion Criteria Not Met	Safety Analysis Set
Listing 16.2.1.4	Visit Dates	Safety Analysis Set
Listing 16.2.2.1	Major and Critical Protocol Deviations	Randomized Participants
Listing 16.2.2.2	All Protocol Deviations	Randomized Participants
Listing 16.2.4.1	Demography	Safety Analysis Set
Listing 16.2.4.2	Baseline Characteristics	Safety Analysis Set
Listing 16.2.4.3	Psychiatric History	Safety Analysis Set
Listing 16.2.4.4	Significant Non-Psychiatric Medical or Surgical History	Safety Analysis Set
Listing 16.2.4.5	Concomitant Antipsychotic Medications	Safety Analysis Set
Listing 16.2.4.6	Other Concomitant Medications	Safety Analysis Set
Listing 16.2.5.1	Treatment Compliance	Safety Analysis Set
Listing 16.2.6.1	PANSS Syndromes	Full Analysis Set
Listing 16.2.6.2	PANSS Individual Syndrome Responses	Full Analysis Set
Listing 16.2.6.3	PANSS Total Score and Subscale Scores	Full Analysis Set
Listing 16.2.6.4	CGI-S and CGI-I	Full Analysis Set
Listing 16.2.6.5	PANSS Marder Factors Scores	Full Analysis Set
Listing 16.2.6.6	BACS Verbal Memory and Verbal Fluency	Full Analysis Set
Listing 16.2.6.7	BACS Composite and Domain Scores	Full Analysis Set
Listing 16.2.6.8	Multidimensional Psychological Questionnaires	Safety Analysis Set
Listing 16.2.6.9	Plasma Concentrations	Safety Analysis Set
Listing 16.2.6.10	Plasma Concentrations of Concomitant Antipsychotic Medications	Safety Analysis Set
Listing 16.2.7.1	Treatment Emergent Adverse Events	Safety Analysis Set
Listing 16.2.7.2	Pre-Treatment Adverse Events	Safety Analysis Set
Listing 16.2.7.3	Participants Experiencing Treatment Emergent Adverse Events by System Organ Class and Preferred term	Safety Analysis Set
Listing 16.2.7.4	Serious Adverse Events	Safety Analysis Set
Listing 16.2.8.1	Laboratory Parameters	Safety Analysis Set
Listing 16.2.8.2	Abnormal Laboratory Parameters by Participant	Safety Analysis Set
Listing 16.2.8.3	Abnormal Laboratory Parameters by Parameter	Safety Analysis Set

Listing Number	Title	Analysis Set
Listing 16.2.8.4	Laboratory Comments	Safety Analysis Set
Listing 16.2.8.5	Laboratory Liver Parameters	Safety Analysis Set
Listing 16.2.8.6	Laboratory Reference Ranges and Toxicity Limits	Safety Analysis Set
Listing 16.2.9.1	Vital Signs – Blood Pressures	Safety Analysis Set
Listing 16.2.9.2	Vital Signs – Heart Rate, Respiratory Rate and Temperature	Safety Analysis Set
Listing 16.2.9.3	Vital Signs – Height, Weight, Waist Circumference and BMI	Safety Analysis Set
Listing 16.2.9.4	Potentially Clinically Significant Changes from Baseline for Vital Signs	Safety Analysis Set
Listing 16.2.10.1	ECG Data – Part 1	Safety Analysis Set
Listing 16.2.10.2	ECG Data – Part 2	Safety Analysis Set
Listing 16.2.10.3	Mealtimes	Safety Analysis Set
Listing 16.2.10.4	Physical Examination	Safety Analysis Set