STATISTICAL ANALYSIS PLAN

A multi-center, open-label clinical pharmacology trial to investigate the pharmacokinetics, tolerability, and safety of brexpiprazole once-weekly (QW) formulation administered as single and multiple oral doses in patients with schizophrenia

NCT Number: NCT04118127
PRT NO.: 331-102-00150
Version Date: 31 Mar 2021 (Version 1.0)

Otsuka Pharmaceutical Co., Ltd.

Investigational New Drug
Brexpiprazole (OPC-34712)

Protocol No. 331-102-00150

A multi-center, open-label clinical pharmacology trial to investigate the pharmacokinetics, tolerability, and safety of brexpiprazole once-weekly (QW) formulation administered as single and multiple oral doses in patients with schizophrenia

Statistical Analysis Plan

Version: 1.0
Date: Mar 31 2021
Protocol Date: Jun 18 2020

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List of Abbreviations and Definition of Terms

Abbreviation	Definition
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body mass index
BUN	Blood urea nitrogen
CGI-I	Clinical Global Impression-Improvement
CGI-S	Clinical Global Impression-Severity of Illness
CPK	Creatine phosphokinase
C-SSRS	Columbia-Suicide Severity Rating Scale
CYP2D6	Cytochrome P450 2D6
CYP3A4	Cytochrome P450 3A4
DIEPSS	Drug-Induced Extrapyramidal Symptoms Scale
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
ECG	Electrocardiogram
IMP	Investigational Medicinal Product
LDH	Lactic dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
PCS	Potentially Clinically Significance
PK	Pharmacokinetic
PT	Preferred Term
QTc	QT corrected for heart rate
QTcF	QT interval as corrected by Fridericia's formula
QW	Quaque (Once) Weekly
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
ULN	Upper Limit of Normal
WHO-DD	World Health Organization Drug Dictionary
AUC	Area under the concentration time curve
AUC_{∞}	Area under the concentration time curve from time zero to infinity
AUC_{∞}/D	Area under the concentration time curve per dose
AUC_%Extrap	Ratio of area under the concentration-time curve from t_{last} to infinity versus AUC_{∞}
AUC_t	Area under the concentration time curve calculated to the last observable concentration at time t
AUC_t/D	AUC_t per dose
AUC_{168h}	Area under the concentration-time curve from time zero to 168 hours
AUC_{168h}/D	AUC_{168h} per dose
CL/F	Apparent clearance of drug from plasma after extravascular administration
CL/F/BW	Apparent clearance of drug from plasma after extravascular administration per body weight
C_{max}	Maximum (peak) plasma concentration of the drug
$C_{max/D}$	C_{max} per dose
LLOQ	Lower limit of quantification
λ_z	Terminal elimination rate constant
λ_z(point)	Number of points used in computing λ_z
λ_z(lower)	Lower limit on time for values to be included in the calculation of λ_z
λ_z(upper)	Upper limit on time for values to be included in the calculation of λ_z

λ_z(RSQ)	Goodness of fit statistic for the terminal elimination phase, adjusted for the number of points used in the estimation of λ_z
$t_{1/2,z}$	Terminal phase elimination half life
t_{last}	Time of the last measurable concentration
t_{max}	Time to maximum (peak) plasma concentration

1 Introduction

This statistical analysis plan describes the statistical methodology and data analysis algorithms and conventions to be applied for statistical analysis in this trial. This plan is based on version 3.0 of Protocol No. 331-102-00150, dated 28 Jan 2020.

2 Trial Objectives

The objective of the clinical trial is to evaluate the PK, tolerability, and safety of brexpiprazole QW formulation administered as single and repeated administration in patients with schizophrenia.

3 Trial Design

3.1 Type/Design of Trial

This is a multi-center, open-label, clinical pharmacology trial to investigate the PK, tolerability, and safety of brexpiprazole QW formulation administered as single and repeated administration in patients with a diagnosis of schizophrenia (295.90) based on the DSM-5®. The trial comprises the single administration period (Cohort 1) and the repeated administration period (Cohort 2). The dose used in the repeated administration period (Cohort 2) will be determined based on plasma drug concentrations obtained in the single administration period (Cohort 1). The single administration period (Cohort 1) comprises Period 1, in which the conventional tablet will be administered, and Periods 2 and 3, in which the QW formulation will be administered. If the single administration period (Cohort 1) fails to produce sufficient plasma drug concentrations, another single administration period (Cohort 1') will be added during which the QW formulation will be administered at higher single doses. Only if progression to the repeated administration period (Cohort 2) is judged to be appropriate based on the results of the single administration period (Cohort 1 and Cohort 1' [as necessary]), will the repeated administration period (Cohort 2) be implemented (see Figure 3.1-1). The repeated administration period (Cohort 2) comprises Period 1, in which subjects will receive a single administration of the conventional tablet, and Period 2, in which subjects will receive 5 administrations of the QW formulation.

In the single administration period (Cohort 1), subjects will receive a brexpiprazole 2 mg conventional tablet on Day 1 of Period 1, the QW formulation at 24 mg on Day 1of Period 2, and the QW formulation at 48 mg on Day 1 of Period 3, all as single administrations in a fasted state.

In the single administration period (Cohort 1'), subjects will receive a brexpiprazole 2 mg conventional tablet on Day 1 of Period 1, the QW formulation at 30 mg on Day 1 of Period 2, and the QW formulation at 60 or 54 mg on Day 1 of Period 3, all as single administrations in a fasted state.

In the repeated administration period (Cohort 2), subjects will receive a single administration of a brexpiprazole 2 mg conventional tablet on Day 1 of Period 1, and repeated administration of the QW formulation on Days 1, 8, 15, 22, and 29 of Period 2. The doses of the QW formulation will be determined based on the results of the single administration period (Cohort 1 and Cohort 1' [as necessary]).

In the single administration period (Cohort 1 and Cohort 1' [as necessary]), subjects will be required to be hospitalized at the trial site from the day of IMP administration (Day 1) through the eighth day following IMP administration (Day 8) in Period 1 (conventional tablet) and Periods 2 and 3 (QW formulation). For the other parts of the single administration period, they may remain in the trial site or make trial visits on an outpatient basis. In Period 1 (conventional tablet) of the repeated administration period (Cohort 2), subjects will be required to be hospitalized at the trial site from the day of IMP administration (Day 1) through the eighth day following IMP administration (Day 8). For the other parts of Period 1, they may remain in the trial site or make trial visits on an outpatient basis. In Period 2 (QW formulation) of the repeated administration period (Cohort 2), subjects will be required to be hospitalized at the trial site from the day of the first IMP administration (Day 1) through Day 16, from Day 22 through Day 23, and from Day 29 through Day 36. For the other parts of Period 2, they may remain in the trial site or make visits on an outpatient basis.

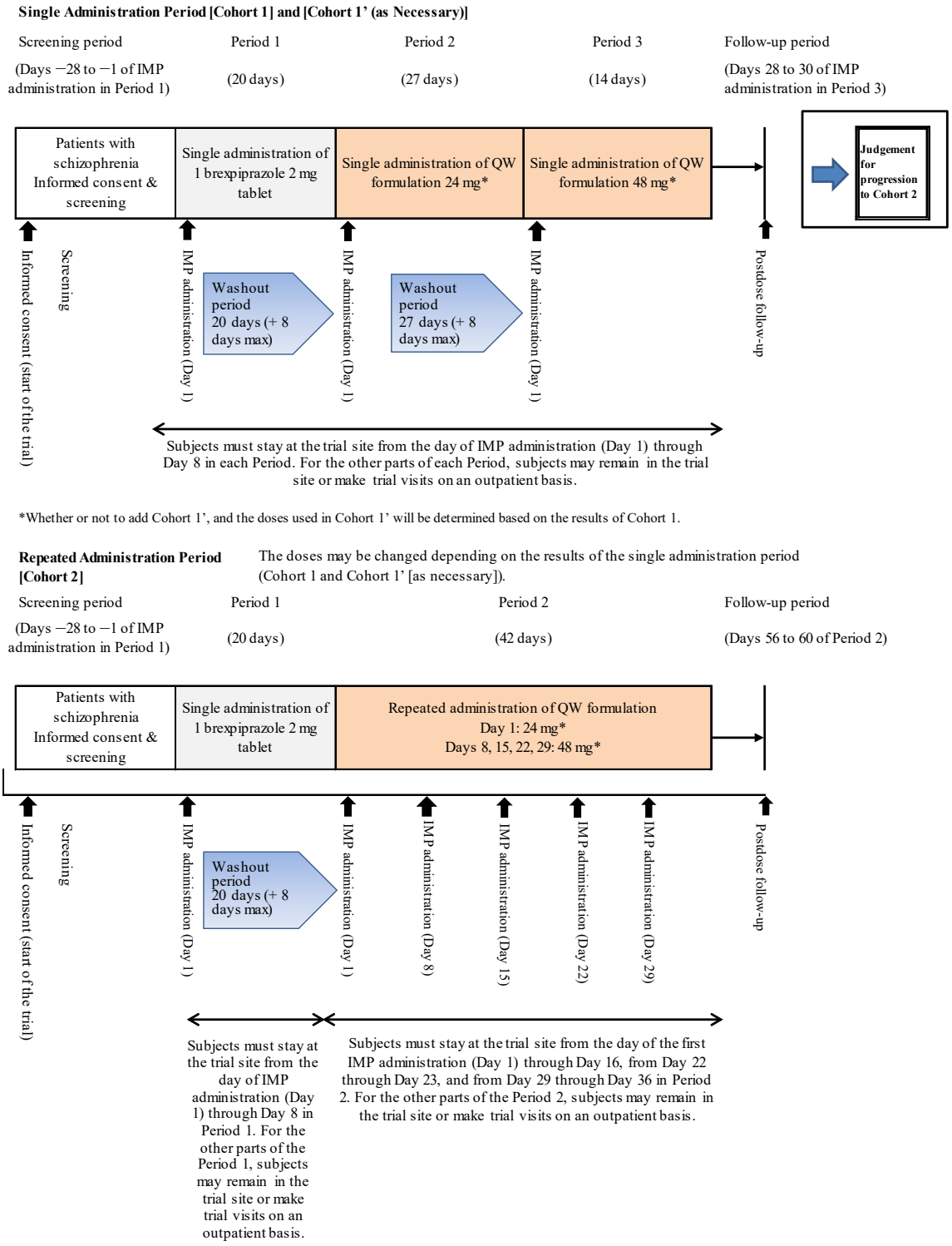

Figure 3.1-1 Trial Design

3.1.1 Cohort 1 (Single Administration Period)

Subjects judged eligible at screening will receive one brexpiprazole 2 mg conventional tablet on Day 1 of Period 1, one 24 mg tablet of the QW formulation on Day 1 of Period 2, and two 24 mg tablets of the QW formulation on Day 1 of Period 3, all as a single oral administration in a fasted state. The trial includes a washout period of 20 days (+ 8 days max) between IMP administration in Period 1 and IMP administration in Period 2 and a washout period of 27 days (+ 8 days max) between IMP administration in Period 2 and IMP administration in Period 3. Brexpiprazole-naïve subjects should be monitored after conventional tablet administration in Period 1 to check if they are free from allergic or hypersensitive reactions. Following administration of the QW formulation in Period 2, safety must be carefully evaluated. Subjects who meet any of the criteria for withdrawal before dose increase as specified in Protocol Section 3.9.3.2 Criteria for Withdrawal Before Dose Increase of the QW Formulation must be withdrawn from the trial and not advance to Period 3. If a subject withdrawn from the trial at the discretion of the sponsor after receiving a brexpiprazole 2 mg conventional tablet in Period 1 and undergoing the examinations scheduled for up to Day 14 of Period 1 subsequently takes part in the trial again, the subject will be allowed to resume participation in the trial from Period 2. If a subject withdrawn from the trial at the discretion of the sponsor after receiving a 24 mg tablet of the QW formulation in Period 2 and undergoing the examinations scheduled for up to Day 14 of Period 2 subsequently takes part in the trial again, the subject will be allowed to resume participation in the trial from Period 3.

3.1.2 Cohort 1’ (Additional Single Administration Period, as Necessary)

A simulation of repeated administration will be performed based on the results of Cohort 1 (single administration period). If steady-state plasma brexpiprazole concentrations of the QW formulation are estimated to fall far below the steady-state trough concentration for the 2 mg conventional tablet, Cohort 1’ will be added.

The design described in Section 3.1.1 Cohort 1 (Single Administration Period) applies to Cohort 1’ as well.

The doses of the QW formulation to be used in Cohort 1’ (as necessary) (single administration period) will be determined according to Protocol Section 3.8 Procedure for Progression to the Repeated Administration Period (Cohort 2) From the Single Administration Period (Cohort 1 and Cohort 1’ [as Necessary]), and the QW formulation will be administered in a fasted state as per regimen 1 or 2 shown in Table 3.2.1.2.2-1. Brexpiprazole-naïve subjects should be monitored after conventional tablet administration in Period 1 to check if they are free from allergic or hypersensitive

reactions. Following administration of the QW formulation in Period 2, safety must be carefully evaluated. Subjects who meet any of the criteria for withdrawal before dose increase as specified in Protocol Section 3.9.3.2 Criteria for Withdrawal Before Dose Increase of the QW Formulation must be withdrawn from the trial not advance to Period 3.

3.1.3 Cohort 2 (Repeated Administration Period)

Subjects judged eligible at screening will receive a single administration of a brexpiprazole 2 mg conventional tablet on Day 1 of Period 1 in a fasted state. The trial includes a washout period of 20 days (+ 8 days max) between IMP administration in Period 1 and IMP administration in Period 2. Subjects will then receive repeated administration of the QW formulation in a fasted state as per one of the regimens 1 to 5 shown in Table 3.2.1.3.2-1 on Days 1, 8, 15, 22, and 29 of Period 2. Brexpiprazole-naïve subjects should be monitored after conventional tablet administration in Period 1 to check if they are free from allergic or hypersensitive reactions.

3.2 Trial Treatments

3.2.1 Dose, Regimen and Treatment Period

3.2.1.1 Cohort 1 (Single Administration Period)

3.2.1.1.1 Administration of Brexpiprazole Conventional Tablet

On Day 1 of Period 1, subjects will receive a single oral administration of a brexpiprazole 2 mg conventional tablet together with approximately 150 mL of water in the morning after at least 10 hours of fasting. Subjects are not to take any food until 4 hours after administration. Subjects are not to take any fluids from 1 hour before administration of the conventional tablet until 2 hours after administration, except for the water taken at the time of administration.

3.2.1.1.2 Administration of Brexpiprazole QW Formulation

On Day 1 of each of Periods 2 and 3 in Cohort 1 (single administration period), subjects will receive a single oral administration of the QW formulation at the dose specified in Table 3.2.1.1.2-1 together with approximately 150 mL of water in the morning after at least 10 hours of fasting. Subjects are not to take any food until 4 hours after administration. Subjects are not to take any fluids from 1 hour before administration of the QW formulation until 2 hours after administration, except for the water taken at the time of administration.

Table 3.2.1.1.2-1 Doses (Cohort 1) (Single Administration Period)						
	Dose					
Treatment period	Period 2			Period 3		
Regimen	Dose	Tablet	No. of Tablets	Dose	Tablet	No. of Tablets
1	24 mg	24 mg tablet	1 tablet	48 mg	24 mg tablet	2 tablets

3.2.1.2 Cohort 1' (as Necessary) (Single Administration Period)

3.2.1.2.1 Administration of Brexpiprazole Conventional Tablet

On Day 1 of Period 1, subjects will receive a single oral administration of a brexpiprazole 2 mg conventional tablet together with approximately 150 mL of water in the morning after at least 10 hours of fasting. Subjects are not to take any food until 4 hours after administration. Subjects are not to take any fluids from 1 hour before administration of the conventional tablet until 2 hours after administration, except for the water taken at the time of administration.

3.2.1.2.2 Administration of Brexpiprazole QW Formulation

On Day 1 of each of Periods 2 and 3 in Cohort 1' (as necessary) (single administration period), subjects will receive a single oral administration of the QW formulation together with approximately 150 mL of water in the morning after at least 10 hours of fasting. Subjects are not to take any food until 4 hours after administration. Subjects are not to take any fluids from 1 hour before administration of the QW formulation until 2 hours after administration, except for the water taken at the time of administration. The doses of the QW formulation to be used in Cohort 1' (as necessary) (single administration period) will be determined according to Protocol Section 3.8 Procedure for Progression to the Repeated Administration Period (Cohort 2) From the Single Administration Period (Cohort 1 and Cohort 1' [as Necessary]), and the QW formulation will be administered in a fasted state as per regimen 1 or 2 shown in Table 3.2.1.2.2-1.

Table 3.2.1.2.2-1 Doses (Cohort 1' [as Necessary] [Single Administration Period])						
	Dose					
Treatment period	Period 2			Period 3		
Regimen	Dose	Tablet	No. of Tablets	Dose	Tablet	No. of Tablets
1	30 mg	30 mg tablet	1 tablet	54 mg	24 mg tablet 30 mg tablet	1 tablet each
2	30 mg	30 mg tablet	1 tablet	60 mg	30 mg tablet	2 tablets

3.2.1.3 Cohort 2 (Repeated Administration Period)

3.2.1.3.1 Administration of Brexpiprazole Conventional Tablet

On Day 1 of Period 1, subjects will receive a single oral administration of a brexpiprazole 2 mg conventional tablet together with approximately 150 mL of water in the morning after at least 10 hours of fasting. Subjects are not to take any food until 4 hours after administration. Subjects are not to take any fluids from 1 hour before administration of the conventional tablet until 2 hours after administration, except for the water taken at the time of administration.

3.2.1.3.2 Administration of Brexpiprazole QW Formulation

In Period 2, subjects will be orally administered the QW formulation together with approximately 150 mL of water in the morning after at least 10 hours of fasting, as per one of regimens 1 to 5 shown in Table 3.2.1.3.2-1 based on the results of the single administration period (Cohort 1 and Cohort 1' [as necessary]). Subjects are not to take any food until 4 hours after administration. Subjects are not to take any fluids from 1 hour before administration of the QW formulation until 2 hours after administration, except for the water taken at the time of administration.

Table 3.2.1.3.2-1 Doses (Cohort 2 [Repeated Administration Period])

	Dose					
Treatment period	**Period 2**					
Day	1			8, 15, 22, and 29		
Regimen	Dose	Tablet	No. of Tablets	Dose	Tablet	No. of Tablets
1	24 mg	24 mg tablet	1 tablet	48 mg	24 mg tablet	2 tablets
2	18 mg	18 mg tablet	1 tablet	36 mg	18 mg tablet	2 tablets
3	24 mg	24 mg tablet	1 tablet	42 mg	18 mg tablet 24 mg tablet	1 tablet each
4	30 mg	30 mg tablet	1 tablet	54 mg	24 mg tablet 30 mg tablet	1 tablet each
5	30 mg	30 mg tablet	1 tablet	60 mg	30 mg tablet	2 tablets

3.3 Trial Population

Patients from 18 years of age to under 65 years of age with a diagnosis of schizophrenia (295.90) based on DSM-5®

3.4 Trial Visit Window

Nominal time points will be used for summary of safety parameters and plasma concentration.

4 Sample Size

The target number of subjects is not based on a statistical hypothesis test. A simulation was performed with the PK model created based on PK data on the conventional tablet and QW-A formulation used in the QW-A formulation group in Trial 331-102-00021 conducted in Japan, and the probability that the mean plasma concentration of brexpiprazole after repeated administration of the QW-A formulation would be within the target range of concentration was determined. On the basis of this probability, the sample size was determined to be 20 subjects each for the single administration period (Cohort 1) and the repeated administration period (Cohort 2). Likewise, the sample size for an additional single administration period (Cohort 1') with a new dose was also determined to be 20 subjects.

5 Statistical Analysis Sets

5.1 Pharmacokinetic Analysis Set

The PK analysis set will consist of subjects who received the QW formulation and had plasma drug concentration measurements. The following subjects will be excluded from the PK analysis set:

- Subjects who vomited within 12 hours postdose

5.2 Safety Analysis Set

The safety analysis set will consist of all subjects who received any QW formulation.

5.3 Handling of Missing Data

Data imputation will not be performed for missing data.

6 Primary and Secondary Outcome Variables:

Plasma drug concentrations and pharmacokinetics parameters of brexpiprazole after single or multiple administrations of the QW formulation.

7 Disposition and Demographic Analysis

7.1 Subject Disposition

The subject dispositions will be summarized for the single administration period (Cohort 1 and Cohort 1' [as necessary]) and the repeated administration period (Cohort 2).

The number of screened subjects will be presented. The numbers and percentages of following subjects will be summarized.

- For the single administration period (Cohort 1 and Cohort 1' [as necessary]):
  1) Subjects treated with conventional tablet
  2) Subjects withdrawn in period 1
  3) Subjects treated with QW formulation in period 2
  4) Subjects withdrawn in period 2
  5) Subjects treated with QW formulation in period 3
  6) Subjects completed in period 3
  7) Subjects withdrawn in period 3
  8) Subjects analyzed for PK
  9) Subjects analyzed for safety
- For the repeated administration period (Cohort 2):
  1) Subjects treated with conventional tablet
  2) Subjects withdrawn in period 1
  3) Subjects treated with QW formulation in period 2
  4) Subjects completed in period 2
  5) Subjects withdrawn in period 2
  6) Subjects analyzed for PK
  7) Subjects analyzed for safety

The denominators for each period are subjects treated with IMP in each period. The denominators for the analysis sets are subjects treated with QW formulation.

The numbers and percentages of subjects withdrawn in each period will also be summarized by primary reason for discontinuation.

Subjects who discontinue by the sponsor's circumstances and participate again will be counted once using final completion status. Listing of information regarding first discontinuation for these subjects will presented.

7.2 Demographic and Baseline Characteristics

Depending on data characteristics, frequency distribution or descriptive statistics of demographic and other baseline characteristics will be produced for the single administration period (Cohort 1 and Cohort 1' [as necessary]) and the repeated administration period (Cohort 2) based on PK and safety analysis sets.

Continuous variables (age, height, weight at screening, and BMI) will be summarized using summary statistics (mean, SD, min, median, max). Categorical variables (sex, race,

detailed ethnicity, country, medical history, complications and CYP2D6 phenotype) will be summarized by number and percentage of subjects.

For subjects who discontinue by the sponsor's circumstances and participate again, data at first screening will be used.

7.3 Medical History

Listing of medical history will be presented.

7.4 Treatment Compliance

Information for administration of IMP is described in Section 7.1 and 9.1.

7.5 Prior and Concomitant Medications

Medications will be coded using World Health Organization Drug Dictionary (WHO-DD) version Sep 2019 Global B3. Listing of prior and concomitant medication will be presented.

7.6 Protocol Deviations

A listing of major protocol deviations will be presented.

8 Efficacy Analysis

Not applicable.

9 Safety Analyses

Each safety endpoint will be summarized for each dose (Periods 2 and 3) of the QW formulation in the single administration period (Cohort 1 and Cohort 1' [as necessary]) and for the repeated administration period (Cohort 2) based on safety analysis set.

The baseline for statistical analysis is defined as data measured immediately prior to IMP administration in Period 2.

Adverse events (AEs) in each period are defined as AEs occurred on or after the IMP administration in each period to before the IMP administration in next period or the end of study.

Potentially clinically significant (potentially clinically significance [PCS]) abnormalities in each period will include the values measured on or after the IMP administration in each period to before the IMP administration in next period or the end of study.

9.1 Extent of Exposure

For the repeated administration period (Cohort 2), the number of administrations will be summarized using frequency distribution.

9.2 Adverse Events

All AEs will be coded by system organ class (SOC) and Medical Dictionary for Regulatory Activities (MedDRA version 23.1) preferred term (PT). If multiple occurrences of the same event are observed in the same subject during the same period, the highest severity will be used for analysis. The incidence of the following events will be summarized by SOC and PT:

- AEs occurring after administration of the QW formulation (treatment-emergent adverse events [TEAEs])
- TEAEs by severity
- TEAEs with an outcome of death
- Serious TEAEs
- TEAEs leading to discontinuations of the trial
- TEAEs by onset time (1-7 and 8-14 for Cohort 1 and Cohort 1' [as necessary]; 1-7 8-14, 15-21, 22-28, 29-35, 36-42 for Cohort 2)

The above summaries will also be prepared for TEAEs potentially causally related to the IMP.

Incidences of the AEs occurring in period 1 will be summarized by SOC and PT for subjects treated with conventional tablet.

9.3 Clinical Laboratory Data

Descriptive statistics of actual measurements and changes from baseline of laboratory test parameters (excluding qualitative urinalysis) at each time point will be produced.

For each laboratory parameter (excluding qualitative parameters), measurements will be classified as "lower than the lower limit of the reference range," "within the reference range," and "higher than the upper limit of the reference range" using the reference range specified by the central laboratory, and a shift table from baseline will be produced.

For qualitative laboratory parameters, a shift table from baseline will be produced.

The number and percentage of subjects with PCS laboratory test abnormalities will be determined. The criteria of PCS laboratory test abnormalities are provided in Appendix 1.

The number and percentage of subjects with abnormal changes in liver function (Hy's Law cases) will be determined.

Definition of Hy's Law Cases:

ALT or AST >= 3xULN (or Baseline) and Bilirubin (total) >= 2xULN or Baseline

9.4 Vital Sign Data

Descriptive statistics of actual measurements and changes from baseline of each parameter at each time point will be produced.

The number and percentage of subjects with PCS in vital signs and weight will be determined. The criteria of PCS vital sign abnormalities are provided in Appendix 2.

9.5 Physical Examination Data

Physical examination findings will be listed by subject.

9.6 Electrocardiogram Data

A shift table from baseline for normal/abnormal finding of 12-lead ECG will be produced.

Descriptive statistics of actual measurements and changes from baseline of each parameter at each time point will be produced.

The number and percentage of subjects with actual measurements of corrected QT interval (QTcF) at each time point being > 450 msec, > 480 msec, and > 500 msec will be determined. The number and percentage of subjects with changes from baseline being > 30 msec and > 60 msec will be determined.

Incidence of PCS ECG abnormalities will also be summarized. The criteria of PCS ECG abnormalities are provided in Appendix 3.

9.7 Other Safety Data

9.7.1 DIEPSS

For the DIEPSS total score (sum of items 1 to 8) and the score for each item, descriptive statistics of actual measurements and changes from baseline at each time point will be produced.

9.7.2 C-SSRS

The number and percentage of subjects with each C-SSRS item (suicidality, suicidal ideation, suicidal behavior, completed suicide, emergence of suicidal ideation, emergence of serious suicidal ideation, worsening of suicidal ideation, and emergence of suicidal behavior) at each time point will be determined.

The definitions for each assessment other than completed suicide are defined as follows.

1) Suicidality: Defined as reporting any suicidal ideation or behavior
2) Suicidal ideation: Defined as reporting any type of suicidal ideation
3) Suicidal behavior: Defined as reporting any type of suicidal behavior
4) Emergence of suicidal ideation: Defined as having no suicidal ideation at baseline and reporting any type of ideation at postbaseline
5) Emergence of serious suicidal ideation: Defined as having no suicidal ideation at baseline and reporting serious suicidal ideation with a score of 4 or 5 on the suicidal ideation severity rating at postbaseline
6) Worsening of suicidal ideation: Defined as having a more severe rating in suicidal ideation rating assessment at postbaseline than at baseline
7) Emergence of suicidal behavior: Defined as having no suicidal behavior at baseline and reporting any type of behavior at postbaseline

10 Pharmacokinetic Analyses

10.1 Statistical Analyses of Primary and Secondary Pharmacokinetic Endpoints

The PK parameters of brexpiprazole (OPC-34712) for the QW formulation and conventional tablet at each dose will be determined using noncompartmental PK analysis. Descriptive statistics of the following variables will be produced.

10.1.1 Brexpiprazole QW Formulation

10.1.1.1 Period 2 of the Single Administration Period (Cohort 1 and Cohort 1' [as Necessary])

1) Plasma concentration of OPC-34712 after a single administration of the QW formulation
2) PK parameters of OPC-34712 after a single administration of the QW formulation
   C_{max}, t_{max}, t_{last}, C_{max}/D
3) Relative C_{max} of OPC-34712 for the QW formulation as compared with a conventional tablet
   Relative C_{max} (%)

= (C_{max} of QW formulation/dose of QW formulation)/(C_{max} of conventional tablet/dose of conventional tablet) × 100

10.1.1.2 Period 3 of the Single Administration Period (Cohort 1 and Cohort 1' [as Necessary])

1) Plasma concentration of OPC-34712 after a single administration of the QW formulation
2) PK parameters of OPC-34712 after a single administration of the QW formulation
   C_{max}, AUC_{∞}, AUC_t, t_{max}, λ_z, AUC_%Extrap, $t_{1/2,z}$, CL/F, CL/F/BW, t_{last}, C_{max}/D, AUC_{∞}/D, AUC_t/D
3) Relative bioavailability of OPC-34712 for the QW formulation as compared with a conventional tablet
   Relative bioavailability (%)
   = (AUC_{∞} of QW formulation/dose of QW formulation)/(AUC_{∞} of conventional tablet/dose of conventional tablet) × 100
4) Relative C_{max} of OPC-34712 for the QW formulation as compared with a conventional tablet
   Relative C_{max} (%)
   = (C_{max} of QW formulation/dose of QW formulation)/(C_{max} of conventional tablet/dose of conventional tablet) × 100

10.1.1.3 Period 2 of the Repeated Administration Period (Cohort 2)

1) Plasma concentration of OPC-34712 after the fifth administration of the QW formulation
2) PK parameters of OPC-34712 after the fifth administration of the QW formulation
   C_{max}, AUC_{168h}, t_{max}, λ_z, $t_{1/2,z}$, CL/F, CL/F/BW, t_{last}, C_{max}/D, AUC_{168h}/D
3) Plasma trough concentrations of OPC-34712 from the first to fifth administration of the QW formulation (C_{168h})

10.1.2 Brexpiprazole Conventional Tablet (for All Cohorts, Period 1)

1) Plasma concentration of OPC-34712 after a single administration of a conventional tablet
2) PK parameters of OPC-34712 after a single administration of a conventional tablet
   C_{max}, AUC_{∞}, AUC_t, t_{max}, λ_z, AUC_%Extrap, $t_{1/2,z}$, CL/F, CL/F/BW, t_{last}, C_{max}/D, AUC_{∞}/D, AUC_t/D

10.2 Technical Details of Pharmacokinetic Statistical Analyses

1) Using the PK analysis set, the following analysis will be performed.
   a) For each concentration in Section 10.1.1.1 1), Section 10.1.1.2 1), Section 10.1.1.3 1) and 3), and Section 10.1.2 1)), descriptive statistics will be calculated by cohort, period, and treatment at each blood collection time point. The descriptive statistics to be calculated will be number of analyzed subjects, number of subjects included in the tabulation, arithmetic mean, standard deviation, coefficient of variation, minimum, median, and maximum. However, the descriptive statistics will be calculated only when the number of subjects included in the tabulation exceeds half of the number of analyzed subjects.
   b) For each parameter in Section 10.1.1.1 2) and 3), Section 10.1.1.2 2), 3), and 4), Section 10.1.1.3 2), and Section 10.1.2 2), descriptive statistics will be calculated by cohort, period, and treatment. For the PK parameters except for t_{max} and t_{last}, the descriptive statistics to be calculated will be number of analyzed subjects, number of subjects included in the tabulation, arithmetic mean, standard deviation, coefficient of variation, geometric mean, minimum, median, and maximum. For t_{max} and t_{last}, descriptive statistics to be calculated will be number of analyzed subjects, minimum, median, and maximum. However, the descriptive statistics will be calculated only when the number of subjects included in the tabulation exceeds half of the number of analyzed subjects. For λ_z and λ_z(Rsq), λ_z(point), λ_z(upper) and λ_z(lower), which is outputted as reference values when calculating λ_z, no descriptive statics will be calculated.
2) Nonacceptance of data will be determined in accordance with the following conditions in this trial.
   a) If blood sampling is conducted outside the time window for the analyses (see Table 3.7-3, Table 3.7-4 Table 3.7-5, Table 3.7-6 in the protocol), the data will be excluded from the calculation of descriptive statistics for plasma concentrations at that time point. However, it will be used for the calculation of PK parameters, and if the calculation of PK parameters is determined to be unsuitable, the parameter will not be adopted.
   b) None of the plasma concentrations after use of drugs or food (see Appendix 3 in the protocol) which may inhibit or induce CYP2D6 or CYP3A4 activity will be used for calculating descriptive statistics at that time.
3) The plasma concentrations below the lower limit of quantitation (LLOQ) that occur prior to the first measurable concentration of IMP administration in each period will be imputed to 0 (ng/mL) and if occur after the first measureable concentration, LLOQ will be set to missing. The LLOQ of OPC-34712 is 0.5000 ng/mL.
4) If the PK sampling at the time of discontinuation is performed within the acceptable time window, the plasma concentrations will be used for the calculation of summary statistics.

5) The PK parameters will be determined by subject and treatment using a noncompartmental PK analysis under the following conditions.
   a) The actual time postdose will be used.
   b) For the λ_z estimation, no weighting will be used for a regression equation.
   c) For the AUC calculation, a linear trapezoidal rule will be used.
   d) For the calculation of the weight correction parameters, the weight immediately before OPC-34712 administration of each period will be used.

11 Pharmacodynamic Analyses

Not applicable.

12 Pharmacogenomic Analyses

Not applicable.

13 Analyses of Other Endpoints

13.1 Clinical Global Impression - Severity of Illness and Clinical Global Impression - Improvement

A list of subjects whose CGI-S or CGI-I has worsened will be provided.

14 Interim Analysis

Not applicable.

15 Changes in the Planned Analyses

The analysis plan in the Protocol Section 6.1.1.3 was corrected as follows.

<Old>

4) Accumulation of brexpiprazole after the fifth administration of the QW formulation as compared with that after the first administration [R5,ac(C_{168h})]

<New>

None

<Reason for the change>

No need to calculate the parameters.

16 References

Not applicable.

Appendix 1 Criteria for Identifying Laboratory Values of Potential Clinical Relevance

Laboratory Tests	Criteria
Chemistry	
AST (SGOT)	≥ 3 x upper limit of normal (ULN)
ALT (SGPT)	≥ 3 x ULN
Alkaline phosphatase	≥ 3 x ULN
LDH	≥ 3 x ULN
BUN	≥ 30 mg/dL
Creatinine	≥ 2.0 mg/dL
Uric Acid	
Men	≥ 10.5 mg/dL
Women	≥ 8.5 mg/dL
Bilirubin (total)	≥ 2.0 mg/dL
CPK	≥ 3 x ULN
Prolactin	> ULN
Hematology	
Hematocrit	
Men	≤ 37% and decrease of ≥ 3 percentage points from Baseline
Women	≤ 32% and decrease of ≥ 3 percentage points from Baseline
Hemoglobin	
Men	≤ 11.5 g/dL
Women	≤ 9.5 g/dL
White blood count	≤ 2,800/ mm^3 or ≥ 16,000/ mm^3
Eosinophils	≥ 10%
Neutrophils	≤ 15%
Absolute neutrophil count	≤ 1,000/ mm^3
Platelet count	≤ 75,000/ mm^3 or ≥ 700,000/ mm^3
Additional Criteria	
Chloride	≤ 90 mEq/L or ≥ 118 mEq/L
Potassium	≤ 2.5 mEq/L or ≥ 6.5 mEq/L
Sodium	≤ 126 mEq/L or ≥ 156 mEq/L
Calcium	≤ 8.2 mg/dL or ≥ 12 mg/dL
Glucose	
Fasting	≥ 100 mg/dL
Non-Fasting	≥ 200 mg/dL
Total Cholesterol, Fasting	≥ 240 mg/dL
Triglycerides, Fasting	≥ 150 mg/dL

Appendix 2 Criteria for Identifying Vital Signs and Body Weight of Potential Clinical Relevance

Variable	Criterion Value[a]	Change Relative to Baseline[a]
Pulse Rate	> 120 bpm < 50 bpm	≥ 15 bpm increase ≥ 15 bpm decrease
Systolic Blood Pressure	> 180 mmHg < 90 mmHg	≥ 20 mmHg increase ≥ 20 mmHg decrease
Diastolic Blood Pressure	> 105 mmHg < 50 mmHg	≥ 15 mmHg increase ≥ 15 mmHg decrease
Weight	-	≥ 7% increase ≥ 7% decrease

[a]In order to be identified as potentially clinically relevant, an on-treatment value must meet the "Criterion Value" and also represent a change from the subject's baseline value of at least the magnitude shown in the "Change Relative to Baseline" column.

Appendix 3 Criteria for Identifying ECG Measurements of Potential Clinical Relevance

Variable	Criterion Value[a]	Change Relative to Baseline[a]
Heart Rate	≥ 120 bpm ≤ 50 bpm	increase of ≥ 15 bpm decrease of ≥ 15 bpm
PR	≥ 200 msec	increase of ≥ 50 msec
QRS	≥ 120 msec	increase of ≥ 20 msec
QTcF	> 450 msec (males and females)	

[a]In order to be identified as potentially clinically relevant, an on-treatment value must meet the "Criterion Value" and also represent a change from the subject's baseline value of at least the magnitude shown in the "Change Relative to Baseline" column.

Appendix 4 List of Summary Tables

CT-1.1	Subject Disposition (Cohort 1)
CT-1.2	Subject Disposition (Cohort 1')
CT-1.3	Subject Disposition (Cohort 2)
CT-2.1.1	Reasons for Discontinuation in Period 1 (Cohort 1)
CT-2.1.2	Reasons for Discontinuation in Period 1 (Cohort 1')
CT-2.1.3	Reasons for Discontinuation in Period 1 (Cohort 2)
CT-2.2.1	Reasons for Discontinuation in Period 2 (Cohort 1)
CT-2.2.2	Reasons for Discontinuation in Period 2 (Cohort 1')
CT-2.2.3	Reasons for Discontinuation in Period 2 (Cohort 2)
CT-2.2.1	Reasons for Discontinuation in Period 3 (Cohort 1)
CT-2.3.2	Reasons for Discontinuation in Period 3 (Cohort 1')
CT-3.1.1	Demographic and Baseline Characteristics - Pharmacokinetic Analysis Set (Cohort 1)
CT-3.1.2	Demographic and Baseline Characteristics - Pharmacokinetic Analysis Set (Cohort 1')
CT-3.1.3	Demographic and Baseline Characteristics - Pharmacokinetic Analysis Set (Cohort 2)
CT-3.2.1	Demographic and Baseline Characteristics - Safety Analysis Set (Cohort 1)
CT-3.2.2	Demographic and Baseline Characteristics - Safety Analysis Set (Cohort 1')
CT-3.2.3	Demographic and Baseline Characteristics - Safety Analysis Set (Cohort 2)
CT-7.1	Extent of Exposure (Cohort 2)
CT-8.1.1	Adverse Events (All Causalities) (Cohort 1)
CT-8.1.2	Adverse Events (All Causalities) (Cohort 1')
CT-8.1.3	Adverse Events (All Causalities) (Cohort 2)
CT-8.2.1.1	Incidence of Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1)
CT-8.2.1.2	Incidence of Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1')
CT-8.2.1.3	Incidence of Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 2)
CT-8.2.2.1	Incidence of Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (Cohort 1)
CT-8.2.2.2	Incidence of Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (Cohort 1')
CT-8.2.2.3	Incidence of Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (Cohort 2)
CT-8.3.1.1	Incidence of Drug-Related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1)
CT-8.3.1.2	Incidence of Drug-Related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1')

CT-8.3.1.3	Incidence of Drug-Related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 2)
CT-8.3.2.1	Incidence of Drug-related Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (Cohort 1)
CT-8.3.2.2	Incidence of Drug-related Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (Cohort 1')
CT-8.3.2.3	Incidence of Drug-related Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Severity (Cohort 2)
CT-8.4.1.1	Incidence of Serious Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1)
CT-8.4.1.2	Incidence of Serious Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1')
CT-8.4.1.3	Incidence of Serious Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 2)
CT-8.4.2.1	Incidence of Serious Drug-related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1)
CT-8.4.2.2	Incidence of Serious Drug-related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1')
CT-8.4.2.3	Incidence of Serious Drug-related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 2)
CT-8.5.1.1	Incidence of Discontinuations due to Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1)
CT-8.5.1.2	Incidence of Discontinuations due to Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1')
CT-8.5.1.3	Incidence of Discontinuations due to Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 2)
CT-8.5.2.1	Incidence of Discontinuations due to Drug-related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1)
CT-8.5.2.2	Incidence of Discontinuations due to Drug-related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 1')
CT-8.5.2.3	Incidence of Discontinuations due to Drug-related Treatment-Emergent Adverse Events by System Organ Class and MedDRA Preferred Term (Cohort 2)
CT-8.6.1.1	Incidence of Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Onset Time (Cohort 1)
CT-8.6.1.2	Incidence of Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Onset Time (Cohort 1')
CT-8.6.1.3	Incidence of Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Onset Time (Cohort 2)
CT-8.6.2.1	Incidence of Drug-related Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Onset Time (Cohort 1)
CT-8.6.2.2	Incidence of Drug-related Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Onset Time (Cohort 1')
CT-8.6.2.3	Incidence of Drug-related Treatment-Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Onset Time (Cohort 2)

CT-8.7.1	Incidence of Adverse Events in Period 1 by System Organ Class and MedDRA Preferred Term (Cohort 1)
CT-8.7.2	Incidence of Adverse Events in Period 1 by System Organ Class and MedDRA Preferred Term (Cohort 1')
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CT-9.1	Listing of Deaths
CT-9.2	Listing of Serious Adverse Events Other Than Death
CT-9.3	Listing of Discontinuations due to Adverse Events
CT-10.1.1.1	Mean Change from Baseline in Clinical Laboratory Test Results - Serum Chemistry (Cohort 1)
CT-10.1.1.2	Mean Change from Baseline in Clinical Laboratory Test Results - Serum Chemistry (Cohort 1')
CT-10.1.1.3	Mean Change from Baseline in Clinical Laboratory Test Results - Serum Chemistry (Cohort 2)
CT-10.1.2.1	Mean Change from Baseline in Clinical Laboratory Test Results - Hematology (Cohort 1)
CT-10.1.2.2	Mean Change from Baseline in Clinical Laboratory Test Results - Hematology (Cohort 1')
CT-10.1.2.3	Mean Change from Baseline in Clinical Laboratory Test Results - Hematology (Cohort 2)
CT-10.1.3.1	Mean Change from Baseline in Clinical Laboratory Test Results - Urinalysis (Cohort 1)
CT-10.1.3.2	Mean Change from Baseline in Clinical Laboratory Test Results - Urinalysis (Cohort 1')
CT-10.1.3.3	Mean Change from Baseline in Clinical Laboratory Test Results - Urinalysis (Cohort 2)
CT-10.2.1.1	Shift Tables of Clinical Laboratory Test Results - Serum Chemistry (Cohort 1)
CT-10.2.1.2	Shift Tables of Clinical Laboratory Test Results - Serum Chemistry (Cohort 1')
CT-10.2.1.3	Shift Tables of Clinical Laboratory Test Results - Serum Chemistry (Cohort 2)
CT-10.2.2.1	Shift Tables of Clinical Laboratory Test Results - Hematology (Cohort 1)
CT-10.2.2.2	Shift Tables of Clinical Laboratory Test Results - Hematology (Cohort 1')
CT-10.2.2.3	Shift Tables of Clinical Laboratory Test Results - Hematology (Cohort 2)
CT-10.2.3.1	Shift Tables of Clinical Laboratory Test Results - Urinalysis (Cohort 1)
CT-10.2.3.2	Shift Tables of Clinical Laboratory Test Results - Urinalysis (Cohort 1')
CT-10.2.3.3	Shift Tables of Clinical Laboratory Test Results - Urinalysis (Cohort 2)
CT-10.3.1	Shift Tables of Clinical Laboratory Test Results - Qualitative Urinalysis (Cohort 1)
CT-10.3.2	Shift Tables of Clinical Laboratory Test Results - Qualitative Urinalysis (Cohort 1')
CT-10.3.3	Shift Tables of Clinical Laboratory Test Results - Qualitative Urinalysis (Cohort 2)
CT-10.4.1.1	Incidence of Potentially Clinically Significant Laboratory Test Abnormalities (Cohort 1)

CT-10.4.1.2	Incidence of Potentially Clinically Significant Laboratory Test Abnormalities (Cohort 1')
CT-10.4.1.3	Incidence of Potentially Clinically Significant Laboratory Test Abnormalities (Cohort 2)
CT-10.4.2	Listing of Potentially Clinically Significant Laboratory Test Abnormalities
CT-10.5.1.1	Incidence of Potential Hy's Law Cases (Cohort 1)
CT-10.5.1.2	Incidence of Potential Hy's Law Cases (Cohort 1')
CT-10.5.1.3	Incidence of Potential Hy's Law Cases (Cohort 2)
CT-10.5.2	Listing of Potential Hy's Law Cases
CT-11.1.1	Mean Change from Baseline in Vital Signs and Weight (Cohort 1)
CT-11.1.2	Mean Change from Baseline in Vital Signs and Weight (Cohort 1')
CT-11.1.3	Mean Change from Baseline in Vital Signs and Weight (Cohort 2)
CT-11.2.1.1	Incidence of Potentially Clinically Significant Vital Sign Abnormalities and Body Weight Changes (Cohort 1)
CT-11.2.1.2	Incidence of Potentially Clinically Significant Vital Sign Abnormalities and Body Weight Changes (Cohort 1')
CT-11.2.1.3	Incidence of Potentially Clinically Significant Vital Sign Abnormalities and Body Weight Changes (Cohort 2)
CT-11.2.2	Listing of Potentially Clinically Significant Vital Sign Abnormalities
CT-11.2.3	Listing of Potentially Clinically Significant Body Weight Changes
CT-12.1.1	Mean Change from Baseline in Electrocardiogram Results (Cohort 1)
CT-12.1.2	Mean Change from Baseline in Electrocardiogram Results (Cohort 1')
CT-12.1.3	Mean Change from Baseline in Electrocardiogram Results (Cohort 2)
CT-12.2.1	Shift Table of Electrocardiogram Findings (Cohort 1)
CT-12.2.2	Shift Table of Electrocardiogram Findings (Cohort 1')
CT-12.2.3	Shift Table of Electrocardiogram Findings (Cohort 2)
CT-12.3.1	Categorical Analysis of Electrocardiogram Parameters (Cohort 1)
CT-12.3.2	Categorical Analysis of Electrocardiogram Parameters (Cohort 1')
CT-12.3.3	Categorical Analysis of Electrocardiogram Parameters (Cohort 2)
CT-12.4.1.1	Incidence of Potentially Clinically Significant ECG Abnormalities (Cohort 1)
CT-12.4.1.2	Incidence of Potentially Clinically Significant ECG Abnormalities (Cohort 1')
CT-12.4.1.3	Incidence of Potentially Clinically Significant ECG Abnormalities (Cohort 2)
CT-12.4.2	Listing of Potentially Clinically Significant ECG Abnormalities
CT-13.1.1	Mean Change from Baseline in DIEPSS (Cohort 1)
CT-13.1.2	Mean Change from Baseline in DIEPSS (Cohort 1')
CT-13.1.3	Mean Change from Baseline in DIEPSS (Cohort 2)
CT-14.1.1	Columbia-Suicide Severity Rating Scale (C-SSRS) - Incidences of Suicidality (Cohort 1)

CT-14.1.2	Columbia-Suicide Severity Rating Scale (C-SSRS) - Incidences of Suicidality (Cohort 1')
CT-14.1.3	Columbia-Suicide Severity Rating Scale (C-SSRS) - Incidences of Suicidality (Cohort 2)
CT-15.1	Listing of Subjects whose CGI-S has Worsened
CT-15.2	Listing of Subjects whose CGI-I has Worsened
PKT-X.X.1.X	Individual and Summary of Plasma Concentration Following Single Administration
PKT-X.X.2.X	Individual and Summary of Plasma Pharmacokinetic Parameters Following Single Administration
PKT-X.X.3.X	Individual and Summary of Plasma Concentration Following Multiple Administration
PKT-X.X.4.X	Individual and Summary of Plasma Trough Concentration Following Administration
PKT-X.X.5.X	Individual and Summary of Plasma Pharmacokinetic Parameters Following Multiple Administration
PKT-X.X.7.X:	Individual and Summary of Pharmacokinetic Parameter Ratios of QW Formulation to Conventional Tablet Following Oral Administration of OPC-34712
PKF-X.X.1.X	Mean Plasma Concentrations Following Single Administration
PKF-X.X.2.X	Median Plasma Concentrations Following Single Administration
PKF-X.X.3.X	Plasma Concentrations Following Single Administration
PKF-X.X.5.X	Mean Plasma Concentrations Following Multiple Administration
PKF-X.X.6.X	Median Concentrations Following Multiple Administration
PKF-X.X.7.X	Mean Plasma Trough Concentrations Following Administration
PKF-X.X.8.X	Median Trough Concentrations Following Administration
PKF-X.X.12.X	Plasma Concentrations Following Multiple Administration
PKF-X.X.13.X	Plasma Trough Concentrations Following Administration
PKF-X.X.19.X	Mean Plasma Concentrations Following Oral Administration of QW Formulation Versus Conventional Tablet
PKF-X.X.20.X	Individual Plasma Concentrations Following Oral Administration of QW Formulation Versus Conventional Tablet

Appendix 5 List of Subject Data Listings

DREAS-1	Discontinued Subjects and Reason for Discontinuation
SUBEX-1	Subjects Excluded From Analysis Set
DEMOG-1	Demographic Characteristics
SMED-1	Study Medication Compliance
AE-1	Adverse Events
LAB-1	Laboratory Test Results - Serum Chemistry
LAB-2	Laboratory Test Results - Hematology
LAB-3	Laboratory Test Results - Urinalysis
LAB-4	Laboratory Test Results - Other
PDATA-1	Inclusion/Exclusion Criteria Not Met
PDATA-2	Treatment Assignment
PDATA-3	Study Completion Status
PDATA-5	Medical History and Complications
PDATA-6.1	Concomitant Medications
PDATA-6.2	Concomitant Therapy
PDATA-8	Physical Examination
PDATA-10	Vital Signs
PDATA-11	Weight
PDATA-12	Electrocardiogram Results
PDATA-13	Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS)
PDATA-14.1	Columbia-Suicide Severity Rating Scale (C-SSRS) - Suicidal Ideation and Intensity
PDATA-14.2	Columbia-Suicide Severity Rating Scale (C-SSRS) - Suicidal Behavior
PDATA-14.3	Columbia-Suicide Severity Rating Scale (C-SSRS) - Actual Attempts
PDATA-15.1	Clinical Global Impression-Severity (CGI-S)
PDATA-15.2	Clinical Global Impression - Improvement (CGI-I)
PDATA-16	Pharmacokinetic Blood Draw Time
PDATA-17	DNA Storage
PDATA-18	CYP2D6 Genetic Test
PDATA-19	Post-treatment Follow-up
PDATA-20	Screen Failures
PDATA-21	Subjects who discontinue by the sponsor’s circumstances and participate again
PDEV-1	Major Protocol Deviations