Statistical Analysis Plan H8H-CD-LAHG (COL MIG-106)

A Phase I, Randomized, Double-Blind, Placebo-Controlled, 5-Period, Cross-Over Study Assessing the Effects of Lasmiditan on Simulated Driving Performance in Normal Healthy Volunteers

NCT03012334

Approval Date: 23-June-2017

16.1.9 Documentation of Statistical Methods

16.1.9.1 Statistical Analysis Plan

16.1.9.2 MiniSim Drive Summary Measures

16.1.9.1 Statistical Analysis Plan

The Safety Statistical Analysis Plan dated 23 June 2017 is attached.

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STATISTICAL ANALYSIS PLAN

For:

CoLucid Pharmaceuticals, Inc.

SPONSOR PROTOCOL No. COL MIG-106

A Phase I, Randomized, Double-Blind, Placebo-Controlled, 5-Period, Cross-Over Study Assessing the Effects of Lasmiditan on Simulated Driving Performance in Normal Healthy Volunteers

Algorithme Project No. CUD-P8-917

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Version: Final 1.0

Date: 2017/06/23

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STATISTICAL ANALYSIS PLAN APPROVAL

We have carefully read this Statistical Analysis Plan and agree it contains the necessary information required to handle the statistical analysis of study data.

PPD

June 26th, 2017
Date

June 26, 2017
Date

June 27, 2017
Date

On behalf of the Sponsor:

PPD

Date

VERSION CONTROL

Version Number	Version Date	Author	Description of Significant Changes from Previous Approved Version
DRAFT 0.1	2017/05/03	PPD	Not Applicable – First Version
DRAFT 0.2	2017/05/25		Updates based on client comments
Draft 0.3	2017/06/13		Updates based on client comments
FINAL 1.0	2017/06/23		Spell Check

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CONTENTS

ABBREVIATIONS

AE	Adverse Event
ANOVA	Analysis of Variance
ATC	Anatomical/Therapeutic/Chemical
BMI	Body Mass Index
CI	Confidence Interval
Cm	Centimeter
CNS	Central Nervous System
CRCDS-MiniSim	Cognitive Research Corporation Driving Simulator-MiniSim
CRF	Case Report Form
CS	Clinically Significant
C-SSRS	Columbia-Suicide Severity Rating Scale
CSR	Clinical Study Report
CVDA	Country Vigilance-Divided Attention
DA	Divided Attention
EOS	End of Study
ICF	Informed Consent Form
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
kg/m^2	Kilogram per meter squared
Km	Kilometer
NCS	Not Clinically Significant
NI	Non-inferiority
PK	Pharmacokinetic(s)
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDC	Symbol Digit Coding
SDLP	Standard deviation of lateral position
SE	Standard Error
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
TFLs	Tables, Figures, and Listings
VAS	Visual Analog Scale
WHO-DDE	WHO Drug Dictionary Enhanced

1. INTRODUCTION

This statistical analysis plan (SAP) provides a detailed description of the statistical methods and procedures to be implemented for the analyses of data from Protocol No. COL MIG-106. The analyses described in the SAP are based upon the final protocol (Amendment 1) dated 2017/01/12.

2. STUDY OBJECTIVES

Primary Objectives

The primary objective of this study is to determine the effects of acute doses of lasmiditan 50 mg, 100 mg and 200 mg compared to placebo and positive control (alprazolam 1.0 mg) on simulated driving performance in healthy subjects as measured by standard deviation of lateral position (SDLP) using the Cognitive Research Corporation Driving Simulator-MiniSim (CRCDS-MiniSim).

Secondary Objective

The secondary objectives of the study are to determine the effects of lasmiditan 50 mg, 100 mg, and 200 mg compared to placebo and positive control (alprazolam 1.0 mg) on other measures of simulated driving performance (e.g., speed deviation, lane exceedance and other measures of lane position and speed control, cornering, collisions, and divided attention [DA]), CogScreen Symbol Digit Coding (SDC) test, and self-report measures (i.e., Karolinska Sleepiness Scale (KSS), Visual Analog Scales addressing motivation and performance, and if the subject feels safe to drive).

3. STUDY DESIGN

General Description

This will be a randomized, single dose, double-blind, placebo-controlled, Latin-square design with 5-period (full) crossover study with subjects randomized to treatment sequences. Subjects will complete all 5 Periods within the treatment sequence that they are randomized to.

The treatments are:

- Treatment A: Lasmiditan 50 mg
- Treatment B: Lasmiditan 100 mg
- Treatment C: Lasmiditan 200 mg
- Treatment D: Alprazolam 1 mg
- Treatment E: Placebo

Subjects will be randomized equally into one of ten treatment sequences:

Treatment Sequence	Period 1	Period 2	Period 3	Period 4	Period 5
1	A	B	E	C	D
2	B	C	A	D	E
3	C	D	B	E	A
4	D	E	C	A	B
5	E	A	D	B	C
6	D	C	E	B	A
7	E	D	A	C	B
8	A	E	B	D	C
9	B	A	C	E	D
10	C	B	D	A	E

Each Period including washout will be approximately 7 days in duration.

Study drug will be administered by site staff on Day 1 of each Period. Subjects will wear a blindfold when taking each dose to maintain the blind. The tablet size and shape are deemed similar enough to maintain the blind with a blindfolded subject.

CRCDS-MiniSim testing is conducted 1.5 hours post-dose (on Days 1, 7, 14, 21, and 28).

Schematic of Design:

Period 1 → Washout 1 → Period 2 → Washout 2 → Period 3 → Washout 3 → Period 4 → Washout 4 → Period 5 → EOS

Day 1 Days 2-6 Day 7 Days 8-13 Day 14 Days 15-20 Day 21 Days 22-27 Day 28 Day 35

A sufficient number of subjects will be enrolled to complete 80 healthy volunteers in the 5-period crossover study.

The positive control (alprazolam 1.0 mg) is included to establish the sensitivity of the study endpoints to detecting residual sedation.

The total duration of study treatment for a participant will be approximately 5 weeks. The total duration of study participation will be in the range of 5-9 weeks depending on the duration of the screening period.

Study procedures

For complete details on the study assessments to be performed for the study, refer to Appendix A.

Randomization and Unblinding Procedure

Prior to dosing, subjects will be randomly assigned to one of ten treatment sequences and dosed with study medication (lasmiditan, alprazolam or placebo) based upon a randomization scheme provided by Algorithme Pharma. Only the qualified person(nel) assigned to prepare and administer the study treatment will have access to the randomization schedule and dispensing records during the study period.

Subjects will wear a blindfold when taking each dose to maintain the blind. The tablet size and shape are deemed similar enough to maintain the blind with a blindfolded subject. Dosing will be observed by a study staff member (qualified party dispenser); no other study personnel will be present at the time of dosing.

4. STUDY ENDPOINTS

Primary Endpoint

The primary endpoint for this study is simulated driving performance as measured by SDLP using the CRCDS-MiniSim.

Secondary Endpoints

The secondary endpoints for this study include other measures of simulated driving performance, KSS and CogScreen SDC test.

- Sleepiness Endpoint – KSS
- Self-reported readiness to drive ("Right now do you feel safe to drive?)
- Visual Analog Scales (VAS) to assess subject's motivation and self-appraisal of their driving performance
- Performance Endpoints
    - CogScreen SDC test
        - Number of correct responses
        - Response Accuracy
        - Standard deviation of reaction time
- Driving Performance Endpoints
    - Lane exceedance; including number, maximum, duration, and area of exceedance
    - Ratio above speed limit, excessive speed count, excessive speed ratio
    - Average speed, speed deviation, speed count, speedings ratio
    - Excessive Ay (cornering speed threshold exceeded)
    - Collision count, off-road crashes, total collisions
    - DA: Correct Responses, Omission Errors, Commission Errors, Reaction Time, Standard Deviation of Reaction Times
- Single-dose plasma drug levels and driving performance

Safety Endpoints

Safety endpoints include:

- Adverse Events
- Clinical Laboratory Tests (hematology, chemistry, urinalysis)
- Vital Signs
- Physical examination
- Concomitant medication
- ECGs
- C-SSRS

The details of the safety endpoints' assessment are presented in Section 10.

Pharmacokinetic Endpoints

The pharmacokinetic endpoint for this study is plasma lasmiditan concentration data.

Sample Size Determination

This study is designed to test non-inferiority of lasmiditan doses relative to placebo, with an alprazolam test versus placebo to confirm the sensitivity of the simulator to detect treatment effects.

The following assumptions were made in the sample size computation:

(a) within-subject standard deviation for SDLP is approximately 6 cm;

(b) the true difference between lasmiditan doses and placebo is 0;

(c) the non-inferiority (NI) margin is proposed to be 4.4 cm, which is the effect seen with 0.05% of blood alcohol content (BAC).

Under these assumptions, a sample of 80 subjects would provide in excess of 90% power to establish non-inferiority of any given dose of lasmiditan compared to placebo in terms of the primary end point, SDLP. This sample size is considered more than adequate to detect alprazolam differences from placebo, which are anticipated to exceed the NI margin.

5. ANALYSIS POPULATIONS

Safety Population:

All subjects who are treated with study medication will be included in the safety population. This population will be used for all demography, background and safety analyses.

Intent-to-treat (ITT) Population:

All subjects who are randomized and treated will be included in the ITT Population. This population will be used for efficacy analyses. Subjects will (in general) be included in all analyses for which data are non-missing.

Pharmacokinetics (PK) Population:

All subjects with evaluable PK data will be included in the pharmacokinetic population.

6. STATISTICAL METHODOLOGY

All analyses will be conducted using the SAS software, version 9.4, or higher

Adverse events and medical history will be classified using the standard MedDRA terminology version 19.1.

Prior and concomitant medications will be coded with the WHO-DDE dictionary version March 01, 2016.

In general, all summary tables will be presented for safety population. Summaries for adverse events will be presented by treatment.

In general, the data listings will include all enrolled subjects up to the point of study completion or discontinuation; exceptions will be listings pertaining to a subset of subjects only (e.g., subjects with blood sampling time deviations) or a subset of records/events (e.g., abnormal laboratory values).

Categorical variables will be summarized using the PROC FREQ procedure. Continuous variables will be summarized using the PROC UNIVARIATE, MIXED, and/or MEANS procedures. For log-transformed endpoints, geometric mean will also be presented.

The following general comments also apply to all statistical analyses and data presentations:

- Duration variables in days will be calculated using the general formula: (end date - start date) +1.
- Individual subject listings of all data represented on the CRFs will be provided to facilitate the investigation of tabulated values and to allow for the clinical review of all efficacy and safety parameters.
- When assessments are repeated for a given timepoint, only the result which is closest to the dosing time will be included in the summary tables.

The analyses described in this plan are considered a priori, that they have been defined prior to database lock. Any analyses performed subsequent to database lock will be considered post hoc and exploratory. Post hoc analyses will be labeled as such in the corresponding statistical output and identified in the clinical study report (CSR).

Analysis Time Points

Unless otherwise specified, the baseline value will be defined as the last non-missing evaluation prior to the first dose of study medication.

Methods for Handling Missing Data

No imputations of values for missing data will be performed. All data recorded on the case report form will be included in the listings that will accompany the CSR.

For subjects that have incomplete data within an assessment, data will be listed but not summarized and/or analyzed for that assessment.

7. STUDY SUBJECTS

Disposition

The subject disposition will be summarized for all subjects enrolled in this study, including:

- The number of subjects screened;
- The number of screen failure subjects;
- The number of subjects randomized;
- The number and percentage of subjects who completed the study;
- The number and percentage of subjects discontinued from the study by primary reason for discontinuation and overall;
- The number and percentage of subjects included in each of the safety, ITT and PK populations.

The percentages will be calculated using the number of subjects randomized as denominator.

A listing of subject's disposition will be provided. A listing of subjects included in each of the analysis populations will also be provided.

Protocol Deviations

Inclusion/exclusion criteria violations will be presented in a listing.

8. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic and Background Characteristics

Demographic data and baseline characteristics will be presented in a data listing and summarized in a table. Quantitative assessments to be summarized are age, height, body weight and body mass index (BMI) at screening. Subject demographics include sex, age, ethnicity, and race. Baseline characteristics include height, weight, and BMI.

Lifestyle

Alcohol and smoking intake history will be recorded and presented in separate listings.

Medical/Social history

Any medical history findings will be recorded and presented in a listing. The listing will include the coding terms (e.g., SOC and Preferred Term).

Prior Medication

Any medications taken including prescription, nonprescription, OTC (cold and antacid medications), dietary supplements, vitamins or herbal medications from screening to the first dose of the study drug will be recorded and presented as prior medications in a listing. The listing will include the coding terms (e.g., ATC and Preferred Term).

9. PHARMACOKINETICS AND PHARMACODYNAMIC ANALYSIS

Pharmacokinetic Analysis

Blood samples for the determination of plasma lasmiditan concentrations will be drawn at the following time points following each dose:

- Days 1, 7, 14, 21, and 28 pre-dose (within 30 minutes prior to dose) of each period
- Days 1, 7, 14, 21, and 28 of each period at 155 minutes (-15 to +30 minutes) after dosing

A summary table will be provided summarizing each time point by treatment.

Pharmacodynamic Analysis

Primary Analysis:

The primary endpoint, SDLP, will be analyzed using a normal theory mixed effects model with fixed effects for sequence, period, and treatment, and a random effect for subject within sequence. A variance component covariance structure and Kenward-Roger degrees of freedom will be used.

Pair-wise comparisons (hypothesis tests) of differences in means, and 95 % confidence intervals on differences will be provided for:

1. Lasmiditan 50 mg versus placebo
2. Lasmiditan 100 mg versus placebo
3. Lasmiditan 200 mg versus placebo
4. Alprazolam 1.0 mg versus placebo
5. Lasmiditan 50 mg versus alprazolam 1.0 mg
6. Lasmiditan 100 mg versus alprazolam 1.0 mg
7. Lasmiditan 200 mg versus alprazolam 1.0 mg

In addition, pair-wise within-subject differences in SDLP greater than 4.4 cm in absolute value (equal to the previously found difference between placebo and 0.05% BAC for the CRCDS) will be compared using McNemar (MM) test. Furthermore, these pair-wise, within subject differences in SDLP will be tested for symmetry about zero (Laska 2012) using the maximally selected McNemar test.

Summary statistics will be provided (mean, SD, median, minimum, maximum) for SDLP for each time point and treatment group. Figures will be provided for the within subject difference scores by treatment and day as both a histogram and scatter plot. Data listings for driving simulator data will be provided.

Secondary Analyses Performed as the Primary Analysis:

Secondary endpoints of VAS, SDC, and driving performance endpoints will be evaluated and presented similarly, however Lane Exceedance will be log transformed (more specifically ln(x+1)) prior to analyses.

Tables will be presented in the same format as the primary output for:

- Visual Analog Scales (VAS) to assess subject's motivation and self-appraisal of their driving performance
- KSS
- Performance Endpoints
    - CogScreen SDC test
        - Number of correct responses

    - Response Accuracy
    - Standard deviation of reaction time
- Driving Performance Endpoints
    - Lane exceedance; including number, maximum, duration, and area of exceedance
    - Ratio above speed limit, excessive speed count, excessive speed ratio
    - Average speed, speed deviation, speed count, speedings ratio
    - Excessive Ay (cornering speed threshold exceeded)
    - DA: Correct Responses, Omission Errors, Commission Errors, Reaction Time, Standard Deviation of Reaction Times

A data listing for the two VASs and SDC results will be provided

Additional Secondary Analyses:

Driving Performance Collision count, off-road crashes, Total Collisions:

Summary statistics will be provided (mean, SD, median, minimum, maximum) for collision count, off-road crashes, and total number of collisions for each time point and treatment group. Additionally, differences in number of collisions/crashes for each pair-wise comparison will be provided with their corresponding Wilcoxon Signed Rank p-value. A bar chart will be provided pooling total number of collisions by 0, 1, 2, or >=3 for all 3 treatment groups.

Self-reported readiness:

Pair-wise comparisons for readiness to drive will be analyzed using McNemar's test. A bar graph for percentage of subjects reporting not safe to drive will be reported by treatment and day.

Plasma drug levels:

The decision as to which plasma samples collected will be assayed for evaluation of pharmacokinetics will be determined by CoLucid Pharmaceuticals, Inc. The correlations between single-dose plasma drug concentrations the morning of the driving simulation and the primary and key secondary end points will be evaluated, data permitting. If indicated, these samples may also be assayed and/or pooled for assay in an exploratory manner for metabolites and/or additional pharmacodynamic markers.

The relationship between single-dose drug levels and all secondary endpoints (excluding self-reported readiness) will be assessed by correlation. Both the Spearman and Pearson correlations will be reported. Figures will be provided for the within subject difference from placebo scores by treatment and day as a scatter plot.

Statistical Analysis

Initially, the statistical significance of alprazolam vs. placebo ($p<0.05$) comparison for SDLP is necessary to validate the experiment as having the ability to detect effects (i.e., assay sensitivity).

To address multiplicity of testing, for the primary endpoint of SDLP, ascending doses of lasmiditan will be interpreted in a sequential manner, starting with the 50 mg dose and proceeding to 100 mg and then 200 mg. Doses of lasmiditan will be considered non-inferior to placebo if the upper 95% confidence limit on the difference in SDLP between that dose and placebo is less than 4.4 cm and lower doses also do not exceed the NI margin. No adjustment to alpha levels will be made for either the comparison of alprazolam to placebo or to lasmiditan, or for secondary endpoints or analyses. Formal statistical tests (where performed) will be two-sided and testing at the alpha=0.05 level of significance.

10. SAFETY

Adverse Events

An AE is defined as any untoward medical occurrence in a subject administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product.

A suspected adverse reaction is any AE for which there is a reasonable possibility that the drug caused the AE. 'Reasonable possibility' means there is evidence to suggest a causal relationship between the drug and the AE. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any AE caused by a drug.

AEs occurring after the initiation of the treatment are referred to as treatment emergent adverse events (TEAEs).

TEAEs will be assigned to a treatment based on the time of occurrence in relation to the last treatment administered prior to the onset of the TEAE. TEAEs will be assigned using the following rules:

- TEAE will be assigned to the last treatment taken by the subject where the date and time of the last treatment dosing is on or before of the start date and time of the event. Such assignment will be performed irrespective of any washout period between the start and stop dates of the TEAE.
- Any TEAE started after the discharge and during the follow-up period will be assigned to the last treatment that the subject has taken during last period.

As an overall summary of AEs, the following will be presented by treatment and overall:

- Number of reported AEs;
- Number of reported TEAEs;
- Number and percentage of subjects experiencing TEAEs;
- Number and percentage of subjects experiencing a drug-related TEAE (i.e. those with a relationship classified as reasonable possibility)
- Number and percentage of TEAEs by relationship to study treatment (i.e. reasonable possibility, no reasonable possibility);
- Number and percentage of TEAEs by severity;
- Number of reported SAEs (serious adverse events);
- Number and percentage of subjects experiencing SAEs;
- Number and percentage of subjects experiencing drug-related SAEs;
- Number and percentage of TEAEs leading to withdrawal; and
- SAEs with an outcome of death.

Frequency tables will be presented by treatment, system organ class and preferred term that summarize all Treatment Emergent Adverse Events (TEAEs), and SAEs. Frequency tables will also be presented by treatment, system organ class, preferred term and maximum severity and by treatment, system organ class, preferred term and relationship to study drug.

Subject listings of all Adverse Events (AEs) including severity and relationship to study drug will be provided. AEs leading to withdrawal and SAEs will also be presented in separate listings.

Concomitant Medications

Medications taken after the first dose of study drug until after discharge from the study will be recorded. Concomitant medications will be presented in a listing. The medication name, active ingredient, dose, units, formulation, route, indication or reason taken, code, date and time taken will be presented. The listing will also include the coding terms (e.g., ATC and Preferred Term).

Extent of Exposure

Details of drug dosing (actual treatment received, actual date and time of administration, dose administered, and route of administration) will be listed by subject.

Clinical Laboratory Evaluations

Planned laboratory analyses include:

- Blood Chemistry: alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total and direct bilirubin, blood urea nitrogen (BUN), creatinine, gamma glutamyltransferase (GGT), glucose, potassium, sodium;
- Hematology: hemoglobin, hematocrit; platelets, prothrombin time (PT), red blood cells (RBC), white blood cells (WBC) with differential (absolute),
- Urinalysis: bilirubin, erythrocytes, glucose, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen
- Other: urine drug screen and serum pregnancy.

Hematology, chemistry and quantitative urinalysis laboratory test results, as well as the change from baseline, will be summarized by sequence, parameter and visit.

Separate listings of all individual data for urinalysis, hematology, chemistry and other laboratory tests will be presented by subject, laboratory test and visit.

Subject listings of abnormal on-study laboratory values will be provided, including demographic information. Similarly, clinically significant on-study laboratory data will be presented in a second listing.

Vital Signs

Vital signs will include the measurement of blood pressure, heart rate, oral temperature, and body weight.

For all vital signs, raw values, as well as the change from baseline, at each time point will be summarized by treatment, parameter and visit. Vital signs data will also be presented in a listing.

Subject listing of abnormal on-study vital signs values (Out-of-Range – Not Clinically Significant (NCS) or Clinically Significant (CS)) will be provided. Similarly, CS on-study vital signs values (Out-of-Range – CS) will be presented in a second listing.

Electrocardiogram

A triplicate 12-lead ECG will be obtained at time points throughout the study. In some cases, repeat abnormal ECGs may be obtained.

Raw values at each time point, as well as the change from baseline, will be summarized by sequence, parameter and visit and will also be presented in a listing.

A subject listing of abnormal on-study ECG assessments (Abnormal – NCS or Abnormal – CS) will be provided. Similarly, CS on-study ECG assessments (Abnormal – CS) will be presented in a second listing.

Physical Examination Findings

A physical examination will be conducted and results will be presented in a listing.

A subject listing of abnormal on-study physical examination results (Abnormal – NCS or Abnormal – CS) will be provided, including demographic information. Similarly, CS on-study physical examination results (Abnormal – CS) will be presented in a second listing.

Columbia-Suicide Severity Rating Scale (C-SSRS)

The Columbia-Suicide Severity Rating Scale (C-SSRS) is a suicidal ideation rating scale. The scale identifies behaviors and thoughts that are associated with an increased risk of suicidal actions in the future. The C-SSRS will be performed at Screening, on Days -1, 6, 13, 20, and 27, and Day 35 or EOS.

Subjects who answer 'Yes' to any of the questions on the C-SSRS questionnaire will be presented in a listing

Epworth Sleepiness Scale

The Epworth Sleepiness Scale assessment will be performed at Screening and results will be presented in a listing.

Simulator Sickness Questionnaire

A simulator sickness questionnaire will be performed at Screening and results will be presented in a listing.

11. INTERIM ANALYSES AND DATA SAFETY MONITORING

There is no interim analysis or safety data monitoring planned for this study.

12. CHANGES TO PROTOCOL-SPECIFIED ANALYSES

There is no change from the planned analysis described in the protocol.

13. GENERAL INFORMATION RELATED TO DATA PRESENTATIONS

All programs used to generate statistical analyses will be validated according to Algorithme Pharma's standard operating procedures.

TFLs will be displayed on letter size paper, 8 ½ inches by 11 inches, using the Courier New font.

In general, summary statistics for raw variables (i.e., variables measured at the study site or central laboratory) will be displayed as follows: if required minima, maxima, means, quartiles, standard deviations and confidence limits will be displayed to the same number of decimal places as the raw data; if required medians will be displayed to one additional decimal place.

Percentages will be displayed to one decimal place. Percentages between 0 and 0.1 (exclusive) will be displayed as '<0.1'. P-values will be displayed to 3 decimal places. P-values that are less than 0.001 will be displayed as '<0.001'.

The numbers of decimal places for summary statistics of derived variables (i.e., variables that are not measured by the study site but are calculated for analysis based on other measured variables) will be determined on a case by case basis. In general, minima and maxima will be displayed to the commonly used unit of precision for the parameter. Means, medians, quartiles, and confidence limits will be displayed to one additional decimal place and standard deviations will be displayed to two additional decimal places.

The formats and layouts of TFLs are provided in subsequent sections. Actual formats and layouts may be altered slightly from those presented in the templates as necessary to accommodate actual data or statistics. Minor format changes will not require updates to the SAP.

The tables and listings listed below are common data displays. Their numbering and general content follow the ICH E3 guidelines. Some of the tables and listings may not be applicable/appropriate/necessary for a particular study. Additional tables and listings may be included, provided the numbering scheme remains consistent with ICH E3.

14. REFERENCE

Laska E, Meisner M, Wanderling J. A maximally selected test of symmetry about zero. Stat Med 2012;31:3178-91.

PLANNED TABLES

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APPENDIX A

STUDY SCHEDULES

Study Procedures	Screening (Within 28 Days Prior to 1st Dose) (Visit 1)	Period 1			Period 2			Period 3			Period 4			Period 5			Follow-Up/EOS
		Day-1 (V2)	Day 1 (V3)	Day 2 (V4)	Day 6 (V5)	Day 7 (V6)	Day 8 (V7)	Day 13 (V8)	Day 14 (V9)	Day 15 (V10)	Day 20 (V11)	Day 21 (V12)	Day 22 (V13)	Day 27 (V14)	Day 28 (V15)	Day 29 (V16)	Day 35 (Visit 17)
Informed consent	X																
Medical/Social history	X																
Subject Eligibility	X	X			X			X			X			X			
Weight/Height[1] (BMI)	X																X
Drug and alcohol screen	X	X			X			X			X			X			
Serum Pregnancy Test	X	X[9]			X[9]			X[9]			X[9]			X[9]			X
Clinical safety labs	X																X[2]
Physical examination	X																X
Epworth Sleepiness Scale	X																
Twelve-lead ECG[3]	X																X
Vital signs[4]	X	X	X		X	X		X	X		X	X		X	X		X
Temperature	X																X
Admission to clinic[5]		X			X			X			X			X			
Discharge from clinic[6]				X			X			X			X			X	
Study Drug Administration			X			X			X			X			X		
PK sampling[7]			X			X			X			X			X		
CogScreen SDC Training/Practice	X	X			X			X			X			X			
Driving Sim Training/Practice	X	X			X			X			X			X			
Simulator Sickness Questionnaire	X																
KSS[8]			X			X			X			X			X		

Self-Perceived Questionnaire (safe to drive)			X			X			X			X			X		
CVDA Drive			X			X			X			X			X		
VAS			X			X			X			X			X		
CogScreen SDC Test			X			X			X			X			X		
C-SSRS	X	X			X			X			X			X			X
Adverse event assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant meds assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[1] Height and BMI will be measured at Screening only.

[2] Safety labs (hematology, chemistry and urinalysis) at Screening and Day 35 or EOS only.

[3] Twelve-lead ECG will be obtained at Screening and Day 35 or EOS only.

[4] Vital signs will be collected at Screening, CRU check-in on Days -1, 6, 13, 20, and 27, pre-dose and 1.17 hours post dose on Days 1, 7, 14, 21, and 28, and at Follow-up/Day 35 or EOS.

[5] Subjects will be inpatient on Days -1, 6, 13, 20, and 27.

[6] Subjects will be discharged approximately 24 hours post-dose.

[7] Plasma PK samples for lasmiditan levels will be collected at the following time-points: Days 1, 7, 14, 21, and 28 pre-dose (within 30 minutes before dosing) and 2.58 hours (155 minutes -15 to +30 minutes) post dosing.

[8] KSS is performed before each drive.

[9] A serum pregnancy test will be performed upon admission to the unit for females of child-bearing potential.

*Days may vary depending on the exact wash-out period.

APPENDIX B

TABLE SHELLS

Table 14.1.1
Subject Disposition
(All Subjects)

		Placebo	Lasmiditan 50 mg	Lasmidit an 100 mg	Lasmidit an 200 mg	Alprazolam 1 mg	Overall
Subjects Screened							xx
Screen Fail Subjects							xx
Subjects Randomized [N]		xx	xx	xx	xx	xx	xx
Subjects Completed the Study [n(%)]	YES	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	NO	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
If No, Reason of Study Discontinuation [n(%)]	Reason 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Reason 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Reason 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Subjects Included in Each Analysis Population [n(%)]	Safety Population	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Intent-to-treat Population	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Pharmacokineti c Population	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The percentages are based on the number of subjects randomized.

Table 14.1.2.1
Summary of Demographic Characteristics
(Safety Population)

		Placebo (N=XX)	Lasmiditan 50 mg (N=XX)	Lasmiditan 100 mg (N=XX)	Lasmiditan 200 mg (N=XX)	Alprazolam 1 mg (N=XX)	Overall (N=XX)
Age (years)	N	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Gender [n(%)]	MALE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	FEMALE						
Ethnicity [n(%)]	HISPANIC/LATINO	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	NOT HISPANIC/NOT LATINO	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race [n(%)]	RACE1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	RACE2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Weight at Screening (kg)	N	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Height (cm)	N	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Body Mass Index as Screening (kg/m^2)	N	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

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Similar Table:

Table 14.1.2.2 Summary of Demographic Characteristics (Intent-to-treat Population)
Table 14.1.2.3 Summary of Demographic Characteristics (Pharmacokinetic Population)

Table 14.2.1.1
Standard Deviation of Lateral Position (SDLP)
(ITT Population)

Statistic	Placebo (N=xx)	Lasmiditan 50 mg (N=xx)	Lasmiditan 100 mg (N=xx)	Lasmiditan 200 mg (N=xx)	Alprazolam 1 mg (N=xx)
N	xx	xx	xx	xx	xx
Mean (SD)	xx.xxxx (xx.xx)	xx.xxxx (xx.xx)	xx.xxxx (xx.xx)	xx.xxxx (xx.xx)	xx.xxxx (xx.xx)
LSMeans*	xx.xxxx	xx.xxxx	xx.xxxx	xx.xxxx	xx.xxxx
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx.xxxx , xx.xxxx	xx.xxxx , xx.xxxx	xx.xxxx , xx.xxxx	xx.xxxx , xx.xxxx	xx.xxxx , xx.xxxx
		Lasmiditan 50 mg vs PBO	Lasmiditan 100 mg vs PBO	Lasmiditan 200 mg vs PBO	Alprazolam 1 mg vs PBO
Diff in LSMean		xx.xxxx	xx.xxxx	xx.xxxx	xx.xxxx
95%CI*		(xx.xx , xx.xx)	(xx.xx , xx.xx)	(xx.xx , xx.xx)	(xx.xx , xx.xx)
p-value*		0.xxxx	0.xxxx	0.xxxx	0.xxxx
		Lasmiditan 50 mg vs Alprazolam 1 mg	Lasmiditan 100 mg vs Alprazolam 1 mg	Lasmiditan 200 mg vs Alprazolam 1 mg	
Diff in LSMean		xx.xxxx	xx.xxxx	xx.xxxx	
95%CI*		(xx.xx , xx.xx)	(xx.xx , xx.xx)	(xx.xx , xx.xx)	
p-value*		0.xxxx	0.xxxx	0.xxxx	

{Repeat table for VAS Motivation (Table 14.2.2.1), VAS self-appraisal (Table 14.2.2.2), SDC number of correct responses (Table 14.2.3.1), SDC Accuracy (Table 14.2.3.2), SDC Standard deviation of reaction time (Table 14.2.3.3), Driving Performance Lane Exceedance number Table 14.2.4.1), maximum (Table 14.2.4.2), duration (Table 14.2.4.3) area of exceedance (Table 14.2.4.4), ratio above speed limit (Table 14.2.4.5), excessive speed count (Table 14.2.4.6), excessive speed ratio (Table 14.2.4.7), average speed (Table 14.2.4.8), speed deviation (Table 14.2.4.9), speed count (Table 14.2.4.10), speedings ratio (Table 14.2.4.11), excessive ay (cornering speed threshold exceeded)(Table 14.2.4.12), Driving Performance Divided Attention – Correct Responses (Table 14.2.4.16), omission errors (Table 14.2.4.17), commission errors (Table 14.2.4.18) reaction time (Table 14.2.4.19), standard deviation of reaction time (Table 14.2.4.20)}

*Mixed effects model with fixed effects for sequence, period, and treatment, and a random effect for subject within sequence, variance component covariance structure, and Kenward-Roger degrees of freedom. Estimated differences are first treatment label listed minus second treatment label.

SAS Program Name: Date: Source Data: Listing 16.2.6.X

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Table 14.2.1.2.1
Standard Deviation of Lateral Position (SDLP) Analysis of Symmetry about Zero (ITT Population – Alprazolam versus Placebo)
(ITT Population)

Threshold	Sign	Low	Neutral	High	McNemar	Nominal P-value
x.xxx	-/+	xx	xx	xx	x.xxxx	0.xxxxxx
x.xxx	-/+	xx	xx	xx	x.xxxx	0.xxxxxx

Repeat table for other comparisons.

Maximally selected McNemar's test statistic (MM) Critical value for n=XX paired differences, at alpha=0.05 (two-tailed) is X.XXX.
Symmetry about zero is rejected if the maximum of the McNemar's test statistics is greater than X.XXX.
If the sum of the high and low values is less than 25, an exact two-sided p-value is computed using the binomial distribution (p=1/2), conditional on the sum of the high and low values (as 2 X the one-sided p-value).
SAS Program Name: Date: Source Data: Listing 16.2.6.1.X

Table 14.2.4.13
Driving Performance Collision Count
(ITT Population)

Statistic	Placebo (N=xx)	Lasmiditan 50 mg (N=xx)	Lasmiditan 100 mg (N=xx)	Lasmiditan 200 mg (N=xx)	Alprazolam 1 mg (N=xx)
N	xx	xx	xx	xx	xx
Mean	x.x	x.x	x.x	x.x	x.x
SD	x.xx	x.xx	x.xx	x.xx	x.xx
Median	x.x	x.x	x.x	x.x	x.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Diff in # of Collisions		Lasmiditan 50 mg vs PBO	Lasmiditan 100 mg vs PBO	Lasmiditan 200 mg vs PBO	Alprazolam 1 mg vs PBO
N		xx	xx	xx	xx
Mean		x.x	x.x	x.x	x.x
SD		x.xx	x.xx	x.xx	x.xx
Median		x.x	x.x	x.x	x.x
Min, Max		xx, xx	xx, xx	xx, xx	xx, xx
p-value*		0.xxxx	0.xxxx	0.xxxx	0.xxxx
Diff in # of Collisions		Lasmiditan 50 mg vs Alprazolam 1 mg	Lasmiditan 100 mg vs Alprazolam 1 mg	Lasmiditan 200 mg vs Alprazolam 1 mg	
N		xx	xx	xx	
Mean		x.x	x.x	x.x	
SD		x.xx	x.xx	x.xx	
Median		x.x	x.x	x.x	
Min, Max		xx, xx	xx, xx	xx, xx	
p-value*		0.xxxx	0.xxxx	0.xxxx	

*Wilcoxon Signed Ranks test.

{Repeat table for off-road crashes (Table 14.2.4.14), and total collisions (Table 14.2.4.15)}

SAS Program Name: Date: Source Data: Listing 16.2.6.X

Table 14.3.1.1
Summary of Adverse Events
(Safety Population)

	Placebo (N=XX)	Lasmiditan 50 mg (N=XX)	Etc.	Overall (N=XX)
Adverse Events (AEs) Reported [n]				xx
Treatment Emergent Adverse Events (TEAEs) Reported [n]	xx	xx	xx	xx
Subjects With At Least One TEAE [n(%)] [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects With At Least One Drug-Related TEAE [n(%)] [1] [3]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
TEAEs Relationship [2]				
Reasonable Possibility [n (%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No Reasonable Possibility	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
TEAEs Severity/Intensity [2]				
Mild [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Moderate [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Severe [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Life-Threatening [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Serious Adverse Events (SAEs) Reported [n] [2]	xx	xx	xx	xx
Subjects With At Least One SAE [n(%)][1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects With At Least Drug-Related SAE [n(%)][1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject With a TEAE Leading to Withdrawal [n(%)] [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death [n(%)] [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Percentages are based on the number of subjects in the Safety population in each treatment group.
[2] Percentages are based on the total number of treatment emergent adverse events reported in each treatment group.
[3] TEAE that was reported with a relationship of "reasonable possibility".

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Table 14.3.1.2
Summary of Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term
(Safety Population)

SOC MedDRA Preferred Term	Placebo (N=XX)	Lasmiditan 50 mg (N=XX)	Etc.
Subjects With At Least One TEAE [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 12 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 13 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 2 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 21 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 22 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 23 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Each treatment emergent adverse event is counted only once for each subject within each System Organ Class and MedDRA Preferred Term.

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Similar Tables:
14.3.1.3 Summary of Serious Adverse Events by System Organ Class and MedDRA Preferred Term (Safety Population)

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Table 14.3.1.4
Summary of Treatment Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Maximum Severity
(Safety Population)

SOC MedDRA Preferred Term	Placebo	Lasmiditan 50 mg	Lasmiditan 100 mg	Lasmiditan 200 mg	Alprazolam 1 mg	Overall
Subjects With At Least One TEAE [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Mild [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Moderate [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Severe [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Life-Threatening [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 21 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 22 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 23 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Mild [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Moderate [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Severe [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Life-Threatening [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Date: VERSION – YYYY-MM-DD

Data Source: XXXX

Table 14.3.1.5
Summary of Treatment Emergent Adverse Events by System Organ Class, MedDRA Preferred Term and Relationship To Study Drug
(Safety Population)

SOC MedDRA Preferred Term	Placebo	Lasmiditan 50 mg	Lasmiditan 100 mg	Lasmiditan 200 mg	Alprazolam 1 mg	Overall
Subjects With At Least One TEAE [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reasonable Possibility	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
NO Reasonable Possibility	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 12 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 2 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 21 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reasonable Possibility	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
NO Reasonable Possibility	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 22 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note(s): Each treatment emergent adverse event is counted only once for each subject under the worst relationship within each System Organ Class and MedDRA Preferred Term.

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.2.1
Listing of Deaths, Other Serious and Significant Adverse Events
(Safety Population)

Subject ID/Gender/ Age	Day Treatment AE #	SOC MedDRA Preferred Term Description of AE	Onset Date Time (Time since Last Dose)	Resolution Date Time (Duration)	I: Maximal Intensity R: Causality Assessment	O: Outcome S: Serious AE D: AE Lead To Discontinuation	Action Taken With Study Treatment / Other Action(s) Taken / Concomitant Given
xxx	xxxxx xxxxx	xxxxxxxxxxxx xxxxxxxxxxxx xxxxxxxxxxxx	YYYY-MM-DD/ HH:MM (DD:HH:MM)	YYYY-MM-DD/ HH:MM (DD:HH:MM)	xxxxxx	xxxxx	xxxxxx

Similar Tables:
14.3.2.2 Listing of Adverse Events Leading to Withdrawal

Table 14.3.4.1
Listing of Abnormal On-Study Laboratory Values
(Safety Population)

Category/ Parameter (Unit)	Reference Range	Subject ID/Gender/Age	Sequence	Visit	Date / Time	Value	Change from Baseline	Out-of-Range Flag	Assessment [1]
Lab Category 1									
Lab Test 11	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Lab Test 12	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Lab Category 2									
Lab Test 21	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Lab Test 22	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Etc.	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx

[1] NCS: Not Clinically Significant / CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled.
Note(s): Abnormal values are determined by applying the reference ranges to the results as reported by the external laboratory analysis.

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.4.2
Listing of Clinically Significant On-Study Laboratory Values
(Safety Population)

Category/ Parameter (Unit)	Reference Range	Subject ID/Gender/Age	Sequence	Visit	Date / Time	Value	Change from Baseline	Out-of-Range Flag	Assessment [1]
Lab Category 1									
Lab Test 11	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Lab Test 12	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Lab Category 2									
Lab Test 21	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Lab Test 22	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx
Etc.	xxx-xxx	xxx		xxxxxx	xxxxxx	xxx	xxx	xxx	xxx

[1] CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled
Note(s): Abnormal values are determined by applying the reference ranges to the results as reported by the external laboratory analysis.

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.4.3
Summary of Blood Chemistry
(Safety Population)

Parameter (unit)	Visit Name		Statistic	Overall (N=XX)
xxx (xxx)	Screening	Value	N	xx
			Mean (SD)	xx.x (xx.xx)
			Median	xx.x
			Min, Max	xx, xx
	Day 35	Value	N	xx
			Mean (SD)	xx.x (xx.xx)
			Median	xx.x
			Min, Max	xx, xx
		Change from Screening	N	xx
			Mean (SD)	xx.x (xx.xx)
			Median	xx.x
			Min, Max	xx, xx

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Similar Tables:
14.3.4.4 Summary of Hematology
14.3.4.5 Summary of Quantitative Urinalysis

Table 14.3.5.1
Listing of Abnormal On-Study Vital Signs Values
(Safety Population)

Assessment (Units)	Subject ID/Gender/Age	Sequence	Visit	Elapsed Time	Position	Date / Time	Value	Change from Baseline	Safety Review
Vital Sign Test 1	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx	xxx
	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx	xxx
Vital Sign Test 2	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx	xxx
	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx	xxx
Etc.	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx	xxx

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.5.2
Listing of Clinically Significant On-Study Vital Signs Values
(Safety Population)

Assessment (Units)	Subject ID/Gender/Age	Sequence	Visit	Elapsed Time	Position	Date / Time	Value	Change from Baseline	Safety Review
Vital Sign Test 1	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx		xxx
	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx		xxx
Vital Sign Test 2	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx		xxx
	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx		xxx
Etc.	xxx		xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx		xxx

Date: VERSION - YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.5.3
Summary of Vital Signs
(Safety Population)

Parameter (unit)	Visit	Timepoint	Statistic	Placebo (N=XX)	Lasmiditan 50 mg (N=XX)	Etc. (N=XX)
Vital Sign Test 1						
	Screening	Value	N			xx
			Mean (SD)			xx (xx.x)
			Median			xx.x
			Min, Max			xx, xx
	Day -1	Value	N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
	xxx	Value				
			N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
		Change from Baseline				
			N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
Etc.	Etc.					

PROGRAMMING NOTE: All visits outlined in Appendix A will be included.

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.6.1
Listing of Abnormal On-Study ECG Assessments
(Safety Population)

Subject ID/Gender/Age	Sequence	Visit	Date / Time	Position	Safety Review	Parameter (Unit)	Value	Change from Baseline
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
			YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
			YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.6.2
Listing of Clinically On-Study ECG Assessments
(Safety Population)

Subject ID/Gender/Age	Sequence	Visit	Date / Time	Position	Safety Review	Parameter (Unit)	Value
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
			YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
			YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.6.3
Summary of ECG Assessments
(Safety Population)

Parameter (unit)	Visit		Statistic	Overall (N=XX)
ECG Assessment Test 1				
	Screening	Value	N	
			Mean (SD)	
			Median	
			Min, Max	
	xxx	Value		
			N	xx
			Mean (SD)	xx (xx.x)
			Median	xx.x
			Min, Max	xx, xx
		Change from Screening		
			N	xx
			Mean (SD)	xx (xx.x)
			Median	xx.x
			Min, Max	xx, xx
Etc.	Etc.			

PROGRAMMING NOTE: All visits outlined in Appendix A will be included.

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.7.1
Listing of Abnormal On-Study Physical Examination Findings
(Safety Population)

Subject ID/Gender/Age	Sequence	Visit	Date / Time	Category	Result (Abnormal Findings)

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Table 14.3.7.2
Listing of Clinically Significant On-Study Physical Examination Findings
(Safety Population)

Subject ID/Gender/Age	Sequence	Visit	Date / Time	Category	Result (Abnormal Findings)

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

APPENDIX C

PHARMACOKINETIC OUTPUTS SHELLS

Table 14.2.7.1
Plasma Concentration by Time Point
(PK Population)

Time Point	Statistic	Lasmiditan 50 mg (N=xx)	Lasmiditan 100 mg (N=xx)	Lasmiditan 200 mg (N=xx)
Predose	N	xx	xx	xx
	Arithmetic Mean	xx.xxx	xx.xxx	xx.xxx
	Geometric Mean	xx.xxx	xx.xxx	xx.xxx
	SD	xx.xxxx	xx.xxxx	xx.xxxx
	%CV	xx.xxxx	xx.xxxx	xx.xxxx
	Median	xx.xxx	xx.xxx	xx.xxx
	Min, Max	xx.xxx , xx.xxx	xx.xxx , xx.xxx	xx.xxx , xx.xxx
Time #2 Postdose	N	xx	xx	xx
	Arithmetic Mean	xx.xxx	xx.xxx	xx.xxx
	Geometric Mean	xx.xxx	xx.xxx	xx.xxx
	SD	xx.xxxx	xx.xxxx	xx.xxxx
	%CV	xx.xxxx	xx.xxxx	xx.xxxx
	Median	xx.xxx	xx.xxx	xx.xxx
	Min, Max	xx.xxx , xx.xxx	xx.xxx , xx.xxx	xx.xxx , xx.xxx

etc.

Predose BLQ values were set to 0.
Standard deviation on the LN scale is approximately equal to CV on raw scale
Geometric CV%= (Std Dev of ln data)*100
SAS Program Name: Date: Source Data: Listing 16.2.5.2

Table 14.2.7.2
Correlation of ln(Plasma Drug Levels) to SDLP
(PK Population)

Statistic	Lasmiditan 50 mg (N=xx)	Lasmiditan 100 mg (N=xx)	Lasmiditan 200 mg (N=xx)
Spearman Correlation	0.xxxx	0.xxxx	0.xxxx
Pearson Correlation	0.xxxx	0.xxxx	0.xxxx

Repeat for all correlation output

SAS Program Name: Date: Source Data: Listings 16.2.5.2 and 16.2.6.X

APPENDIX D

LISTING SHELLS

Listing 16.2.1
Listing of Study Disposition

Subject ID/Gender/Age	Sequence	Date of Completion or Discontinuation	Subject Status	Specify	AE #	Date of Death

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.3
Listing of Analysis Populations

Subject ID/Gender/Age	Sequence	Safety Population	PK Population	Intent-to-treat Population	Reason if Excluded from one Population

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.4.1
Listing of Demographic Characteristics

Subject ID	Sequence	Age	Date of Birth	Gender	Ethnicity	Race	Other Race	Weight at Screening (kg)	Height (cm)	BMI at Screening (kg/m^2)

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.4.2
Listing of Screen Failures

Subject ID	Date	Specify Primary Reason

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.5.1
Listing of Investigational Product Administration

Subject ID/Gender/Age	Sequence	Visit	Start Date/Time	Treatment	Route	If Any Dosing Issues, Specify

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.5.2
Listing of Lasmiditan Plasma Concentrations

Treatment:

Subject ID/Gender/Age	Sequence	Visit	Time Point	Date / Time	Value

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.7
Listing of Adverse Events

Subject ID/Gender/Age	Visit Treatment AE #	SOC MedDRA Preferred Term Description of AE	Onset Date Time (Time since Last Dose)	Resolution Date Time (Duration)	I: Maximal Severity R: Causality Assessment	O: Outcome S: Serious AE D: AE Leading To Discontinuation	Action Taken With Study Treatment / Other Action(s) Taken / Concomitant Given
		xxxxxxxxxxxx xxxxxxxxxxxx	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM			
xxx	xxxxx xxxxx	xxxxxxxxxxxx	(DD:HH:MM)	(DD:HH:MM)	xxxxxx	xxxxx	xxxxxx

Listing 16.2.8.1
Listing of Blood Chemistry

Subject ID/Gender/Age	Sequence	Lab Test Name (Units)	Reference Range	Visit	Date / Time	Value	Change from Baseline	Out-of-Range Flag	Assessment [1]

[1] CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled

Date: VERSION - YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Similar listing(s):

L16.2.8.2 Listing of Hematology
L16.2.8.3 Listing of Urinalysis
L16.2.8.4 Listing of Urine Drug Screen
L16.2.8.5 Listing of Pregnancy Test

Listing 16.2.9.1
Listing of Alcohol Habits

Subject ID/Gender/Age	Sequence	Intake Status	Quantity	Frequency	Start Date	End Date

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.2
Listing of Smoking Habits

Subject ID/Gender/Age	Sequence	Intake Status	Quantity	Frequency	Start Date	End Date

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.3
Listing of Prior Medication

Subject ID/Gender/ Age	Sequence	Related to AE#/MH#	ATC / PT / Medication Name	Indication	Dose (unit)	Frequency	Formulation	Total Daily Dose	Route	Start Date/ Time	End Date/ Time

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Similar Listing:

Listing 16.2.9.4 Listing of Concomitant Medications

Listing 16.2.9.5
Listing of Physical Examination

Subject ID/Gender/Age	Sequence	Visit	Date / Time	Body System Examined	Result (Abnormal Findings)

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.6
Listing of Vital Signs

Subject ID/Gender/Age	Sequence	Visit	Time Point	Position	Date Time	/ Assessment (Units)	Value	Change from Baseline	Safety Review

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.7
Listing of ECG Assessments

Subject ID/Gender/Age	Sequence	Visit	Date / Time	Position	Safety Review	Parameter (Unit)	Value	Change from Baseline
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
			YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
			YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			
xxxxx		xxxxxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx			

Date: VERSION - YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.8
Listing of Screening Summary

Subject ID/Gender/Age	Does the subject continue to be eligible?

Date: VERSION – YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.9
Listing of Medical History

Subject ID/Gender/Age	Sequence	Description of Medical History	Start Date	End Date

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.10
Listing of Columbia-Suicide Severity Rating Scale (C-SSRS)

Subject ID/Gender/Age	Sequence	Visit	Category	Question	Answer

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.11
Listing of Epworth Sleepiness Scale

Subject ID/Gender/Age	Sequence	Visit	Date	Total Score

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

Listing 16.2.9.12
Listing of Simulator Sickness Questionnaire

Subject ID/Gender/Age	Sequence	Visit	Date	Result

Date: VERSION – YYYY-MM-DD Data Source: XXXX Program Source: XXXXX.sas

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