Statistical Analysis Plan

Long-Term Study of DSP-5423P in Patients with Schizophrenia
[Phase 3]

Protocol: D4904040

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Modification History

Version	Study Biostatistician	Date of the Document Version	Approvers	Significant Changes from Previous Authorized Version
1.0	[redacted]	25APR2017	[redacted]	Not Applicable – First Version
2.0	[redacted]	On the cover	[redacted]	• Since the discontinuation rate after DSP-5423P patch initiation was less than 50%, rates of subjects continued Week 28 and/or Week 52 were added in analysis of DSP-5423P treatment duration. (Section 9.11.4, 10.1) • Table 14.2.5 Time to All-Cases Treatment Discontinuation by Prior Antipsychotics was added. • The sum of cohort was added in the summary of plasma drug concentration. (Section 9.14.1)

Contents

1. Introduction

This statistical analysis plan describes the statistical analysis of protocol No. D4904040 in detail and the planned analysis needed. When separately analyzing the pharmacokinetics and PK-PD, the details of the analytical procedures will be specified in an analysis plan and if appropriate pooled analysis with other studies will be performed and reported separately.

2. Abbreviation

Abbreviation	Full description
ALT	Alanine aminotransferase (alanine aminotransferase)
ALP	Alkaline phosphatase (alkaline phosphatase)
AST	Aspartate aminotransferase (aspartate aminotransferase)
ATC	Anatomical Therapeutic Chemical classification
BMI	Body Mass Index
BUN	Blood urea nitrogen (blood urea nitrogen)
CGI-S	Clinical Global Impression –Severity of Illness (Global Impressions Rating Scale-severity)
CK	Creatine phosphokinase (creatine phosphokinase)
Cl	Chlorine (Chloride)
C-SSRS	Columbia-Suicide Severity Rating Scale (Columbia Suicide Rating Scale)
DAI-10	Drug Attitude Inventory-10
DIEPSS	Drug-Induced Extrapyramidal Symptoms Scale (Pharmacogenicity extrapyramidal symptom Rating Scale)
ECG	Electrocardiogram (ECG)
EDC	Electronic data capture (electronic information-gathering systems)
EQ-5D	EuroQol-5 Dimension
GCP	Good Clinical Practice (Good clinical study Practice)
γ-GTP	γ-glutamyl transpeptidase (Glutamyltranspeptidase)
HbA1c	Hemoglobin A1c (Hb A1c)
IPDs	Important protocol deviations (deviation from critical clinical study plans)
K	Potassium (K)
LDH	Lactate dehydrogenase (lactate dehydrogenase)
LLN	Lower limit of normal
LOCF	Last Observation Carried Forward
MAPLV	Markedly Abnormal Post-Baseline Laboratory Values
MAPVS	Markedly Abnormal Post-Baseline Vital Signs
MedDRA	Medical Dictionary for Regulatory Activities

Abbreviation	Full description
Na	Sodium (Na)
PANSS	Positive and Negative Syndrome Scale (Positive and Negative symptom Rating Scale)
PK-PD	Pharmacokinetics-Pharmacodynamics
PT	Preferred Term
QTc	QT interval corrected for heart rate (corrected QT)
QTcB	QTcB - Bazett's Correction Formula
QTcF	QTcF - Fridericia's Correction Formula
SD	Standard Deviation
SE	Standard Error
SOC	System Organ Class
TEAE	Treatment emergent adverse event
ULN	Upper limit of normal
WHO	World Health Organization

3. Change from analysis specified in study protocol

No changes were made.

4. Objective of the study

4.1 Primary objective

To evaluate the safety of DSP-5423P (40-80 mg/day) for 52-week treatment.

4.2 Secondary objective

- To evaluate the safety and effectiveness of switching from DSP-5423 (tablet) to DSP-5423P.
- To evaluate the effectiveness and pharmacokinetics of DSP-5423P (40-80 mg/day) for 52-week treatment.

4.3 Overall study design of clinical study

This clinical study is a multicenter, perform uncontrolled, open-label, long-term administration study consisting of two cohorts. The study schematics of clinical study are presented in Figures 1 (cohort 1) and 2 (cohort 2). Details of the study assessment and other procedures (assessment, observation, laboratory test) to be performed are presented in Tables 2 (cohort 1), 3 (cohort 2) and Chapter 11 in the protocol. In both cohorts, Day 1 is defined as the day of the initial application of DSP-5423P.

Cohort 1, consisting of DSP-5423 (tablet) treatment period and DSP-5423P treatment period, and cohort 2, consisting only of DSP-5423P treatment period, will be conducted in different subjects,

and cohort 2 will be initiated after enrollment in cohort 1 has been completed. Enrollment in cohort 1 will be terminated when the number of total subjects whose DSP-5423P treatment duration is 6 weeks or more reached 50. At the completion of enrollment in cohort 1 and at the initiation of enrollment in cohort 2, the sponsor will notify the participating study centers of that.

4.3.1 Cohort 1

Cohort 1 consists of 3 periods: DSP-5423 (tablet) treatment period (6 weeks), DSP-5423P treatment period (52 weeks) and follow-up period (1-2 weeks). Prior to initiation of DSP-5423 (tablet) treatment period, washout period (up to 4 weeks) will be arranged according to the dose of prior antipsychotics (haloperidol equivalent).

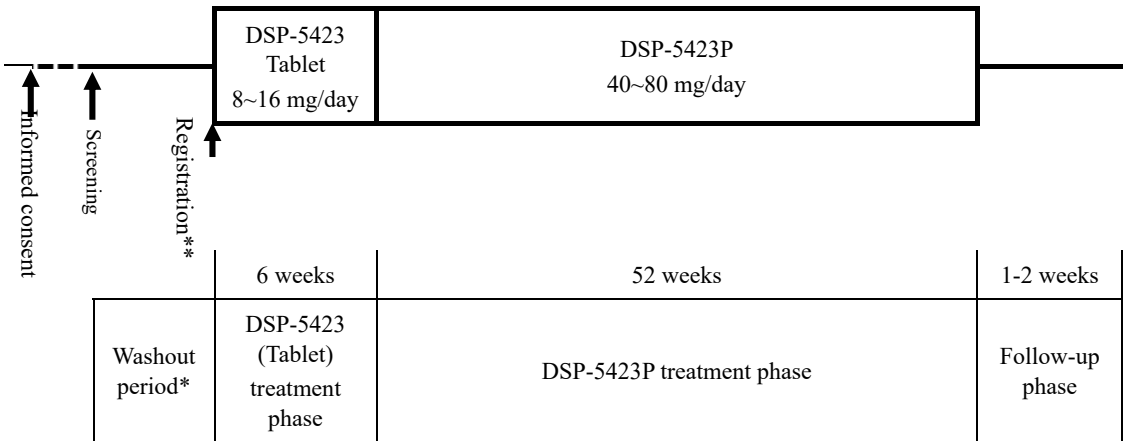
1) DSP-5423 (tablet) treatment period

DSP-5423 (tablets) will be administered orally twice daily after breakfast and evening meal for 6 weeks. The initial dose of DSP-5423 (tablet) will be 8mg/day. DSP-5423 (tablet) will be administered as flexible dose (8, 12, 16 mg/day) according to the dose adjustment criteria.

2) DSP-5423P treatment period

DSP-5423P will be applied once daily for 52 weeks. The study drug will be applied to the subject's back, chest, or abdomen. Start DSP-5423P application with the dosage according to the final dosage of DSP-5423. DSP-5423P will be applied as flexible dose (40, 60, 80 mg/day) according to the dose adjustment criteria.

Figure 1 Study schematic (cohort 1)



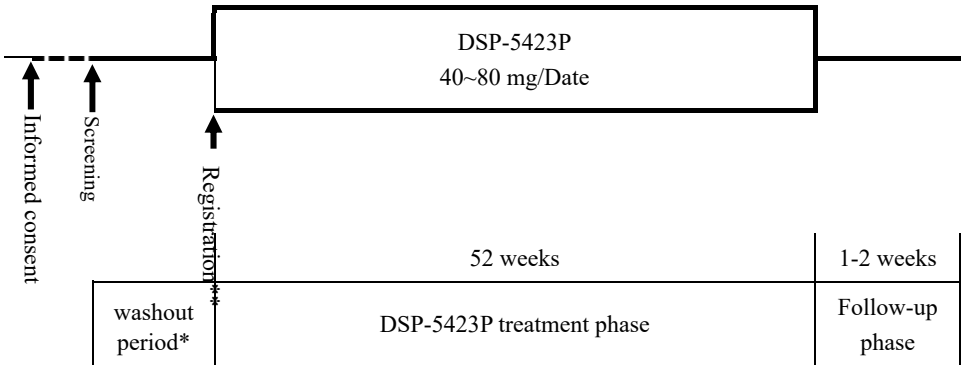
* If the dose of the prior antipsychotics is 12.0 mg/day or less (haloperidol equivalent), to initiate the administration of the DSP-5423 (tablet) after termination of the prior antipsychotics. Washout period may be arranged and down-titration would be done as needed prior to termination.
If the dose of the prior antipsychotics exceeds 12.0 mg/day (haloperidol equivalent), washout period will be arranged. First, the dose is reduced to 12.0 mg/day or less, then down-titration would be done as needed. After termination of the prior antipsychotics, to initiate the administration of the DSP-5423 (tablet).
Washout period should be up to 4 weeks (28 days) from the screening.

** The registration procedure is presented in section 10 in the protocol.

4.3.2 Cohort 2

Cohort 2 consists of 2 period: DSP-5423P treatment period (52 weeks) and follow-up period (1-2 weeks). During the DSP-5423P treatment period, DSP-5423P will be applied once daily for 52 weeks. The study drug will be applied to the subject's back, chest, or abdomen. The initial dose of DSP-5423P will be 40 mg/day. DSP-5423P will be applied as flexible dose (40, 60, 80 mg/day) according to the dose adjustment criteria. Prior to initiation of DSP-5423P treatment period, a washout period (up to 4 weeks) will be arranged according to the dose of prior antipsychotics (haloperidol equivalent).

Figure 2 Study schematic (cohort 2).



* If the dose of the prior antipsychotics is 12.0 mg/day or less (haloperidol equivalent), to initiate the application of the DSP-5423P after termination of the prior antipsychotics. Washout period may be arranged and down-titration would be done as needed prior to termination.
If the dose of the prior antipsychotics exceeds 12.0 mg/day (haloperidol equivalent), washout period will be arranged. First, the dose is reduced to 12.0 mg/day or less, then down-titration would be done as needed. After termination of the prior antipsychotics, to initiate the administration of the DSP-5423P.
Washout period should be up to 4 weeks (28 days) from the screening.

** The registration procedure is presented in section 10 in the protocol.

4.4 Schedule of assessments

Table 1 Schedule of Assessments (Cohort 1)

			DSP-5423 (tablet) treatment phase (6 weeks)					DSP-5423P treatment phase (52 weeks)													Discontinuation	Follow-up phase (1-2 weeks)
Visit No.	-	1	2	3	4	5	6	101	102	103	104	105	106	107	108	109	110	111	112	113		Follow-up visit
Study timeline [a] Week	-	Screening	Timeline from initiation of DSP-5423 (tablet) administration					Timeline from initiation of DSP-5423P application													Discontinuation	6 ~ 17 days after completion of treatment or dicontinuation
			Tab-Baseline	Tab-Week 1	Tab-Week 2	Tab-Week 4	Tab-Week 6 /baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 36	Week 44	Week 52		
Visit window (Day)		Tab -28-	Tab -2-1	Tab 5-11	Tab 12-18	Tab 26-32	Tab 40-43	5-11	12-18	26-32	40-46	54-60	78-92	106-120	134-148	162-176	190-204	239-267	295-323	351-379	At discontinuation +5	
Obtain informed consent	X																					
Patient demographics and medical history		X																				
Dispense study drug			X[d]	X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X			
Study treatment compliance				X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PANSS		X	X[d]	X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X[g]	X[g]	
CGI-S		X	X[d]	X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X[g]	X[g]	
DIEPSS			X[d]	X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X[g]	X[g]	
C-SSRS			X[d]	X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X[g]	X[g]	
DAI-10							X[e]				X						X			X	X	
EQ-5D							X[e]				X						X			X	X	
Skin irritation assessment							X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Laboratory test [b]		X	X[d]		X		X[e]		X		X		X		X		X	X	X	X[g]	X[g]	
Pregnancy test [c]		X																		X	X	
12-lead ECG		X	X[d]		X		X[e]		X		X		X		X		X	X	X	X[g]	X[g]	
Body weight		X	X[d]	X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Body temperature, blood pressure, pulse rate		X	X[d]	X	X	X	X[e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse event monitoring			←																		→	

			DSP-5423 (tablet) treatment phase (6 weeks)					DSP-5423P treatment phase (52 weeks)													Discontinuation	Follow-up phase (1-2 weeks)
Visit No.	-	1	2	3	4	5	6	101	102	103	104	105	106	107	108	109	110	111	112	113		Follow-up visit
Study timeline [a)] Week	-	Screening	Timeline from initiation of DSP-5423 (tablet) administration Tab-Baseline	Tab-Week 1	Tab-Week 2	Tab-Week 4	Tab-Week 6 /baseline	Timeline from initiation of DSP-5423P application Week 1	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 36	Week 44	Week 52		6 ~ 17 days after completion of treatment or dicontinuation
Visit window (Day)		Tab -28~	Tab -2~1	Tab 5~11	Tab 12~18	Tab 26~32	Tab 40~43	5~11	12~18	26~32	40~46	54~60	78~92	106~120	134~148	162~176	190~204	239~267	295~323	351~379	At discontinuation +5	
Blood sampling for PK					X		X [e)]				X						X			X	X	
Questionnaire																				X	X	

a) DSP-5423 (tablet) date of initial administration is the Tab-Day 1, and DSP-5423P patch initiation/beginning Date is the Day 1.

b) DSP-5423 (tablet) Visit 2 before administration initiation/beginning (perform), DSP-5423 (tablet) at the end of administration period (Visit 6) and at the end of DSP-5423P patch period (Visit 113) always in in fasting state/conditions (End fast 10 hours prior to blood collection/drawing/sampling). Perform to in fasting state/conditions as much as possible in the rest of the Visit.

c) Pregnancy only perform in premenopausal women available.

d) Perform prior to administration initiation/beginning of DSP-5423 (tablet). Prior therapy If antipsychotics are present, prior therapy after termination of antipsychotics, perform prior to DSP-5423 (tablet) administration initiation/beginning.

e) Perform prior to initiation/beginning of attachment of the DSP-5423P.

f) In the event of termination to DSP-5423 (tablet) administration period, treatment compliance status, DIEPSS, C-SSRS, laboratory test, bone pregnancy laboratory test, 12-lead electrocardiogram, body weight, bone termination, and Visit survey, observation, and laboratory test of the survey, observation, and laboratory test of the adverse event at the time of body temperature ・blood pressure ・pulse rate, among others, perform status, laboratory test, pregnancy, laboratory test, 12-lead electrocardiogram.

g) Investigational drug except perform prior to administration initiation/beginning of antipsychotics.

Table 2 Schedule of Assessments (Cohort 2)

			DSP-5423Ptreatment phase (52 weeks)														Discontinuation	Follow-up phase (1-2 weeks)
Visit No.	-	1	2	101	102	103	104	105	106	107	108	109	110	111	112	113		Follow-up visit
Timeline from initiation of DSP-5423P application	-	Screening	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 36	Week 44	Week 52		6 ~ 17 days after completion of treatment or dicontinuation
Visit window (Day)		-28~	-2~1	5~11	12~18	26~32	40~46	54~60	78~92	106~120	134~148	162~176	190~204	239~267	295~323	351~379	At discontinuation +5	
Obtaining informed consent	X																	
Patient demographics and medical history		X																
Dispense study drug			X[d]	X	X	X	X	X	X	X	X	X	X	X	X			
Study treatment compliance				X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PANSS		X	X[d]	X	X	X	X	X	X	X	X	X	X	X	X	X[e]	X[e]	
CGI-S		X	X[d]	X	X	X	X	X	X	X	X	X	X	X	X	X[e]	X[e]	
DIEPSS			X[d]	X	X	X	X	X	X	X	X	X	X	X	X	X[e]	X[e]	
C-SSRS			X[d]	X	X	X	X	X	X	X	X	X	X	X	X	X[e]	X[e]	
DAI-10			X[d]				X						X			X	X	
EQ-5D			X[d]				X						X			X	X	
Skin irritation assessment			X[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Laboratory test [b]		X	X[d]		X		X		X		X		X	X	X	X[e]	X[e]	
Pregnancy laboratory test [c]		X														X	X	
12-lead ECG		X	X[d]		X		X		X		X		X	X	X	X[e]	X[e]	
Body weight		X	X[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Body temperature, blood pressure, pulse rate		X	X[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse event monitoring			←	—	—	—	—	—	—	—	—	—	—	—	—	—	—	→
Blood sampling for PK							X						X			X	X	
Questionnaire																X	X	

a) The Day 1 is a DSP-5423P patch initiation/beginning Date.

b) Before the initiation/beginning of DSP-5423P attachment (Visit 2) and at the completion of the period of DSP-5423P attachment (Visit 113), perform should be performed at the in fasting state/conditions (End fast 10 hours before blood collection/drawing/sampling). Perform to in fasting state/conditions as much as possible in the rest of the Visit.

c) Pregnancy only perform in premenopausal women available.
d) Perform prior to initiation/beginning of attachment of the DSP-5423P. Prior therapy If antipsychotics are present, prior therapy after termination of antipsychotics, perform prior to initiation/beginning of DSP-5423P placement.
e) Investigational drug except perform prior to administration initiation/beginning of antipsychotics.

5. Target sample size

Number of subjects enrolled: 200 subjects

- Number of subjects treated with DSP-5423P for 6 weeks and more in cohort 1: 50 subjects
- Number of subjects treated with DSP-5423P for 52 weeks in either cohort 1 or cohort 2: 100 subjects

The new enrollment can be terminated at the time when 100 subjects with 52-week exposure of DSP-5423P are collected, together with a separate confirmatory study [Confirmatory Study of DSP-5423P in Patients with Schizophrenia <Phase 3> (protocol: D4904020)].

6. Analysis population

Prior to database hard lock, a data review meeting will be conducted and subject assignments to analysis set/population will be determined.

6.1 Safety analysis population

Subjects with at least one application of DSP-5423P.

Efficacy analysis will also be performed based on the safety analysis population.

6.2 Pharmacokinetic analysis population

Subjects with at least one application of DSP-5423P, and with measurements of plasma bronanserin concentration after application of DSP-5423P.

7. Endpoints

7.1 Efficacy endpoints

1) Change in PANSS total score from baseline [note 1)]
2) Change in PANSS subscale total scores from baseline [note 1)]
3) Change in by PANSS 5 Factor Model total score from baseline [note 1)]
4) Change in CGI-S scores from baseline [note 1)]
5) Time to treatment discontinuation from the initial application of DSP-5423P

Note 1) Baseline of DSP-5423P treatment period

7.1.1 PANSS

The PANSS is an interview-based measure of the severity of psychopathology in adults with psychotic disorders. A person, who will be a certified rater for PANSS assessments, will receive specific training and education for the PANSS assessment provided by the Sponsor and will be certified by the Sponsor before his/her initial assessment of PANSS. The certified rater will rate 30 items on a 7-point scale of 1 to 7 and record dates and results of the assessments in the CRFs.

When the study treatment is completed or prematurely discontinued, PANSS will be rated before starting post-treatment with other antipsychotics.

The PANSS total score is the sum of all 30 item scores.

PANSS subscale

Positive subscale: Delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution, and hostility

Negative subscale: Blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking

General psychopathology subscale:
Somatic concern, anxiety, guilt feelings, tension, mannerisms and posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgment and insight, disturbance of volition, poor impulse control, preoccupation, and active social avoidance

Each PANSS subscale score is the sum of item scores defined respectively as each subscale.

PANSS 5 factors models

Negative symptoms: Blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, lack of spontaneity and flow of conversation, and active social avoidance

Excitement: Excitement, hostility, tension, and poor impulse control

Cognitive disorders: Conceptual disorganization, difficulty in abstract thinking, mannerisms and posturing, disorientation, and poor attention

Positive symptoms: Delusions, grandiosity, suspiciousness/persecution, and unusual thought content

Anxiety/depression: Hypochondria, anxiety, feelings of guilt, depression, and preoccupation

PANSS 5 factor model score is the sum of item scores defined respectively as each factor.

7.1.2 Clinical Global Impression – Severity of Illness (CGI-S)

CGI-S is a research rating tool of the subject's current disease state on a 7-point scale of 1 to 7. The Investigators will receive specific training before their initial assessment of CGI-S. Dates of the assessments and the results will be recorded in the CRFs.

When the study treatment is completed or prematurely discontinued, CGI-S will be rated before the first post-treatment with other antipsychotics.

7.1.3 DSP-5423P patch duration

The treatment duration of DSP-5423P will be the one from the initial application date to the last application date of DSP-5423P. Termination of application (for any reason) will be an event and

completion of treatment will be a censor. That is to say, time to event based on treatment duration from start to termination of treatment will be analyzed. In this analysis, subjects who complete study treatment will be censored not as an event, considering those subjects can pursue study treatment even after treatment completion.

7.2 Safety endpoints

1) Adverse events (AEs) and adverse drug reaction (ADRs)
2) Extrapyramidal AEs and ADRs
3) Skin-related AEs and ADRs at the application site
4) Assessment of skin irritation reaction at the application site
5) Change in Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS) Total Score (excluding overall severity) from baseline
6) Change in individual DIEPSS scores from baseline
7) Serum prolactin concentration
8) Electrocardiogram (ECG) parameters (QTc)
9) Concomitant use of antiparkinson drug
10) Assessment of suicides using Columbia-Suicide Severity Rating Scale(C-SSRS)
11) Laboratory test values, vital signs and body weight

7.2.1 Adverse event

In this study, relevant events occurred from the treatment initiation of DSP-5423 (tablet) to follow-up visit in cohort 1 and ones occurred from the initiation of DSP-5423P application to follow-up visit in cohort 2 will be captured as adverse events. An AE can, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease occurring after the administration of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product.

In the cohort 1, AEs that occur during the DSP-5423 (tablet) treatment period and worsen during the DSP-5423P application period will be recorded as both AEs in the DSP-5423 (tablet) administration period and also as AEs in the DSP-5423P application period with start date as the onset date of the worsening AE. AEs that occur during the DSP-5423 (tablet) treatment period without further worsening in the DSP-5423P application period will be recorded as AEs only in the DSP-5423 (tablet) treatment period

7.2.2 Concomitant drug and concomitant therapy

The following information on all medications used from initiation of DSP-5423(tablet) treatment until the follow-up visit in cohort1 or initiation of DSP-5423P application until the follow-up visit

in cohort 2 will be recorded in the CRFs. For antipsychotics and antiparkinson drugs, the information on the usage for 7 days before screening and during wash-out period will also be recorded in the CRFs.

- Drug name, Route, Start date, Stop date, The reason for concomitant use, Drug category
- Daily dose (for antipsychotics and antiparkinson drugs only)

7.2.3 Laboratory test

Blood and urine samples will be collected for clinical laboratory tests. The Investigators will record the date of collection and whether or not the subject is under fasting conditions (at least 10 hours after the last meal) in the CRFs. All clinical laboratory tests will be performed centrally.

The clinical laboratory tests required by the protocol are listed in Table 3. Detailed instructions regarding clinical laboratory procedures, sampling, shipping, and reporting can refer to the instructions manual provided by the Sponsor.

Table 3 Contents of laboratory variables

Hematology test	white blood cell count, red blood cell count, hemoglobin, hematocrit, platelet count, differential white blood cell count (neutrophils, eosinophils, basophils, monocytes, and lymphocytes)
Biochemical laboratory test	total protein, total bilirubin, AST, ALT, ALP, γ-GTP, LDH, total cholesterol, triglycerides, BUN, creatinine, CK, Na, K, Cl, blood glucose, HbA1c, serum prolactin
Urinalysis (qualitative)	glucose, protein, occult blood, urobilinogen
Pregnancy test (premenopausal women of childbearing potential only)	Urine chorionic gonadotropin

7.2.4 Vital Sign and Body Weight

Investigator measure the following variable and record Dates of measurements and the results in the CRFs

- Systolic and diastolic blood pressures (sitting), pulse rate, body temperature (axilla), and body weight

7.2.5 12-lead ECGs

The Investigator will perform 12-lead ECG at rest and record the dates and times of assessments in the CRFs. The Investigator will retain ECG tracings and send them electronically to the central ECG reader. The central ECG reader will analyze ECG tracings and calculate the following ECG parameters: RR interval, QT interval, PR interval, QRS interval, and QTc interval (QTc Fridericia [QTcF] and QTc Bazett [QTcB]). The central ECG reader will report analysis results and ECG

parameters to the Sponsor and the Investigator. Detailed instructions regarding12-lead ECG can refer to the instructions manual provided by the Sponsor

The principal ECG analyst will comprehensively evaluate the effect of study treatment on QTc prolongation.

- Bazett: QT_cB (msec) = QT (msec) / (RR (sec) x 1000)$^{1/2}$
- Fridericia: QT_cF (msec) = QT (msec) / (RR (sec) x 1000)$^{1/3}$

7.2.6 Drug-Induced Extrapyramidal Symptom Scale (DIEPSS)

The DIEPSS is a rating tool of extrapyramidal symptoms induced by antipsychotics and consists of 8 individual items; gait, bradykinesia, sialorrhea, muscle rigidity, tremor, akathisia, dystonia, and dyskinesia; and one global assessment; overall severity. The severity of each item is on a 5-point scale of 0 to 4. Dates of the assessments and the results will be recorded in the CRFs.

The DIEPSS total score (excluding overall severity) are the sum of the eight symptom scores.

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

The C-SSRS is a rating tool designed to systematically assess and track suicidal behavior and suicidal ideation throughout the study. The C-SSRS can comprehensively identify suicidal events and limit the over-identification of suicidal behavior.

The Investigators will receive specific training before their initial assessment of C-SSRS. Date of the assessments and the results will be recorded in the CRFs.

7.2.8 Skin irritation assessment

The Investigator will evaluate any skin reactions at the application sites according to the Table 4 and record the score in the CRFs. If more than one skin reaction from + − to ++++ is observed at the application sites, the stronger reaction will be scored and recorded in the CRFs.

Table 4 Scoring of Skin Reactions

Skin condition		Score
No response	Negative	−
Erythema of the mild	Faint erythema	+ −
Erythema	Erythema	+
Erythema + edema	Erythema + Edema	+ +
Erythema + edema + papules, serous papules, vesicles	Erythema + Edema + Papules, Serous papules, Vesicles	+ + +
Bulla major	Coalescing vesicles	+ + + +

7.3 Other assessments

7.3.1 DAI-10

DAI-10's is an assessment for evaluating a drug adherence by adding the patient’s attitude to the drug treatment compliance. Investigator will survey the subject's drug attitude ("true" or "false") for the following 10 items and record the assessment Date and the results to CRFs.

1) Good things about medication outweigh the bad
2) Feel like a zombie
3) Take of my own free choice
4) Feel more relaxed
5) Feel tired and sluggish
6) Take only when sick
7) Feel more normal
8) Unnatural for my mind and body to be controlled by medications
9) Thoughts are clearer
10) By staying on medication I can prevent a breakdown

7.3.2 EQ-5D

EQ-5D's is a self-administered, comprehensive rating scale developed to measure health-related quality of life. Investigator will use the questionnaire to investigate the following 5 items and record the assessment Date and the result to CRFs.

1) MOBILITY
   1: I have no problems in walking about,
   2: I have slight problems in walking about,
   3: I have moderate problems in walking about,
   4: I have severe problems in walking about,
   5: I am unable to walk about
2) SELF-CARE
   1: I have no problems washing or dressing myself,
   2: I have slight problems washing or dressing myself,
   3: I have moderate problems washing or dressing myself,
   4: I have severe problems washing or dressing myself,
   5: I am unable to wash or dress myself
3) USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)
   1: I have no problems doing my usual activities,
   2: I have slight problems doing my usual activities,
   3: I have moderate problems doing my usual activities,

4: I have severe problems doing my usual activities,

5: I am unable to do my usual activities.

4) PAIN / DISCOMFORT

1: I have no pain or discomfort,

2: I have slight pain or discomfort,

3: I have moderate pain or discomfort,

4: I have severe pain or discomfort,

5: I have extreme pain or discomfort

5) ANXIETY / DEPRESSION

1: I am not anxious or depressed,

2: I am slightly anxious or depressed,

3: I am moderately anxious or depressed,

4: I am severely anxious or depressed,

5: I am extremely anxious or depressed

7.3.3 Questionnaire on dosage form

Investigator will ask Question 1 and Question 2 regarding the patch dosage form of antipsychotic, Question 3 regarding the DSP-5423P, and record the assessment Date and the results to CRFs.

- Would you like the patch dosage form to be available??
  Response) "Yes" or "No"
- Is it easy for you to continue treatment with patches compared with tablets?
  Response) "Yes," "Equal" or "No."
- Question 3 Would you like to use the patches that you used during this study in the future?
  Response) "Yes" or "No"

7.4 Pharmacokinetic variable

7.4.1 Measurement

- Plasma concentration of bronanserin
- Plasma metabolite concentration

Cohort 1: M-1 (N-de-ethylated), M-2 (N-oxide), M-3 (7OH) (hydroxide), M-3 (8OH) (hydroxide), M-4 (ethylenediamine), and M-8 (carboxylic acid)

Cohort 2: M-1 (N-de-ethylated)

7.4.2 Survey variable

Investigator will record the following variable in CRFs. When subjects early terminate the study treatment, investigator will record the survey variables according to period at the time of termination [DSP-5423(tablet) or DSP-5423P].

DSP-5423 (tablet) treatment period:

Dates and times of blood sample collection, Dates and times of the last two administrations of DSP-5423 (tablet) before blood sample collection, DSP-5423 (tablet) doses of the last two administrations before blood sample collection, Yes or no for the question whether had a meal immediately before administrations of DSP-5423 (tablet) of the last two administrations before blood sample collection

DSP-5423P application period:

Dates and times of blood sample collection, Dates and times of the last two applications of DSP-5423P before blood sample collection, DSP-5423P doses of the last two applications before blood sample collection, Locations for the last two applications of DSP-5423P before blood sample collection

8. Statistical Analysis

8.1 General Considerations

For categorical variables, the number of subjects and percentage for each category will be calculated. Unless otherwise specified, all options in a category in CRFs should be presented regardless of whether they are actually selected. Missing (if no option in CRFs was selected) are presented as missing unless otherwise specified. The percentages are rounded to one decimal place. However, 0% is set to be a blank.

For continuous variables, summary statistic (n, Mean, SD, Min, Median, Max) will be calculated unless otherwise specified. Unless otherwise specified, mean and median should be rounded to one more decimal place of the observed value and SDs to two more of the observed value. If the summary statistic cannot be calculated (e.g., if the standard deviation is calculated with single data), period (.) should be presented. In summary of plasma drug concentration, the Geometric mean is rounded to one mode decimal place of observed value, and the CV% and Geometric CV% are rounded to one decimal place.

In summary of observed values and change, subjects with both baseline and each visit values are utilized for analysis.

All analyses will be conducted using SAS (Statistical Analysis System: SAS Institute, North Carolina, USA) version 9.4 or higher

8.2 Derived variables

When analysis is performed using derived variables, derived variables are handled without rounding, and the results are expressed with pre-specified digits. The derived variables in listing are presented based on pre-specified digits.

- BMI (kg/m²): Weight (kg) / (height (m) x height (m)). [one decimal point]
- Age at initial onset of schizophrenia (years): FLOOR ((onset date of initial episode – date of

birth)/365.25). [integer]

- Duration of illness (years): (date of informed consent – onset date of initial episode)/365.25. [integer]
- Duration of current episode (months): (date of informed consent – onset date of current episode)/ (365.25/12). [integer]

The following item are calculated for DSP-5423 (tablet) treatment period and DSP-5423P treatment period, respectively.

- Duration of exposure (days): Last dose date –first dose date +1 [integer]
- The first dose date and last dose date: the initial administration date and the final administration date for each period. The final application date for patch and the date for completion of the patch are identical and those are the final application date for patch, not final removal date for patch.
- Treatment compliance (%): (total number of tablets/patches actually taken/applied x 100) / total number of tablets/patches that should have been taken/applied during each treatment period. [integer] If number of tablets/patches actually taken/applied is unknown, the treatment compliance is set to a missing.
- Mean daily dose (mg/day): Average of prescribed daily dose (mg). [integer]
- Maximum daily dose (mg/day): Maximum of prescribed daily dose (mg). [integer]
- Modal daily dose (mg/day): Most frequently of prescribed daily dose (mg/day). In the case that two or more dose are the most frequent dose, the maximum of them will be the modal daily dose.
- Last daily dose (mg/day): Prescribed daily dose of the last dose date (mg/day). [integer]
- Cumulative dose (mg): Sum of prescribed daily dose (mg/day) x duration of each prescription (days). [integer]

  In calculation for number of tablets that should have been taken, if last date of prior description period and start date of following description period are same, prior description period are seen as up to day before of its last date. That is, the number of tablets prescribed and dose at last date of prior description period are seen as the number of tablets prescribed and dose in the subsequent period, and utilized for calculations.
- DAI-10 total score: sum of 1 (item 1,3,4,7,9, or 10 are true and item 2,5,6, or 8 are false) and −1 for other cases. [integer]
- Ratio of plasma metabolite concentration to plasma blonanserin concentration: plasma concentration of metabolite/plasma concentration of blonanserin [three decimal places]

8.3 Day 1

Day 1 is defined as the day of the initial application of DSP-5423P for each subject. Tab-Day1 is defined as the day of initial administration of DSP-5423(tablet) for subjects in Cohort 1.

8.4 Baseline

Baseline value for analysis (for the DSP-5423P treatment period) is defined as the last non-missing data on or prior to Day 1.

Regarding to Cohort 1, baseline value for the DSP-5423 (tablet) administration period (Tab-Baseline) is defined as the last non-missing data on or prior to the day of initial administration of DSP-5423(tablet).

8.5 Analysis Visit

Data of DSP-5423P treatment period is defined as the data captured on Day 1 through 7 days after the final application of DSP-5423P.

All data will be organized and analyzed according to the scheduled timing as outlined in Tables 1 and 2 Schedule of Assessments and according to the visit denoted in the CRFs. Unscheduled visits may not be used for any analysis unless otherwise specified. However, the data collected at the discontinuation visit within 7 days from the final application of study drug are mapped to the next scheduled visit of the actual discontinuation date. In listing, all data including unscheduled visit data should be presented.

1) CRF discontinuation visits in DSP-5423 (tablet) treatment period

Assessments and tests	Relative Day	Analysis Visit
PANSS, CGI-S, DIEPSS, body weight, body temperature, blood pressure, pulse rate	Tab-Day 1 to 11	Tab-W1, 2, 4, 6
	Tab-Day 12 to 18	Tab-W2, 4, 6
	Tab-Day 19 to 32	Tab-W4, 6
	Tab-Day 33 or later	Tab-W6
Laboratory test, ECG	Tab-Day 1 to 18	Tab-W2, 6
	Tab-Day 18 or later	Tab-W 6

The Tab-Day 1 is defined as the date of initial administration of DSP-5423 (tablet). CRF discontinuation visits in DSP-5423 (tablet) treatment period is defined as data on first non-missing (ex. no visit or results are missing) visit which meets all above requirements. Laboratory test and vital sign (body temperature, blood pressure, pulse rate) are performed visit handling for each item. Others are not considered as missing if they have any one component.

2) CRF discontinuation visits in DSP-5423P application period

Assessments and tests	Relative Day	Analysis Visit
PANSS, CGI-S, DIEPSS, C-SSRS,	Day 1 to 11	W1, 2, 4, 6, 8, 12, 16, 20, 24, 28, 36, 44, 52
	Day 12 to 18	W2, 4, 6, 8, 12, 16, 20, 24, 28, 36, 44, 52

Assessments and tests	Relative Day	Analysis Visit
Skin irritation assessment, body weight, body temperature, blood pressure, pulse rate	Day 19 to 32	W4, 6, 8, 12, 16, 20, 24, 28, 36, 44, 52
	Day 33 to 46	W6, 8, 12, 16, 20, 24, 28, 36, 44, 52
	Day 47 to 60	W8, 12, 16, 20, 24, 28, 36, 44, 52
	Day 61 to 92	W12, 16, 20, 24, 28, 36, 44, 52
	Day 93 to 120	W16, 20, 24, 28, 36, 44, 52
	Day 121 to 148	W20, 24, 28, 36, 44, 52
	Day 149 to 176	W24, 28, 36, 44, 52
	Day 177 to 204	W28, 36, 44, 52
	Day 205 to 267	W36, 44, 52
	Day 268 to 323	W44, 52
	Day 324 or later	W52
Laboratory test, ECG	Day 1 to 18	W2, 6, 12, 20, 28, 36, 44, 52
	Day 19 to 46	W6, 12, 20, 28, 36, 44, 52
	Day 47 to 92	W12, 20, 28, 36, 44, 52
	Day 93 to 148	W20, 28, 36, 44, 52
	Day 149 to 204	W28, 36, 44, 52
	Day 205 to 267	W36, 44, 52
	Day 268 to 323	W44, 52
	Day 324 or later	W52
DAI-10, EQ-5D, Plasma drug concentration	Day 1 to 46	W2, 6, 12, 20, 28, 36, 44, 52
	Day 47 to 204	W28, 36, 44, 52
	Day 205 or later	W52

Day 1 is defined as the day of the initial application of DSP-5423P for each subject. CRF discontinuation visits in DSP-5423P treatment period is defined as data on first non-missing (ex. no visit or results are missing) visit which meets all above requirements. Laboratory test and vital sign (body temperature, blood pressure, pulse rate) are performed visit handling for each item. Others are not considered as missing if they have any one component.

8.6 LOCF endpoint

The last observation from Day 1 through 7 days after the final application of DSP-5423P, except for baseline data defined in section 8.4, will be carried forward and will be defined as the Week 52 (LOCF).

8.7 Missing data

Individual missing item in any scale will not be imputed. For the rating scales that consist of more than one item, if any item is missing, then the total and subscale scores will also be handled as missing. In case that any value derived in EDC and one calculated along with the SAP are different, the later will be adopted for the analysis.

Missing/partial date will be imputed according to the following rules. In the listings, the original date without any imputation will be presented. The last visit date is the last date of visit among all visits including follow-up visits and unscheduled visits.

1) Adverse event

   End date should be imputed first, and then Start date will be imputed based on imputed end date.

   End Date:

   1. If ongoing is checked, no imputation will be performed.
   2. If ongoing is not checked and end date is totally missing or year is missing, then end date will be imputed as the last visit date.
   3. If only day of end date is missing, end date will be imputed as the earlier one of following dates: the last day of that month and the last visit date.
   4. If both month and day (or only month) of end date is missing, end date will be imputed as the earlier one of following dates: the last day (Dec31) in that year or the last visit date.

   Start Date:

   1. If start date is totally missing and end date is also missing (ongoing), no imputation will be performed. For subjects applied DSP-5423P, although the events are summarized as TEAE, those are not included in summaries by the initial onset date of the event.
   2. If start date is totally missing and end date is not missing, start date will be imputed as the earlier one of following dates: end date of AE or date of the initial application date of DSP-5423P.
   3. If only day of start date is missing, and start date is in the same year and month of initial application date of DSP-5423P, start date will be imputed as earlier one of following non-missing dates: end date of AE or date of the initial application date of DSP-5423P.
   4. If only day of start date is missing, and start date is not in the same month of initial application date of DSP-5423P, start date will be imputed as the first day in that month.
   5. If both month and day (or only month) of start date is missing, and start date is in the same year of initial application date of DSP-5423P, start date will be imputed as earlier

one of following non-missing dates: end date of AE or date of the initial application date of DSP-5423P.

6. If both month and day (or only month) of start date is missing, and start date is not in the same year of initial application date of DSP-5423P, start date will be imputed as the first day (Jan01) in that year.

2) Prior/Concomitant Medication

End Date:

1. If ongoing is checked, no imputation will be performed.
2. If ongoing is not checked and end date is totally missing or year is missing, then end date will be imputed as the last visit date.
3. If only day of end date is missing, end date will be imputed as the earlier one of following dates: the last day of that month and the last visit date.
4. If both month and day (or only month) of end date is missing, end date will be imputed as the earlier one of following dates: the last day (Dec31) in that year or the last visit date.

Start Date:

1. If the medication is 'started prior to study' (checked in the CRF), no imputation will be performed (That medication should be defined as prior medication).
2. If the medication is not 'started prior to study' (checked in the CRF) and start date is totally missing, no imputation will be performed (That medication should be defined as neither prior medication nor concomitant medication).
3. If only day of start date is missing, start date will be imputed as the first day in that month.
4. If both month and day (or only month) of start date is missing, start date will be imputed as the first day (Jan01) in that year.

3) Initial/Current Episode of Schizophrenia

For the purpose of the estimation of Duration of illness and duration of current episode, the day of onset date of initial/current episode will be imputed according to the followings;

1. If onset date is totally missing, no imputation will be performed.
2. If only date of onset date is missing, onset date will be imputed as the first day in that month.
3. If only month of onset date is missing, and onset date is in the same year of informed consent, onset date will be imputed as previous day of informed consent.
4. If only month of onset date is missing, and onset date is not in the same year of informed consent, onset date will be imputed as June 30th.

9. Statistical Method

All efficacy, safety and other analysis are based on Safety Analysis Population, and PK analysis are based on PK analysis population. All subjects and data collected will be presented in listings.

9.1 Subject Disposition

The subject will be categorized for each cohort.

1) Cohort 1

   Subjects with informed consent, subjects discontinued before administration of DSP-5423P (tablet), subjects took DSP-5423 (tablet) in DSP-5423 (tablet) treatment period, subjects who didn't apply DSP-5423P after completion of DSP-5423 (tablet), subjects who applied DSP-5423P in DSP-5423P application period, subjects who completed DSP-5423P application period, and subject who early terminated from DSP-5423P application period.

2) Cohort 2

   Subjects with informed consent, subjects discontinued before application of DSP-5423P, subjects took DSP-5423P in DSP-5423P application period, subjects who completed DSP-5423P application period, and subject who early terminated from DSP-5423P application period.

List of the study disposition, list of subject who discontinued the treatment of DSP-5423 (tablet) treatment period, and list of subject who discontinued the treatment of DSP-5423P application period.

9.2 Analysis Population

The number and percentage of subjects who are included in each analysis population or treated with DSP-5423P will be summarized for each cohort and cohort total. The list of analysis population and subjects who excluded from each population will be presented.

9.3 Important Protocol Deviations

IPDs will be discussed and determined at a blind data review meeting before DBL. Potential IPDs will be identified through data review by programmatically and manually and review for the deviation log. Subjects with potential IPDs can be, but not limited to:

- Subject who deviated inclusion/exclusion criteria
- Subject who took prohibited concomitant medication/therapy

The number of IPDs, and the number and percentage of subjects with IPD will be summarized by cohort and IPDs defined in Table 5. For Cohort1, IPDs in DSP-5423(tablet) treatment period and ones in DSP-5423P application period will be summarized separately. If a subject has same IPD multiple times, the subject will be counted only one times as such IPD. IPDs will be listed.

Table 5 Important Protocol Deviation Terminology

Categorized important protocol deviation
Deviation from the GCP
Deviation from the eligibility criteria
Use any prohibited medication or therapy
Others

9.4 Demographics and Other Baseline Characteristics

Demographic and baseline characteristics will be summarized based on each analysis population for each cohort and cohort total. They will be also listed. Baseline weight and BMI for Cohort 1 should be the one of DSP-5423(tablet) treatment period.

Sex: Female, Male

Age (years): summary statistics

Age by category: < 65; >= 65

Race: American Indian or Alaska Native; Asian; Black or African American;
Native Hawaiian or Other Pacific Islander; White; Other

Ethnicity: Hispanic or Latino; Not Hispanic or Latino

Height (cm): summary statistics

Weight (kg): summary statistics

BMI (kg/m^2): summary statistics

Any concomitant disease: No; Yes

Inpatient at informed consent: Inpatient; Outpatient

9.5 Psychiatric History

The summary statistic and the number and percentages will be summarized based on each analysis population for each cohort and cohort total. They will be also listed. Baseline PANSS, CGI-S and DIEPSS for Cohort 1 should be the one of DSP-5423(tablet) treatment period.

Number of episodes of schizophrenia: summary statistics

Number of episodes of schizophrenia: 1; 2; 3; 4; 5 or more, Unknown

Age at initial onset of schizophrenia (years): summary statistics

Age at initial onset of schizophrenia (years):
19 or less; 20 to 29; 30 to 39; 40 to 49; 50 or more

Duration of illness (years)*: summary statistics

Duration of illness (years)*:
< 1; >= 1 to < 5; >= 5 to < 10; >= 10 to < 20; >= 20 to < 30; >= 30, Unknown

Duration of current episode (months): summary statistics

PANSS composite subscale at baseline: Positive subscale score > Negative subscale score;
Positive subscale score = Negative subscale score;
Positive subscale score < Negative subscale score

Baseline PANSS total score: summary statistics

Baseline PANSS total score: 59 or less, 60 to 79, 80 or above

Baseline CGI-S score: summary statistics and frequency

Baseline DIEPSS total score (excluding overall severity): summary statistics

* at informed consent, 1 year = 365.25 days

9.6 Medical History

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) [Version 19.1], and number and percentage of subjects with any medical history by system organ class (SOC) and preferred term (PT), as well as ones of subjects with any concomitant disease, will be summarized for each cohort and cohort total. All medical history will be listed.

9.7 Prior and Concomitant Medications

For Cohort 1, prior medications are defined as those taken prior to initial dose of DSP-5423 (tablet). For Cohort 2, prior medications are defined as those taken prior to initial application of DSP-5423P. Prior medications will include medications that had been used before participation of the study, which are collected as “Started prior to study” on the CRF.

For Cohort 1, concomitant medications during DSP-5423 (tablet) treatment period are defined as those taken from the initial dose date of DSP-5423 (tablet) through the last dose date of DSP-5423 (tablet). For both Cohort 1 and Cohort 2, concomitant medications during DSP-5423P application period are defined as those taken from the initial application date of DSP-5423P through the last application date of DSP-5423P. Note that the concomitant and prior medications are not mutually exclusive, ie, a medication can be classified as both prior and concomitant medication.

Prior and concomitant medications will be coded using the WHO Drug Dictionary [March 1, 2014 version], Anatomical Therapeutic Chemical (ATC) Classification codes and preferred term (PT, Standardized Medication Name), and summarized for each cohort and cohort total. The number and percentage of subjects who took prior or concomitant medications will be summarized as well.

Prior and concomitant medications will be summarized as the number and percentage of subjects by ATC level and PT for each cohort. If a subjects took same medications in terms of ATC level or PT multiple times, the subject will be counted one time into associated ATC level or PT. In addition, Prior and concomitant medications will be summarized as to following categories defined on the CRF;

Antipsychotics

Antiparkinson drugs

Psychotropic drugs

Hypnotic drugs

The number and percentage of subjects with concomitant use of antiparkinson drugs will be summarized by cohorts and visits. Denominator for visit base summary will be subjects who received DSP-5423 (tablet) during relevant periods or subjects who received DSP-5423P during relevant periods. Note that denominator at Day -1 and one for overall period will be all subjects in Safety Analysis Population. Subgroup analysis for subjects who didn't use antiparkinson drugs at Day -1 will be repeated in the same fashion.

DSP-5423 (tablet) treatment period: (overall)

DSP-5423P application period: Day -1, Week 1 to 2, 3 to 4, 5 to 6, 7 to 12, 13 to 24, 25 to 36, 37 or later, overall (Week 1=Day 1 to 7, Week 2=Day 8 to 14)

Prior or concomitant mediations will be listed respectively.

9.8 Treatment Compliance

The percentage of treatment compliance will be calculated for DSP-5423 (tablet) or DSP-5423P according to derivation in section 8.2. Treatment Compliant is defined as a subject with 80% to 120% compliance in condition with no rounding for treatment compliance. Other subjects and also subjects with missing treatment compliance will be seen as non-compliant to study treatment. Summary statistics of treatment compliance will be calculated by visits for each cohort and cohort total as well as the number and percentage of subjects who dropped into the following categories. Treatment compliance will be listed with rounding to one decimal point.

Treatment Compliance: <80%; 80% to 120%; >120%

9.9 Duration of Exposure

Duration of exposure will be calculated following section 8.2. Summary statistics will be calculated by visits for each cohort and cohort total as well as the number and percentage of subjects who dropped into the following categories. Duration of exposure will be listed.

Duration of Exposure (days):

DSP-5423 (tablet) treatment period: 1 to 7; 8 to 14; 15 to 28; 29 to 43; 44 or more

DSP-5423P application period:

1 to 42; 43 to 84; 85 to 168; 169 to 252; 253 to 336; 337 or more

9.10 Daily dose and Cumulative dose

Each kind of daily dose will be calculated following section 8.2. Mean daily dose (mg/day), Maximum daily dose (mg/day) and Modal daily dose (mg/day) will derived as specified in section

8.2. Those summary statistics will be calculated by visits for each cohort and cohort total, and also the number and percentage of subjects with each dose will be summarized. Those daily doses will be listed.

Cumulative dose will be calculated as specified in section 8.2 and its summary statistics will be calculated by visits for each cohort and cohort total. Cumulative dose will be listed.

9.11 Efficacy Analysis

The efficacy analysis will be performed for each cohort based on safety analysis population.

9.11.1 PANSS Total Score

Observed PANSS total score and change from baseline of DSP-5423P application period will be summarized by visits (including LOCF endpoint) for each cohort. The overtime change of mean of the change from baseline of DSP-5423P application period will be plotted for each cohort with +/-SD.

For DSP-5423(tablet) treatment period in Cohort 1, observed PANSS total score and change from baseline of DSP-5423(tablet) treatment period will be summarized by visits. For both DSP-5423(tablet) and DSP-5423P periods in Cohort 1, the overtime change of mean of the change from baseline of DSP-5423(tablet) treatment period will be plotted with +/-SD.

PANSS score will be listed.

9.11.2 PANSS subscale scores and PANSS five-factor model scores

PANSS subscale scores and PANSS five-factor model scores will be summarized in same fashion as PANSS total score, and listed.

9.11.3 Clinical Global Impression - Severity of Illness (CGI-S)

Observed CGI-S score and change from baseline of DSP-5423P application period will be summarized by visits (including LOCF endpoint) for each cohort. The overtime change of mean of the change from baseline of DSP-5423P application period will be plotted for each cohort with +/-SD.

For DSP-5423(tablet) treatment period in Cohort 1, observed CGI-S score and change from baseline of DSP-5423(tablet) treatment period will be summarized by visits. For entire period in Cohort 1, the overtime change of mean of the change from baseline of DSP-5423(tablet) treatment period will be plotted with +/-SD.

CGI-S score will be listed.

9.11.4 Time to Treatment Discontinuation

All cause discontinuation of DSP-5423P is considered as an event and completion of DSP-5423P

application is considered as a censor, and Kaplan-Meier estimate for 50 percentiles and its 95% CI for time to event will be analyzed. Also the number and percentage of subjects who applied DSP-5423P for 28 weeks or 52 weeks will be summarized. Those analyses will be performed for each cohort overall and also by use of prior antipsychotics (Blonanserin and Other/None).

The final application date of DSP-5423P can be either event date or date of censored. Kaplan-Meier plots for each cohort will be provided. One for each cohort by use of prior antipsychotics will also be provided. Time to Treatment Discontinuation will be listed.

9.11.5 Subgroup analysis for efficacy

For each subgroup, observed PANSS total score and change from baseline of DSP-5423P application period will be summarized by visits (including LOCF endpoint) for each cohort.

Subgroups include Sex, Age (years), use of Prior antipsychotics, Hospitalization status at Screening, Duration of illness (years), and Baseline PANSS total score specified as following. A subject with missing value will not be included in appropriate summary and then 'missing' category is not expected to be presented in the tables.

Sex: Male, Female

Age (years): < 65, >= 65

Prior antipsychotics: No, Yes

Duration of illness (years): < 5, >= 5 to < 10, >= 10 to < 20, >= 20, Unknown

Hospitalization status at Screening: Inpatient, Outpatient

Baseline PANSS total score: 59 or less, 60 to 79, 80 or above

9.12 Safety Analysis

Safety analysis will be performed for each cohort and cohort total based on safety population, besides C-SSRS summaries only for each cohort.

9.12.1 Adverse event

The adverse event will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), Version 19.1. Treatment-emergent adverse event (TEAE) is defined as adverse events with start date on or after Day 1. Regardless of cohort, adverse events occurred on same date as the initial date of application of DSP-5423P will be defined as TEAE. All adverse events, regardless of TEAE or not, will be listed. A treatment-related TEAE is defined as a TEAE for which the causal relationship to the study treatment is either 'definite', 'probable', or 'possible'.

The summary of TEAE will include the number of event, and the number and percentage of subjects which are classified in the following TEAE or treatment-related TEAE categories. Extrapyramidal (EPS) adverse event will be defined based on MedDRA PT and determined at blinded data review meeting. The skin-related adverse event will be defined as an adverse event

with any application sites collected on EDC.

Adverse event (any TEAE)

Death (TEAE leading to death)

Serious adverse event (serious TEAE)

Adverse event leading to treatment discontinuation
(TEAE leading to treatment discontinuation)

Severe adverse event (severe TEAE)

Extrapyramidal adverse event (extrapyramidal TEAE)

Skin-related adverse event at the application site (skin related TEAE)

The number and percentage of subjects who have TEAE or treatment-related TEAE will be summarized by SOC/PT for each cohort. If a subject has multiple events categorized in same SOC/PT, the subject will be counted only one time into the SOC/PT. SOCs are sorted by alphabetically and PTs are sorted within SOC in descending order of frequency of cohort total. If there are ties, PTs are sorted by alphabetically. TEAE leading to treatment discontinuation will be summarized in the same manner.

Common TEAE are PT of TEAEs experienced by 2% or more subjects in cohort total. Common TEAE and common treatment-related TEAE will be summarized by SOC/PT.

The number and percentage of subjects who have TEAE or treatment-related TEAE will be summarized by SOC/PT and maximum severity. For this summaries, if a subject experienced more than one episode of a TEAE within a PT, the subject is counted only once in the PT at the maximum severity. If the maximum severity is missing, the episode will be kept as missing (not specified). In determining maximum severity, severities are ranked from missing (not specified), mild, moderate, to severe.

The number and percentage of subjects who have TEAE or treatment-related TEAE will be summarized by SOC/PT and first onset date. If a subject experienced more than one event within a PT, the subject is counted only once in the PT based on the earliest event started on the same or closer to Day 1. Denominator of percentage for each period of interest is the number of subjects who were treated with DSP-5423P in each period.

Onset: Day 1 to 7, Day 8 to 14, Day 15 to 28, Day 29 to 42; Week 1 to 6;
Week 1 to 13; Week 14 to 26; Week 27 to 39; Week 40 or later
(Week 1=Day 1 to 7, Week 2=Day 8 to 14)

As TEAE of interests, Extrapyramidal TEAE and skin related TEAE will be summarized by SOC/PT. Additionally, those TEAE will be summarized by maximum severity or first onset date in same manner as summaries of TEAE. In summary tables, the frequencies for entire TEAE related to extrapyramidal symptoms or TEAE related to skin, not just by SOC/PT, will be presented.

Adverse events and extrapyramidal adverse events started during DSP-5423(tablet) treatment period of Cohort 1, meaning Tab-Day 1 to Day -1 will be summarized by SOC/PT.

Listings for adverse events, AE leading to death, SAE, AE leading to treatment discontinuation, Extrapyramidal AE and skin related AE will be generated. Both TEAE and pre-treatment event which started before Day 1, will be included in those listings. In the listing for skin related AE, the application site will also be presented.

The adverse events during DSP-5423(tablet) treatment period of Cohort 1 will be listed.

9.12.2 Laboratory test

Observed values and changes from baseline at DSP-5423P application period for the hematology, and blood chemistry parameters will be summarized by visits including LOCF endpoints. For urinalysis parameters, the number and percentage of subjects in each category of parameters will be summarized at baseline of DSP-5423P application period, each visit, and LOCF endpoint. All laboratory parameters and any abnormal laboratory values, which are all values beyond its own normal range at least one time whenever in DSP-5423P application period, will be listed respectively.

Criteria for Markedly Abnormal Post-Baseline Laboratory Values(MAPLV) for abnormal values in the hematology, and blood chemistry parameter can be found in Table 6. The frequencies and percentages of subjects who met MAPLV at least once in the post-baseline of DSP-5423P (including unscheduled visits), will be presented.

Table 6 Criteria for Markedly Abnormal Post-Baseline Laboratory Values

Hematology Parameter	**Markedly Abnormal Range**
Hemoglobin	Male: <= 11.5 g/dL
	Female: <= 9.5 g/dL
Hematocrit	Male: <= 37%
	Female: <= 32%
WBC	<= 2.8 x 10^3/uL
	>= 16 x 10^3/uL
Platelets	<= 75 x 10^3/uL
	>= 700 x 10^3/uL
Chemistry Parameter	**Markedly Abnormal Range**
ALT	>= 3 x ULN
AST	>= 3 x ULN
Alkaline Phosphatase	>= 1.5 x ULN
Na/Sodium	< 130 mEq/L

	> 150 mEq/L
K/Potassium	< 3 mEq/L
	> 5.5 mEq/L
Cl/Chloride	< 90 mEq/L
	> 115 mEq/L
Blood Glucose (fasting)	< 50 mg/dL
	> 250 mg/dL
HbA1c	>= 7.5%
Total Bilirubin	> 2 x ULN
Blood Urea Nitrogen	> 30 mg/dL
Creatinine	> 2.0 mg/dL
CK	> 3 x ULN
Serum Prolactin	>= 5 x ULN
Triglycerides (fasting)	> 300 mg/dL
Total Cholesterol (fasting)	> 300 mg/dL

Note: A value is considered MAPLV if it is outside the Markedly Abnormal Range.
Note: Blood glucose, triglycerides, and total cholesterol are limited for blood samples collected in fasting state.

Box plot of observed value of the hematology and blood chemistry parameters will be provided by visits including baseline of DSP-5423P application period and LOCF endpoint.

For DSP-5423(tablet) treatment period in Cohort 1, observed values and changes from baseline at DSP-5423(tablet) treatment period for the hematology, and blood chemistry parameters will be summarized by visits including LOCF endpoints. For urinalysis parameters, the number and percentage of subjects in each category of parameters will be summarized at baseline of DSP-5423(tablet) treatment period, each visit, and LOCF endpoint. Box plot of observed value of the hematology and blood chemistry parameters will be provided by visits including baseline of DSP-5423(tablet) treatment period.

9.12.3 Vital sign and body weight

BMI is calculated based on the height at Screening and weight at each visit.

Observed values and changes from baseline at DSP-5423P application period for the vital sign, weight and BMI will be summarized by visits including LOCF endpoints. The vital sign, weight and BMI will be listed.

Criteria for Markedly Abnormal Post-Baseline Vital Signs (MAPVS) for abnormal values in the vital sign can be found in Table 7. The frequencies and percentages of subjects who met MAPVS criteria at least once in the DSP-5423P post-baseline (including unscheduled visits) will be

presented. Weights for subjects with values met MAPVS criteria in DSP-5423P post-baseline period (including unscheduled visits) will be listed.

Table 7 Criteria for Markedly Abnormal Post-Baseline Vital Signs

Parameter	Unit	Markedly low	Markedly high
Weight	Kg	>= 7% decreased from baseline	>= 7% increased from baseline

Box plot of observed value of the vital sign, weight and BMI will be provided by visits including baseline at DSP-5423P application period and LOCF endpoint.

For DSP-5423(tablet) treatment period in Cohort 1, observed values and changes from baseline in DSP-5423(tablet) treatment period for the vital sign, weight and BMI will be summarized by visits including LOCF endpoints. Box plot of observed value of the vital sign, weight and BMI will be provided by visits including baseline of DSP-5423(tablet) treatment period for both DSP-5423(tablet) treatment period and DSP-5423P application period in Cohort 1.

9.12.4 12-lead ECGs

Observed values and changes from baseline in DSP-5423P treatment period for ECG parameters (RR interval, QT interval, PR interval, QRS interval, and QTc interval (QTc Fridericia [QTcF] and QTc Bazett [QTcB]) will be summarized by visits including LOCF endpoints. Interpretation, which is 'Normal', 'Abnormal', or 'Not evaluable', will be summarized based on the number and percentage of subjects by visits including LOCF endpoints. In case that finding are identified in a subject, and his/her interpretation is 'Normal', the subject will be summarized as 'Normal'. The ECG parameters will be listed. The ECG parameters for subjects who experienced 'Abnormal' at least once in the DSP-5423P post-baseline (including unscheduled visits) will be listed.

The number and percentage of subjects met have QTcB or QTcF criteria in Table 8 will be summarized. The ECG parameters for subjects who met the criteria in Table 8 at least once in the DSP-5423P post-baseline (including unscheduled visits) will be listed.

Table 8 QT Prolongation

QTc Prolongation
QTc > 450 msec
QTc > 480 msec
QTc > 500 msec
Increased from baseline > 30 msec
Increased from baseline > 60 msec

For DSP-5423(tablet) treatment period in Cohort 1, observed values and changes from baseline in DSP-5423(tablet) treatment period for the ECG parameters will be summarized by visits including LOCF endpoints.

9.12.5 DIEPSS

Observed values and changes from baseline in DSP-5423P application period in DIEPSS total score excluding overall severity and item scores will be summarized by visits (including LOCF endpoint). The overtime change from baseline of DSP-5423P application period in DIEPSS total score excluding overall severity will be plotted for each cohort with +/-SD.

For DSP-5423(tablet) treatment period in Cohort 1, observed value and change from baseline in DSP-5423(tablet) treatment period in DIEPSS total score excluding overall severity and item scores will be summarized by visits. For both DSP-5423(tablet) and DSP-5423P periods in Cohort 1, the overtime change from baseline of DSP-5423(tablet) treatment period in DIEPSS total score excluding overall severity will be plotted with +/-SD.

DIEPSS total score and item scores will be listed.

9.12.6 C-SSRS

C-SSRS will be summarized for each cohort and cohort total, and baseline for Cohort 1 is defined as baseline at DSP-5423(tablet) treatment period and one for Cohort 2 is defined as baseline at DSP-5423P application period.

For ‘Suicidal ideation’, the number and percentage of subjects by items, with any suicidal ideation, with no suicidal ideation, with serious suicidal ideation defined as ‘Yes’ in item 4 or item 5, will be summarized at baseline, each visit, entire DSP-5423(tablet) treatment period, and entire DSP-5423P application period.

Suicidal ideation

1. Wish to be dead
2. Non-specific active suicidal thoughts
3. Active suicidal ideation with any methods [not plan] without intent to act
4. Active suicidal ideation with some intent to act, without specific plan
5. Active suicidal ideation with specific plan and intent

For ‘Suicidal behavior’, the number and percentage of subjects by items, with any suicidal behavior, and with no suicidal behavior will be summarized at baseline, each visit, entire DSP-5423(tablet) treatment period, and entire DSP-5423P application period.

Suicidal behavior

1. Any actual attempts

2. Any interrupted attempts
3. Any aborted attempts
4. Any preparatory acts or behavior

The number and percentage of subjects with either suicidal ideation or suicidal behavior as 'any suicidality', and with no suicidality will be summarized at baseline, each visit, entire DSP-5423(tablet) treatment period, and entire DSP-5423P application period.

The subjects* with 'emergence of suicidal ideation' defined as subjects without suicidal ideation at baseline, but not in post-baseline of DSP-5423P application period, subjects* with 'serious emergence of suicidal ideation' defined as subjects with 'No' in both item 4 and item 5**, but not in post-baseline of DSP-5423P application period, subjects* with 'emergence of suicidal behavior' defined as subjects with no suicidal behavior at baseline, but not in post-baseline of DSP-5423P application period, subjects* with "emergence of suicidality" defined as subjects with neither suicidal ideation nor suicidal behavior, but either/both in post-baseline of DSP-5423P application period, subjects with 'any completed suicide', will be summarized based on the number and percentages.

* Subject with 'Yes' at baseline are not included in the denominator of percentages.

** If item 2 of suicidal ideation is 'No', and item 3, 4, and 5 are null, item 3, 4, and 5 are counted as 'No'. The C-SSRS is designed to ask item 3, 4, and 5 to subjects only when item 2 is 'Yes'.

C-SSRS will be listed.

9.12.7 Skin irritation assessment

The number and percentages of subjects in each score of skin irritation assessment will be summarized by visits, baseline in DSP-5423P application period, each visit, LOCF endpoint, and also maximum score throughout the DSP-5423P post-baseline period. Skin irritation assessment scores will be listed.

9.12.8 Subgroup analysis for safety

The summary of TEAE and treatment-related TEAE and also their summary by SOC/PT will be presented by subgroups. The subgroups include Sex, Age(years), Duration of illness (years), and Hospitalization status at Screening defined as below. Subjects with missing data for any subgroup categories will not be included subgroup analysis without setting 'missing' category.

Sex: Male, Female

Age (years): < 65, >= 65

Duration of illness (years): < 5, >= 5 to < 10, >= 10 to < 20, >= 20, Unknown

Hospitalization status at Screening: Inpatient, Outpatient

9.13 Analysis of Other endpoints

All analysis of other endpoints will be conducted based on Safety population by each cohort and cohort total.

9.13.1 DAI-10

DAI-10 item scores will be summarized at baseline of DSP-5423P application period, each visit, and LOCF endpoints using number and percentage of subjects. For DAI-10 total score, the number and percentage of subjects and also descriptive summaries in change from baseline of DSP-5423P application period will be provided by each visit including LOCF endpoints. DAI-10 will be listed.

9.13.2 EQ-5D

For EQ-5D item scores, the number and percentage of subjects by scores will be summarized at baseline of DSP-5423P application period, each visit and LOCF endpoint. Observed value and change from baseline of DSP-5423P application period in EQ-5D Index value （QS.QTESTCD=EQTOT）will be summarized by each visit and LOCF endpoints. EQ-5D will be listed.

9.13.3 Questionnaire on dosage form

The number and percentage of subjects by each question at LOCF endpoint will be summarized. Summary will be repeated for subjects who completed the study, discontinued the study, and overall. Questionnaire on dosage form will be listed.

9.14 Pharmacokinetic analysis

9.14.1 Plasma drug concentration

Summary statistics of plasma concentrations of blonanserin and metabolites specified in section 7.4.2, will be calculated by visits for each cohort and cohort total. Summary statistics will include n, Mean, SD, Min, Median, Max, CV%, Geometric Mean and Geometric CV%. This analysis will be repeated by visits, cohorts including cohort total, the latest dose prior to the PK sampling (ie, 40, 60, or 80 MG), and the latest application site (abdomen, back, chest, overall). For DSP-5423(tablet) administration period in Cohort 1, this analysis will also be repeated by fasting status, fasting, non-fasting and overall. The BLQ will not be included in the summary statistics.

Additionally, Summary statistics of the ratio of plasma concentration of metabolites to blonanserin (ie, M1/blonanserin) will be calculated by visits for each cohort and cohort total.

Plasma drug concentration and the ratio of plasma concentration of metabolites to blonanserin will be listed.

9.14.2 Subgroup analysis

Summary statistics of plasma concentration of blonanserin, and metabolites will also be summarized by subgroup. Subgroups will include sex and age group.

Sex: Male; Female

Age (years): < 65; >= 65

10. Appendix

10.1 SAS Code

Kaplan-Meier

```
Proc lifetest plots=survival(atrisk) outsurv=sdf;
   Strata COHORT;
   Time TTE*CENSOR(1);
   Ods output quartiles=MST;
* TTE is time to discontinuation (ie, the last dose date – the first dose date + 1);
* If completer then CENSOR=1; else CENSOR=0;
* SURVIVAL, SDF_LCL, SDF_UCL variables in OUTSURV dataset will be tabulated where the TTE
is closest (and smaller) to 28 weeks (196 days) and 52 weeks (364 days);
```

10.2 Title of Tables, Listings, and Figures

No	Title	Population
Table 14.1.1	Disposition	All Patients
Table 14.1.2	Analysis Population	Subjects treated with DSP-5423P
Table 14.1.3.1	Important Protocol Deviations – DSP-5423P Treatment Phase	Subjects treated with DSP-5423P
Table 14.1.3.2	Important Protocol Deviations – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.1.4.1	Demographics and Baseline Characteristics	Safety Population
Table 14.1.4.2	Demographics and Baseline Characteristics	PK Analysis Population
Table 14.1.5.1	Psychiatric History	Safety Population
Table 14.1.5.2	Psychiatric History	PK Analysis Population
Table 14.1.6	Concomitant Diseases	Safety Population
Table 14.1.7.1	Prior Medications by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.2	Prior Medications of Special Interest (Antipsychotics) by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.3	Prior Medications of Special Interest (Antiparkinson Drugs) by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.4	Prior Medications of Special Interest (Psychotropic Drugs) by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.5	Prior Medications of Special Interest (Hypnotic Drugs) by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.6	Concomitant Medications in DSP-5423P Treatment Phase by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.7	Concomitant Medications in DSP-5423 (tablet) Treatment Phase by ATC Classification and Preferred Name	Subjects treated with DSP-5423 (tablet)
Table 14.1.7.8	Concomitant Medications of Special Interest (Antipsychotics) by ATC Classification and Preferred Name	Safety Population

No	Title	Population
Table 14.1.7.9	Concomitant Medications of Special Interest (Antiparkinson Drugs) by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.10	Concomitant Medications of Special Interest (Psychotropic Drugs) by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.11	Concomitant Medications of Special Interest (Hypnotic Drugs) by ATC Classification and Preferred Name	Safety Population
Table 14.1.7.12	Concomitant Use of Antiparkinson Drugs – DSP-5423P Treatment Phase	Safety Population
Table 14.1.7.13	Concomitant Use of Antiparkinson Drugs – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.1.8.1	Treatment Compliance – DSP-5423P Treatment Phase	Safety Population
Table 14.1.8.2	Treatment Compliance – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.1.9.1	Duration of Exposure to Study Drug – DSP-5423P Treatment Phase	Safety Population
Table 14.1.9.2	Duration of Exposure to Study Drug – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.1.10.1	Daily Dose and Cumulative Dose of Study Drug – DSP-5423P Treatment Phase	Safety Population
Table 14.1.10.2	Daily Dose and Cumulative Dose of Study Drug – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.2.1.1	Positive and Negative Syndrome Scale (PANSS) Total Score – DSP-5423P Treatment Phase	Safety Population
Table 14.2.1.2	Positive and Negative Syndrome Scale (PANSS) Total Score – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.2.2.1	Positive and Negative Syndrome Scale (PANSS) Subscale Scores – DSP-5423P Treatment Phase	Safety Population
Table 14.2.2.2	Positive and Negative Syndrome Scale (PANSS) Subscale Scores – DSP-5423 (tablet) Treatment Phase	Subjects treated with

No	Title	Population
		DSP-5423 (tablet)
Table 14.2.2.3	Positive and Negative Syndrome Scale (PANSS) 5 Factor Scores – DSP-5423P Treatment Phase	Safety Population
Table 14.2.2.4	Positive and Negative Syndrome Scale (PANSS) 5 Factor Scores – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.2.3.1	Clinical Global Impression-Severity of Illness (CGI-S) – DSP-5423P Treatment Phase	Safety Population
Table 14.2.3.2	Clinical Global Impression-Severity of Illness (CGI-S) – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.2.4	Time to All-Cases Treatment Discontinuation – DSP-5423P Treatment Phase	Safety Population
Table 14.2.5	Time to All-Cases Treatment Discontinuation by Prior Antipsychotics – DSP-5423P Treatment Phase	Safety Population
Table 14.2.5.1	Positive and Negative Syndrome Scale (PANSS) Total Score by Sex – DSP-5423P Treatment Phase	Safety Population
Table 14.2.5.2	Positive and Negative Syndrome Scale (PANSS) Total Score by Age – DSP-5423P Treatment Phase	Safety Population
Table 14.2.5.3	Positive and Negative Syndrome Scale (PANSS) Total Score by Prior Antipsychotics Status – DSP-5423P Treatment Phase	Safety Population
Table 14.2.5.4	Positive and Negative Syndrome Scale (PANSS) Total Score by Duration of Illness – DSP-5423P Treatment Phase	Safety Population
Table 14.2.5.5	Positive and Negative Syndrome Scale (PANSS) Total Score by Hospitalization Status at Screening – DSP-5423P Treatment Phase	Safety Population
Table 14.2.5.6	Positive and Negative Syndrome Scale (PANSS) Total Score by Baseline PANSS Total Score – DSP-5423P Treatment Phase	Safety Population
Table 14.3.1.1	Summary of Treatment-Emergent Adverse Events	Safety Population
Table 14.3.1.2	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Safety Population
Table 14.3.1.3	Common (>=2%) Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Safety Population

No	Title	Population
Table 14.3.1.4	Treatment-Emergent Adverse Events by Maximum Severity, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.5	Common (>=2%) Treatment-Emergent Adverse Events by Maximum Severity, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.6	Treatment-Emergent Adverse Events by First Onset Time, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.7	Common (>=2%) Treatment-Emergent Adverse Events by First Onset Time, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.8	Treatment-Emergent Adverse Events Related to Study Treatment by First Onset Time, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.9	Common (>=2%) Treatment-Emergent Adverse Events Related to Study Treatment by First Onset Time, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.10	Treatment-Emergent Extrapyramidal Adverse Events by System Organ Class and Preferred Term	Safety Population
Table 14.3.1.11	Treatment-Emergent Adverse Events Related to Skin by System Organ Class and Preferred Term	Safety Population
Table 14.3.1.12	Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term	Safety Population
Table 14.3.1.13	Summary of Treatment-Emergent Adverse Events by Sex	Safety Population
Table 14.3.1.14	Summary of Treatment-Emergent Adverse Events by Age	Safety Population
Table 14.3.1.15	Summary of Treatment-Emergent Adverse Events by Duration of Illness	Safety Population
Table 14.3.1.16	Summary of Treatment-Emergent Adverse Events by Hospitalization Status at Screening	Safety Population
Table 14.3.1.17	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term by Sex	Safety Population
Table 14.3.1.18	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term by Age	Safety Population
Table 14.3.1.19	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term by Duration of Illness	Safety Population
Table 14.3.1.20	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term by Hospitalization Status	Safety Population

No	Title	Population
	at Screening	
Table 14.3.1.21	Adverse Events in DSP-5423 (tablet) Treatment Phase by System Organ Class and Preferred Term	Subjects treated with DSP-5423 (tablet)
Table 14.3.1.22	Extrapyramidal Adverse Events in DSP-5423 (tablet) Treatment Phase by System Organ Class and Preferred Term	Subjects treated with DSP-5423 (tablet)
Table 14.3.1.23	Treatment-Emergent Extrapyramidal Adverse Events by Maximum Severity, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.24	Treatment-Emergent Adverse Events Related to Skin by Maximum Severity, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.25	Treatment-Emergent Extrapyramidal Adverse Events by First Onset Time, System Organ Class, and Preferred Term	Safety Population
Table 14.3.1.26	Treatment-Emergent Adverse Events Related to Skin by First Onset Time, System Organ Class, and Preferred Term	Safety Population
Table 14.3.4.1	Clinical Laboratory Data – Blood Chemistry – DSP-5423P Treatment Phase	Safety Population
Table 14.3.4.2	Clinical Laboratory Data – Blood Chemistry – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.3.4.3	Clinical Laboratory Data – Hematology – DSP-5423P Treatment Phase	Safety Population
Table 14.3.4.4	Clinical Laboratory Data – Hematology – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.3.4.5	Clinical Laboratory Data – Urinalysis – DSP-5423P Treatment Phase	Safety Population
Table 14.3.4.6	Clinical Laboratory Data – Urinalysis – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)

No	Title	Population
Table 14.3.4.7	Markedly Abnormal Post-Baseline Clinical Laboratory Values – DSP-5423P Treatment Phase	Safety Population
Table 14.3.5.1	Vital Signs and Body Weight – DSP-5423P Treatment Phase	Safety Population
Table 14.3.5.2	Vital Signs and Body Weight – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.3.5.3	Markedly Abnormal Post-Baseline Vital Signs – DSP-5423P Treatment Phase	Safety Population
Table 14.3.6.1	Electrocardiogram Parameters – DSP-5423P Treatment Phase	Safety Population
Table 14.3.6.2	Electrocardiogram Parameters – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.3.6.3	Electrocardiogram Abnormality – DSP-5423P Treatment Phase	Safety Population
Table 14.3.6.4	Markedly Abnormal Post-Baseline Values - Electrocardiogram – DSP-5423P Treatment Phase	Safety Population
Table 14.3.7.1	Drug-Induced Extrapyramidal Symptom Scale (DIEPSS) Total Score – DSP-5423P Treatment Phase	Safety Population
Table 14.3.7.2	Drug-Induced Extrapyramidal Symptom Scale (DIEPSS) Total Score – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.3.7.3	Drug-Induced Extrapyramidal Symptom Scale (DIEPSS) Symptom Scores – DSP-5423P Treatment Phase	Safety Population
Table 14.3.7.4	Drug-Induced Extrapyramidal Symptom Scale (DIEPSS) Symptom Scores – DSP-5423 (tablet) Treatment Phase	Subjects treated with DSP-5423 (tablet)
Table 14.3.8.1	Columbia Suicide Severity Rating Scale (C-SSRS) Suicidal Ideation	Safety Population
Table 14.3.8.2	Columbia Suicide Severity Rating Scale (C-SSRS) Suicidal Behavior	Safety Population
Table 14.3.8.3	Columbia Suicide Severity Rating Scale (C-SSRS) Incidences of Suicidality	Safety Population
Table 14.3.8.4	Columbia Suicide Severity Rating Scale (C-SSRS) Emergence of Suicidality – DSP-5423P Treatment Phase	Safety Population
Table 14.3.9	Skin Irritation Assessment – DSP-5423P Treatment Phase	Safety Population
Table 14.4.1	Drug Attitude Inventory-10 (DAI-10) Total Score – DSP-5423P Treatment Phase	Safety Population

No	Title	Population
Table 14.4.2	Drug Attitude Inventory-10 (DAI-10) – DSP-5423P Treatment Phase	Safety Population
Table 14.4.3	Drug Attitude Inventory-10 (DAI-10) Total Score Compared to Baseline Assessment – DSP-5423P Treatment Phase	Safety Population
Table 14.4.4	EuroQol-5 Dimension (EQ-5D) Index Value – DSP-5423P Treatment Phase	Safety Population
Table 14.4.5	EuroQol-5 Dimension (EQ-5D) – DSP-5423P Treatment Phase	Safety Population
Table 14.4.6	Questionnaire for Formulation – DSP-5423P Treatment Phase	Safety Population
Table 14.5.1.1	Plasma Concentration of Blonanserin and Metabolites	PK Analysis Population
Table 14.5.1.2	Ratio of Plasma Concentration of Metabolites to Blonanserin	PK Analysis Population
Table 14.5.2.1	Plasma Concentration of Blonanserin and Metabolites by Sex	PK Analysis Population
Table 14.5.2.2	Plasma Concentration of Blonanserin and Metabolites by Age	PK Analysis Population
Table 14.5.3	Plasma Concentration of Blonanserin and Metabolites by Most Recent Dose and Administration Site	PK Analysis Population
Listing 16.2.1.1	Patients Who Discontinued Study Treatment – DSP-5423 (tablet) Treatment Phase	All Patients
Listing 16.2.1.2	Patients Who Discontinued Study Treatment – DSP-5423P Treatment Phase	All Patients
Listing 16.2.1.3	Patient Disposition	All Patients
Listing 16.2.1.4	Analysis Population	All Patients
Listing 16.2.2	Important Protocol Deviations	All Patients
Listing 16.2.3	Patients Who Excluded from Efficacy Analysis	All Patients
Listing 16.2.4.1	Demographics and Baseline Characteristics	All Patients
Listing 16.2.4.2	Psychiatric History	All Patients
Listing 16.2.4.3	Concomitant Diseases	All Patients
Listing 16.2.4.4	Prior Medications	All Patients

No	Title	Population
Listing 16.2.4.5	Concomitant Medications Used in DSP-5423 (tablet) Treatment Phase	All Patients
Listing 16.2.4.6	Concomitant Medications Used in DSP-5423P Treatment Phase	All Patients
Listing 16.2.5.1	Treatment Compliance	All Patients
Listing 16.2.5.2	Treatment Exposure – Mean Daily Dose and Cumulative Dose	All Patients
Listing 16.2.5.3	Treatment Exposure	All Patients
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No	Title	Population
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No	Title	Population
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