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Document History

Not applicable currently.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

Abbreviation	Definition
ADNM	Adjustment Disorder New Module
AE	adverse event
AjD	adjustment disorder
AjDA	adjustment disorder with anxiety
ANCOVA	analysis of covariance
ATC	Anatomical Therapeutic Chemical
CGI-I	Clinical Global Impression-Improvement
CGI-S	Clinical Global Impression-Severity
CI	confidence interval
CRF	case report form
CSR	clinical study report
C-SSRS	Columbia Suicide Severity Rating Scale
DSM-5	Diagnostic and Statistical Manual of Mental Disorders
ECG	electrocardiogram
eCRF	electronic case report form
EMA	European Medicines Agency
ET	end of treatment
FDA	food and drug administration

Abbreviation	Definition
HAM-A	Hamilton Anxiety Scale
IADQ	International Adjustment Disorder Questionnaire
ICE	intercurrent event
ICH	International Conference on Harmonization
IND	Investigational New Drug
IP	investigational product
ITT	intent-to-treat
IWRS	interactive web response system
LS	least squares
LSAS	Liebowitz Social Anxiety Scale
MADRS	Montgomery-Asberg Depression Rating Scale
MedDRA	Medical Dictionary for Regulatory Activities
MINI	Mini International Neuropsychiatric Review
PGI-C	Patient Global Impression of Change
PWC-20	20-item Physician Withdrawal Checklist
QTc	QT interval corrected for heart rate
QTcF	QT interval corrected for heart rate using Fridericia's formula
RR	respiratory rate or relative rate
SAE	serious adverse event

Abbreviation	Definition
SAP	statistical analysis plan
SAS	Statistical Analysis System software
SD	standard deviation
SE	standard error
SIGH-A	Structured Interview Guide for the HAM-A
SOC	system organ class
TEAE	treatment emergent adverse event
WHO-DD	World Health Organization Drug Dictionary

1. Overview

This draft statistical analysis plan (SAP) describes the planned analysis and reporting for VistaGen Therapeutics, Inc. protocol number PH94B-CL029 A Phase 2a Double-blind, Placebo-controlled, Parallel Study of PH94B Nasal Spray in the Treatment of Anxiety in Adults with Adjustment Disorder with Anxiety, Version 2.0, dated 30-Aug-2021. Reference materials for this draft statistical plan include the protocol. The final SAP will include accompanying sample data collection documents (currently under development). Operational aspects related to collection and timing of planned clinical assessments are included in the study protocol.

The structure and content of the final SAP will provide sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials (ICH, 1998). All work planned and reported for the final SAP will follow internationally accepted guidelines.

The planned analyses identified in this draft SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post-hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data. Any post-hoc or unplanned, exploratory analysis performed will be clearly identified as such in the final CSR.

The statistical plan described hereafter is an *a priori* plan. It will be finalized and approved before any unblinded inferential or descriptive analysis of data pertaining to VistaGen Therapeutics, Inc.'s study PH94B-CL029 is conducted.

2. Study Objectives and Endpoints

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective of this Phase 2a study is to evaluate the efficacy of PH94B Nasal Spray (PH94B) administered 4 times per day over 4 weeks for the treatment of anxiety in adult subjects with adjustment disorder with anxiety (AjDA).

2.1.2. Secondary Objective

The secondary objective of the study is to evaluate safety and tolerability of PH94B.

2.1.3. Exploratory Objective

An exploratory objective of the study is to evaluate efficacy of PH94B over time during the 4-week treatment period.

2.2. Study Endpoints

2.2.1. Efficacy Endpoints

2.2.1.1. Primary Efficacy Endpoint

The primary efficacy endpoint is mapped to the primary objective as follows:

Primary Objective	Primary Efficacy Endpoint
The primary objective of this Phase 2a study is to evaluate the efficacy of PH94B administered 4 times per day over 4 weeks for the treatment of anxiety in adult subjects with AjDA.	The primary efficacy endpoint of the study is change from baseline in anxiety level as measured by the Hamilton Anxiety Scale (HAM-A) at the end of the 4-week treatment period.

2.2.1.2. Secondary Efficacy Endpoint(s)

The secondary efficacy endpoints are mapped to the primary objective as follows:

Primary Objective	Secondary Efficacy Endpoints
The primary objective of this Phase 2a study is to evaluate the efficacy of PH94B administered 4 times per day over 4 weeks for the treatment of anxiety in adult subjects with AjDA.	Secondary efficacy endpoints of the study include the following: Individual subject improvement as assessed by the Clinical Global Impression-Improvement (CGI-I) scale. Values for comparison will be the proportion of "responders" in each group, defined as subjects receiving scores of 1 (Very much improved) or 2 (Much improved) at the end of treatment with PH94B. Individual subject improvement as assessed by the subject's self-assessment of improvement (by Patient Global Impression of Change [PGI-C] scale) at the end of treatment compared to baseline. Values for comparison will be the proportion of "responders" in each group, defined as subjects receiving scores of 1 (Very much improved) or 2 (Much improved) at end of treatment with PH94B. Individual subject improvement on the Adjustment Disorder New Module (ADNM) scale at the end of treatment compared to baseline. Individual subject improvement on the International Adjustment Disorder Questionnaire (IADQ) at end of treatment compared to baseline.

2.2.1.3. Exploratory Efficacy Endpoint(s)

The exploratory efficacy endpoints are mapped to the exploratory objective as follows:

Exploratory Objective	Exploratory Efficacy Endpoints
An exploratory objective of the study is to evaluate efficacy of PH94B over time during the 4-week treatment period.	Summaries and changes from baseline in HAM-A at Weeks 1, 2, and 3. Summaries and changes from baseline in ADNM subscales at Week 4. Summaries of CGI-I and PGI-C at Weeks 1, 2, 3, and 4 (each week).

2.2.2. Safety Endpoints

The safety endpoints are mapped to the secondary objective as follows:

Secondary Objective	Safety Endpoints
The secondary objective of the study is to evaluate the safety and tolerability of PH94B.	Incidence and severity of adverse events (AEs), AEs leading to discontinuation, and serious adverse events (SAEs). Changes in clinical laboratory values. Changes in 12-lead electrocardiogram (ECG) results. Changes in physical examination findings. Changes in vital signs results. Changes in Montgomery-Asberg Depression Rating Scale (MADRS) scores. Changes in suicidal ideation scores, as documented using the Columbia Suicide Severity Rating Scale (C-SSRS).

3. Overall Study Design and Plan

3.1. Overall Design

This is a double-blind, placebo-controlled, parallel group, Phase 2a clinical study in adult subjects diagnosed with AjDA. Subjects diagnosed with AjDA by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria and a HAM-A of 20 or greater are to be enrolled.

3.2. Experimental procedures

Subject participation in the Study will last a total of 6 to 10 weeks, depending on the duration of the screening period and whether they need a washout of concomitant anxiolytics. Upon signing an investigation review board approved informed consent, all subjects will complete Visit 1 (Screening) and enter a screening period [redacted] that could include tapering of concomitant anxiolytics, if necessary. Visit 1 (Screening) will consist of subject demographics recording, safety assessments (medical and psychiatric history, prior and concomitant medications recording, physical examination, vital signs, ECG, blood tests and urinalysis, urine drug screen, urine pregnancy test [if appropriate]) and psychiatric assessments (Mini-International Neuropsychiatric Interview [MINI], MADRS, HAM-A, Liebowitz Social Anxiety Scale [LSAS], Clinical Global Impression-Severity [CGI-S], and C-SSRS) to determine eligibility. Subjects will then return to complete Visit 2 (Baseline). At this visit, subjects will complete all psychiatric assessments (ADNM, IADQ, MADRS, HAM-A, CGI-S, C-SSRS), adverse event recording, concomitant medications recording, vital signs, blood tests and urinalysis, urine drug screen, and urine pregnancy test (if appropriate). If the subject continues to meet the inclusion criteria and none of the exclusion criteria, the subject will be randomized 1:1 to PH94B or placebo. The subject will be trained on using the investigational product (IP) and will be dispensed a 1-week supply of PH94B or placebo. Subjects will then commence 4 weeks of double-blind treatment with the randomized IP four times per day.

Subjects will return for weekly site visits (Visits 3, 4, and 5), in which the subject will return the IP vial dispensed at the previous visit and receive a new vial. At Visits 2, 3, 4, and 5, when the subjects will be dispensed 2 vials of the appropriate IP, the vial weights will be recorded before dispensing to a subject. Study personnel will also record the weight of all returned vials. Concomitant medications and adverse events (AEs) will be recorded. During these visits, the HAM-A, PGI-C, CGI-I, CGI-S, and C-SSRS will be completed. Vital signs will be collected, and nasal passages will be examined.

When the subject returns for Visit 6 (End of Treatment), besides the assessments completed at Visits 3 through 5, the subjects will also complete the MADRS, ADNM, and IADQ; and have a physical examination, ECG, blood tests and urinalysis, urine drug screen, and urine pregnancy test (if appropriate). Any remaining IP vials will be collected.

The subject will then come back after a one-week washout period for Visit 7 (Follow-up). During this visit, AEs concomitant medications since the last visit, and vital signs will be collected. In addition, the HAM-A, C-SSRS, and 20-item Physician Withdrawal Checklist (PWC-20) will be administered.

Subjects who discontinue prior to Visit 6 (End of Treatment), will undergo a Visit 6 (Early Termination) visit, and provide all Visit 6 outcome measures and safety assessments for the efficacy analysis.

[redacted]

3.4. Study Population

The study population includes males and females, age ≥18 years, with a current diagnosis of AjDA as defined in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition.

3.5. Treatments Administered

Subjects will receive one of the treatments listed in Table 1 at Visit 2 (Baseline).

Table 1: Treatment Definitions

Treatment Description	Treatment Abbreviation
PH94B nasal spray self-administered as an intranasal solution in the amount of [redacted] to each nostril for a total dose of 3.2 µg [redacted]. Dose is to be administered 4 times per day separated by at least 2 hours (targeting morning, noon, early evening, and bedtime).	PH94B
Placebo nasal spray self-administered as an intranasal solution in the amount of 100 µL to each nostril for a total of 200 µL. Spray is to be administered to each nostril 4 times per day separated by at least 2 hours (targeting morning, noon, early evening, and bedtime).	Placebo

3.6. Method of Assigning Subjects to Treatment Groups

At Visit 2 (Baseline), subjects who meet study entry criteria will be randomly assigned to placebo or PH94B in a 1:1 ratio at each study site. The randomization schedule will be computer generated using a permuted block algorithm to randomly allocate IP to randomization numbers,

stratified by study site. A central interactive web response system (IWRS) will assign randomization numbers sequentially to subjects that are entered into the study. The randomization schedule will be prepared by Premier Research before the start of the study. No one involved in the study performance will have access to the randomization schedule before official unblinding of treatment assignment. No subject will be randomized into this study more than once.

3.7. Blinding and Unblinding

This is a double-blind study throughout. All subjects, investigators, and study personnel involved in the conduct of the study, including data management, will be blinded to treatment assignment with the exception of a specified unblinded statistician and a member of the Interactive Response Technology team from Premier Research who will have access to the randomization code. Unblinded study personnel will not participate in study procedures or data analysis prior to the official unblinding of the study data to all study-related personnel. If an interim analysis is to be conducted, then unblinded personnel who are not otherwise involved in the study will prepare the data for review.

Study personnel will make every effort to safeguard the integrity of the study blind to minimize bias in the conduct of the study. Treatment unblinding is discouraged if knowledge of the treatment assignment will not materially change the planned management of a medical emergency. Unblinding will be permitted in a medical emergency that requires immediate knowledge of the subject's treatment assignment. All IP containers will be provided with a code that will unblind the contents in an emergency. Procedures for emergency unblinding will be outlined in the Study Procedures Manual for PH94B-CL029.

The Investigator or designee will record the date and reason for treatment unblinding on the appropriate electronic case report form (eCRF) for that subject. If treatment assignment is unblinded for an individual subject, study personnel will be notified of that subject's treatment assignment without unblinding the treatment assignments for the remaining subjects in the study. Thus, the overall study blind will not be compromised. Overall unblinding will take place at the end of the study only after database lock has been achieved.

3.8. Schedule of Events

Please see protocol PH94B-CL029, A Phase 2a Double-blind, Placebo-controlled, Parallel Study of PH94B Nasal Spray in the Treatment of Anxiety in Adults with Adjustment Disorder with Anxiety for a detailed schedule of events.

4. Statistical Analysis and Reporting

This study is considered a Phase 2a exploratory study under an Investigational New Drug (IND) application for PH94B targeting AjDA. Statistical tests will be applied and interpreted to determine feasibility and best approaches for potential Phase 2b and Phase 3 studies.

The final study analysis will be conducted only after all subjects have completed the study as

described in the referenced protocol, a thorough blind review of all collected data has been conducted and approved, and a final SAP has been approved and signed prior to unblinding of the data.

4.1. Introduction

Data processing, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will primarily use Statistical Analysis System Software (SAS) (release 9.4 or higher). If the use of other software is warranted, the final SAP and the statistical methodology report will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with non-missing values, mean, SD, median, minimum, and maximum. The minimum and maximum will be reported with the same degree of precision (i.e., the same number of decimal places) as the observed data. Measures of location (mean and median) will be reported to 1 degree of precision more than the observed data and measures of spread (SD) will be reported to 2 degrees of precision more than the observed data.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the category or each possible value. The denominator for the percentage calculation will be based upon the total number of subjects in the study population for the treatment groups unless otherwise specified. Percentages will be presented to 1 decimal place. Counts of zero will be presented without percentages.

Unless otherwise indicated, all statistical tests will be conducted at the 0.05 significance level using 2-tailed tests, and *p* values will be reported. Corresponding 95% confidence intervals (CIs) will be presented for statistical tests. All *p* values will be displayed in four decimals and rounded using standard scientific notation (e.g., 0.XXXX). If a *p* value less than 0.0001 occurs it will be shown in tables as < 0.0001; similarly, if a *p* value greater than 0.9999 occurs, it will be shown in tables as > 0.9999. Confidence intervals will be reported to 1 degree of precision more than the observed data.

This study is considered a Phase 2a exploratory study under an IND application for PH94B targeting AjDA. Statistical tests will be applied and interpreted to determine feasibility and best approaches for potential Phase 2b and Phase 3 studies.

4.2. Interim Analysis and Data Monitoring

No interim analyses or data monitoring are planned.

5. Analysis Populations

The following analysis populations are planned for this study:

- **All Subjects Population:** All subjects who sign an informed consent, participate in a Visit 1 (Screening), and are entered into the eCRF will be included in the All Subjects

population. The All Subjects population will be used for summaries of subject disposition.

- **Safety Population:** The Safety population includes all subjects who are dispensed IP and reported administering at least 1 dose of IP. The Safety population will be used for safety analyses. For analyses of the Safety population, each subject will be analyzed by the actual treatment received, even if it differs from the subject's randomized treatment assignment.
- **Intent-to-Treat (ITT) Population:** The ITT population includes all subjects who are randomized and have one documented dose of IP at Visit 2 (Baseline). The ITT population will be used for efficacy analyses. For analyses of the ITT population, each subject will be analyzed by their randomized treatment assignment, even if the subject did not receive the assigned treatment or did not follow the protocol until completion.

Assignment of subjects to populations will be confirmed at a blinded data review meeting to be held before the study database is locked. All protocol deviations that occur during the study will be considered for their severity/impact and will be taken into consideration when subjects are assigned to analysis populations.

6. General Issues for Statistical Analysis

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

Baseline for each study assessment (where applicable) is defined in Table 2.

Table 2: Baseline Definitions

Parameters	Baseline
Safety parameters including physical examinations and ECGs.	The last non-missing assessment before the first dose of study drug. This assessment will be at Visit 1 (Screening).
Safety parameters including vital signs, clinical laboratory tests, MADRS, and C-SSRS.	The last non-missing assessment before the first dose of study drug at Visit 2 (Baseline).
Efficacy parameters including HAM-A total score, ADNM total score, and IADQ total score.	The last non-missing assessment before the first dose of study drug at Visit 2 (Baseline).

6.1.2. Adjustments for Covariates

For applicable efficacy models comparing change from baseline in efficacy measures of PH94B to placebo, the baseline value of the respective scale will be included as a covariate.

6.1.3. Multiple Comparisons

For the primary efficacy endpoint, group differences will be assessed at alpha = 0.05. No adjustments will be made for comparison of secondary or exploratory efficacy endpoints as the study is exploratory.

6.1.4. Handling of Dropouts or Missing Data

Data will be included in the analysis according to the analysis visit windows described in Section 6.1.5.

Treatment of intercurrent events (ICEs) will be as described in Table 3. Briefly, subjects who withdraw from the study after treatment begins will be encouraged to complete an Early Termination Visit where all Visit 6 assessments will be performed. If the subject is lost to follow-up or otherwise unable to complete the Visit 6 assessments or if the subject uses a prohibited medication prior to the planned end of treatment, the Visit 6 HAM-A score will be set to missing. If the fraction of missing change from baseline to Visit 6 HAM-A total scores in the ITT population is ≤0.05, missing change scores will be imputed with treatment group mean change scores for the primary efficacy analysis. If the fraction of missing change scores is greater than 0.05, multiple imputation of the change from baseline to Visit 6 HAM-A total scores will be carried out for the primary efficacy analysis. The fraction of missing change from baseline to Visit 6 HAM-A total scores will be computed as described in Section 6.1.7.2. The multiple imputation procedure will not impute individual HAM-A item scores or HAM-A total scores; only change from baseline to Visit 6 HAM-A total scores will be imputed. Other efficacy and safety data will not be imputed and will be analyzed as observed.

Table 3: Strategies for Intercurrent Events

ICE	Strategy for Addressing ICE
Treatment discontinuation following randomization but prior to Week 4.	<u>While on Treatment Strategy</u> The research objectives seek to understand the response to PH94B compared to placebo while subjects are actively using the study medication. Subjects who discontinue will undergo an Early Termination Visit and provide all Visit 6 outcome measures and safety assessments for the efficacy analysis.

ICE	Strategy for Addressing ICE
Treatment discontinuation following randomization but prior to Week 4 (subject lost to follow-up).	Hypothetical Strategy Measurement following ICE is unavailable and will be considered missing. Multiple imputation of the change from baseline to Visit 6 HAM-A scores will be carried out for the primary efficacy analysis using important subject variables and treatment assignment, if the fraction of missing change from baseline to Visit 6 HAM-A scores in the ITT population is greater than 0.05. In addition, the primary efficacy measure will be subjected to sensitivity analysis (complete case comparison and control-case using mean change from baseline HAM-A from the placebo group).
Use of prohibited medication prior to Week 4.	Hypothetical Strategy Measurement following ICE is not of interest and will be considered missing. Multiple imputation of the change from baseline to Visit 6 HAM-A scores will be carried out for the primary efficacy analysis using important subject variables and treatment assignment, if the fraction of missing change from baseline to Visit 6 HAM-A scores in the ITT population is greater than 0.05. In addition, the primary efficacy measure will be subjected to sensitivity analyses (complete case comparison and control-case using mean change from baseline HAM-A from the placebo group).

Abbreviations: HAM-A = Hamilton Anxiety Scale; ICE = intercurrent event.

The imputation approach has 2 broad components: i) the multiple imputation process for the placebo and PH94B data; and ii) the analysis method that will be used to draw inference regarding the primary estimand (Table 4), along with the method for combining the results across the multiply-imputed datasets. The primary estimand is defined in Section 8.1.

The imputation for the primary efficacy endpoint will be carried out in SAS using the fully conditional specification (FCS) method with a regression model approach (Carpenter and Kenward, 2013). The method assumes data are missing at random (MAR). Thus, subjects with missing values will have imputed values similar to other subjects with comparable observed profiles in the regression variables. The imputation will be carried out separately within each

treatment group. The regression model will include the following variables: baseline HAM-A total score, sex, age, LSAS total score, and analysis site. For each imputation process, a total of 25 complete datasets will be created. The random seeds to be used in the imputation process are 813616018 for the PH94B treatment group and 80521516 for the placebo treatment group.

The analysis method for the multiple imputation will match that described for the primary efficacy analysis in Section 8.1. Results from the multiply-imputed datasets will be combined using the standard Rubin's rules for multiple imputation (Little and Rubin, 1987) and will be done in SAS using PROC MIANALYZE.

Two sensitivity analyses will be performed to assess robustness of the multiple imputation results to changes in missing data assumptions. The sensitivity analyses include 1) a complete case analysis where only subjects with non-missing change from baseline in HAM-A total scores will be included, and 2) a control-case analysis, where missing change from baseline in HAM-A total scores will be imputed by the mean change from baseline for the placebo group. Sensitivity analyses are detailed in Section 8.1.1.

6.1.5. Analysis Visit Windows

Efficacy data will not be windowed and will be analyzed as per the nominal visit present in the database. Efficacy data includes scores on HAM-A, CGI-I, PGI-C, ADNM, and IADQ. As described in the Protocol, a ±2-day window will be allowed for each visit following Baseline (Visit 2). If a subject attends a visit outside of the window specified in the Protocol, this will be considered an out-of-window visit protocol deviation. Subjects who come in for a visit later than the 2-day window specified in the Protocol, who may have missed days of taking the IP, will be assessed on a case-by-case basis to determine whether they will be included in the analysis. Safety and baseline medical or psychiatric data will not be windowed and will be analyzed as per the nominal visit present in the database. These data include physical examinations, vital signs, clinical laboratory tests, ECGs, adverse events, prior and concomitant medications, and data from the MINI, MADRS, PWC-20, C-SSRS, LSAS, and CGI-S. Unscheduled assessments of safety parameters will be included in listings only.

6.1.6. Pooling of Sites

Analysis sites (pooled sites) will be created if any site has fewer than 6 randomized subjects. Site 004 will be one analysis site and all other sites will be combined into a second analysis site. The final determination of pooled sites will be made prior to database lock. Should the condition for multiple imputation be met, analysis site will be used in the multiple imputation model.

6.1.7. Derived Variables

6.1.7.1. General

- **Age:** Age will be calculated as the integer difference in years between the subject's date of informed consent and the date of birth.

- **Baseline:** The last observation prior to the first dose of study drug. See Section 6.1.1 for more detail.
- **Change from baseline:** The value at the target time point minus the value at baseline.
- **Prior and concomitant medications:** All medications taken in the month prior to Visit 1 (Screening) or in the time interval between Visit 1 (Screening) and Visit 2 (Baseline) will be considered prior medications, whether or not they were stopped before Visit 2 (Baseline). Any medications continuing or starting after Visit 2 (Baseline) will be considered concomitant. If a medication starts before Visit 2 (Baseline) and continues after Visit 2 (Baseline) it will be considered both prior and concomitant.
- **Study day:** For analysis purposes, Study day is calculated relative to the date of first dose of study drug.
- **Treatment emergent adverse event (TEAE):** Treatment emergent adverse events are defined as 1) AEs with onset at the time of or following the start of treatment with IP through Visit 7 (Follow-Up) or 2) AEs starting prior to the start of treatment but increasing in severity or relationship at the time of, or following, the start of treatment with IP through Visit 7 (Follow-Up).
- **Total vial weight dispensed (grams):** Subjects will be dispensed 2 vials of the appropriate IP at Visits 2, 3, 4, and 5. The vial weights will be recorded prior to dispensation. For each subject and visit where vials were dispensed, calculate the total vial weight dispensed as the sum of the weight of the 2 vials prior to dispensation. If a subject is missing a weight for one or both vials at a visit, then the total vial weight dispensed at that visit will be set to missing.
- **Total vial weight returned (grams):** At Visits 3, 4, 5, and 6, subjects will return the IP vials that were dispensed at the previous visit. The weights of the returned vials will be recorded. For each subject and visit where vials were returned, calculate the total vial weight returned as the sum of the weight of the 2 vials returned. If a subject is missing a weight for one or both vials at a visit, then the total vial weight returned at that visit will be set to missing.
- **Difference in vial weight (grams):** For each subject, for Visits 3, 4, 5, and 6, the difference in vial weight will be calculated as: total vial weight returned at current visit minus total vial weight dispensed at previous visit. For example, the difference in vial weight at Visit 3 will be calculated as the difference in total vial weight returned at Visit 3 minus the total vial weight dispensed at Visit 2. If a subject is missing a value for total vial weight returned or total vial weight dispensed needed for the computation of difference in vial weight for a given visit, then the value of difference in vial weight for that visit will be set to missing.
- **Doses missing:** The number of doses missing will be computed for each subject and each visit where vials are returned (Visits 3, 4, 5, and 6). Doses missing for a given visit will be calculated as the absolute value of the difference in vial weight for the visit, divided by 0.2. If the difference in vial weight for a given subject and visit is missing, then the number of doses missing will be set to missing.

6.1.7.2. Hamilton Anxiety (HAM-A) Scale

At each visit, subjects will be asked to complete the HAM-A questionnaire to assess anxiety. The HAM-A questionnaire consists of 14 items, each scored on a 5-point scale (0="Not present", 1="Mild", 2="Moderate", 3="Severe", 4="Very severe"). It is completed by trained personnel over a 15-to-20-minute period. The Structured Interview Guide for the HAM-A (SIGH-A) will be used.

The Hamilton Anxiety Scale (HAM-A) total score is calculated as the sum of the 14 individual scores, ranging from 0 to 56 where <17 indicates mild severity, 18-24 mild to moderate severity, and 25-30 moderate to severe.

The fraction of missing change from baseline to Visit 6 HAM-A total scores is calculated as the number of missing values of change from baseline to Visit 6 HAM-A total scores across all subjects in the ITT population divided by the total number of expected change scores (1 per subject in the ITT population). The fraction of missing change from baseline to Visit 6 HAM-A total scores is used to compute the threshold for determining whether to implement the multiple imputation procedure, as described in Section 6.1.4.

6.1.7.3. Clinician's Global Impression – Improvement (CGI-I) Scale

The CGI scale is a clinician-rated scale assessment of the clinician's view of the subject's global health prior to and after participation in a clinical study. The improvement component (CGI-I) asks the clinician to respond to the following question:

> *"Rate total improvement whether or not, in your judgement, it is due entirely to drug treatment. Compared to his condition at admission to the project, how much has he changed?"*

The rating is on an 8-point scale (0="Not assessed", 1="Very much improved", 2="Much improved", 3="Minimally Improved", 4="No change", 5="Minimally worse", 6="Much worse", 7="Very much worse").

Subjects with scores of 1 (Very much improved) or 2 (Much improved) at the end of treatment with PH94B will be categorized as "responders". The proportion of CGI-I responders will be calculated as the number of CGI-I responders divided by the number of subjects with non-missing CGI-I scores in the population of interest.

6.1.7.4. Patient's Global Impression of Change (PGI-C)

The PGI-C is a self-administered instrument that measures change in subjects' overall improvement with treatment. The subject will respond to the following question using the same scale as is used for the CGI-I (Section 6.1.7.3):

> "*Since the start of the study, my overall status is _____.*"

Subjects reporting scores of 1 (Very much improved) or 2 (Much improved) at the end of treatment with PH94B will be categorized as "responders". The proportion of PGI-C responders

will be calculated as the number of PGI-C responders divided by the number of subjects with non-missing PGI-C scores in the population of interest.

6.1.7.5. Adjustment Disorder New Module (ADNM) Scale

The ADNM is a newer scale that has been validated for classification of severity of adjustment disorder (AjD). It consists of an 18-item stressful life event checklist and a list of 20 statements about which reactions these types of events can trigger. Subjects are also asked to indicate how often the statements apply to them on a 4-point scale (1="never", 2="rarely", 3="sometimes", and 4="often").

The ADNM total score is calculated as the sum of the 20 statement frequency scores. The subscale scores will be calculated as the sum of the statement frequency scores indicated below.

- Preoccupation Subscore: 2, 4, 13, and 15
- Failure to Adapt Subscore: 10, 17, 19, and 20
- Avoidance Subscore: 3, 7, 11, and 14
- Depressed Mood Subscore: 1, 5, and 18
- Anxiety Subscore: 6 and 16
- Impulse Disturbance Subscore: 8, 9, and 12

6.1.7.6. International Adjustment Disorder Questionnaire (IADQ)

The IADQ is a recently validated questionnaire to measure AjD symptoms defined by the new International Classification of Disorders (ICD-11) definition. The subject completes a 9-item checklist of potential stressful events, and if they have experienced any stressful events, they then complete a 3-item list of potential problems suffered over the last month (Preoccupation subscale), a 3-item list of potential social impacts from the stressors (Failure to Adapt subscale), 1 regarding timing of symptoms, and a 3-item list of potential functional impairments (Functional Impairment). The Preoccupation, Failure to Adapt, and Functional Impairment items are scored on a 5-point scale (0="Not at all", 1="A little bit", 2="Moderately", 3="Quite a bit", and 4="Extremely").

The IADQ total score is calculated as the sum of the 6 Preoccupation and Failure to Adapt items (items 10 through 15). The Preoccupation and Failure to Adapt subscale scores will be calculated as the sums of the individual scores for items 10, 11, and 12 (Preoccupation) and 13, 14, and 15 (Failure to Adapt), respectively. An additional Functional Impairment subscale score will be calculated as the sum of the individual scores on items 17, 18, and 19 (not included in the total score).

6.1.7.7. Liebowitz Social Anxiety Scale (LSAS)

The LSAS is a clinician-rated scale that has been shown to be sensitive to treatment-related change in social phobia symptoms. The time frame for rating symptomatology is the past week. The scale consists of 24 items. Each item is given 2 ratings: fear or anxiety on scale of 0 to 3 and avoidance on a scale of 0 to 3, with a total maximum overall score of 144. The "Total

Performance (P) Subscore – Fear or Anxiety" and the "Total Performance Subscore (P) – Avoidance" are the sums of the fear or anxiety or avoidance scores, respectively, on items 1-4, 6, 8, 9, 13, 14, 16, 17, 20, and 21. The "Total Social (S) Subscore – Fear or Anxiety" and "Total Social (S) Subscore – Avoidance" are the sums of the fear or anxiety or avoidance scores, respectively, on items 5, 7, 10-12, 15, 18, 19, and 22-24. The "Total Anxiety Subscore" and the "Total Avoidance Subscore" are the sums of performance and social subscores for fear or anxiety and avoidance scales, respectively. The LSAS total score for each subject is the sum of all ratings across both scales.

6.1.7.8. Montgomery-Asberg Depression Rating Scale (MADRS)

The MADRS is a validated instrument used to measure the severity of depressive episodes. A higher MADRS score indicates more severe depression. The MADRS includes 10 items and uses a 0 to 6 severity scale.

The MADRS total score will be calculated as the sum of the 10 items and will range from 0 to 60.

6.1.7.9. Columbia-Suicide Severity Rating Scale (C-SSRS)

The C-SSRS is a semi-structured interview that captures the occurrence, severity, and frequency of suicide-related thoughts and behaviors during the assessment period. The interview includes definitions and suggested questions to solicit the type of information needed to determine if a suicide-related thought or behavior has occurred. The C-SSRS has a "baseline" version, which will be completed at Visit 1 (Screening), and a "since last visit" version that will be completed at all subsequent visits.

There are a maximum of 19 items to be completed: 7 that are required, 10 potential additional items if there is a positive response to a required item, and 2 items for suicide/suicide behavior present during the interview. The C-SSRS uses dichotomous scales (i.e., yes or no), Likert scales, and text or narrative are used to further describe the thoughts or behaviors.

Subjects are considered to have had suicidal ideation during a time period (lifetime, last 6 months, since last visit) if they respond "Yes" to any of the 5 suicidal ideation questions listed below for that time period:

- Wish to be dead (Category 1)
- Non-specific active suicidal thoughts (Category 2)
- Active suicidal ideation with any methods (Category 3)
- Active suicidal ideation with some intent to act, without specific plan (Category 4)
- Active suicidal ideation with specific plan and intent (Category 5)

Subjects are considered to have had suicidal behavior during a time period if they respond "Yes" to any of the 5 suicidal behavior questions listed below for that time period:

- Completed suicide
- Actual attempt

- Interrupted attempt
- Aborted attempt
- Preparatory acts or behavior

Subjects are considered to have suicidal ideation or behavior during a time period if they responded "Yes" to any of the suicidal ideation or behavior questions for that time period.

A subject's maximum suicidal ideation score is the maximum suicidal ideation category to which they responded "Yes". Subjects are considered to have treatment emergent suicidal ideation if their maximum suicidal ideation score increased from a previous visit to the next visit after treatment with study drug.

Subjects are considered to have treatment emergent suicidal behavior if they did not have suicidal behavior prior to treatment with study drug but did have suicidal behavior at any visit after treatment with study drug.

6.1.7.10. Physician Withdrawal Checklist (PWC-20)

The PWC-20 is a 20-item simple instrument for assessing anxiolytic discontinuation symptoms. It consists of 20 questions related to withdrawal from benzodiazepines or other anti-anxiety compounds rated on a 4-point scale (0="Not Present", 1="Mild", 2="Moderate", 3="Severe"). The symptoms measured are based on those that are potentially related to anxiolytic withdrawal: gastrointestinal, mood, sleep, motor, somatic, perception and cognition. The questions will cover any symptoms that might occur during the week following discontinuation of PH94B.

The PWC-20 total score will be calculated as the sum of the 20 items and will range from 0 to 60.

Subjects with any score >0 will be categorized as having a withdrawal symptom. The proportion of subjects with withdrawal symptoms will be calculated as the number of subjects with any score >0 divided by the total number of subjects in the population of interest.

6.1.8. Data Adjustments/Handling/Conventions

All collected data will be presented in listings. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included only in the data listings.

Medical history and AEs (all types) will be coded using the current version of the Medical Dictionary for Regulatory Activities (MedDRA) and WHO Drug Dictionary (WHO-DD) Anatomical Therapeutic Chemical (ATC) classes and preferred terms.

For quantitative laboratory values reported as '<X' or '≤X', 1/2 times the lower limit of quantitation will be used for analysis. For values reported as '>X' or '≥X', 3/2 times the upper limit of quantitation will be used. Values above or below the limit of quantitation will not be flagged as abnormal unless they are outside the normal range for that laboratory test, as described in Section 9.2.

A treatment related AE is any AE with a reasonable possibility of being related to the study drug. Medical judgement will be used to determine relatedness, considering all relevant factors, including pattern of reaction, temporal relationship, relevant medical history, and confounding factors such as co-medication or concurrent diseases.

If partial dates occur for treatment emergent AEs, prior medications, or concomitant medications, the convention for replacing missing information for the purpose of statistical analysis is as follows.

Adverse Events

- If the event start date is completely missing, or if the subject was not treated, no imputation will be conducted.
- If the event start date is missing day and month, the treatment start date is not missing, and event start year is the same as the treatment start year, set the event start date to the treatment start date.
- If the event start date is missing day and month and the treatment start date is missing, the event start year is not the same as the treatment start year, or if there is information indicating that the event ended before the treatment start date (e.g., the event end date is before the treatment start date), then set the event start month and day to January 1st.
- If only the event start day is missing, the treatment start date is not missing, and the event start month and year are the same as the treatment start month and year, set the event start day to the treatment start day.
- If only the event start day is missing and the treatment start date is missing, or the event start month and year is not the same as the treatment start month and year, or if there is information to indicate that the event ended before the treatment start date, then set the event start day to the first day of the start month.
- End dates will not be imputed.

Prior and Concomitant Medications

Medication start and stop dates will not be imputed. Instead, available information will be used to assign the following categories to each medication: prior versus concomitant versus both. If a missing date part leads to uncertainty in how to assign categories, the medication will be considered concomitant.

For example, if the medication start year or end year is after the start of treatment, the medication will be considered concomitant even if the start month and/or day are missing. Likewise, if the medication start year occurs in the same year as the treatment start year, and the medication start

month or end month is after the treatment start month, then the medication will be considered concomitant even if the medication start day or end day is missing.

7. Study Patients/Subjects and Demographics

7.1. Disposition of Patients/Subjects and Withdrawals

Disposition will include tabulations of the number and percentage of subjects randomized into each treatment group, completing the study, and withdrawing from the study, along with reasons for withdrawal overall and by treatment group. Additionally, the number and percentage of subjects assigned to each analysis population will be displayed. Tabulations will be for all subjects and will be displayed by the planned treatment.

Additionally, inclusion and exclusion criteria not met will be listed for screen failures.

7.2. Protocol Violations and Deviations

Protocol deviations will be tracked, recorded, and reviewed prior to database lock, following the Protocol Deviation Guidance Plan for this study. The deviation list will be stored in the Remarque system and transferred to the biostatistics team for analysis.

Protocol deviations will be classified as "Important" or "Non-Important". An important deviation poses a possible safety issue to the participant, or it has a potential impact on the statistical analysis of the clinical data. A non-important deviation is identified as any protocol deviation that does not meet the criteria for an important deviation.

Examples of important deviations include but are not limited to:

- Violation of inclusion/exclusion criteria
- Randomization or dosing error
- Use of prohibited medications
- Assessment conducted by unqualified personnel
- Missing baseline efficacy or safety assessments
- Lack of adherence to study drug dosing
- Controlled substance inappropriate handling

Examples of non-important deviations include but are not limited to:

- Lack of data collection due to subject non-compliance
- Subjects who fail to make scheduled visits
- Extension of screening period to clarify diagnoses or verify laboratory values
- Incorrect storage of study drug
- Failure to follow up on subjects who drop out

Subjects with at least 1 deviation classified as "Important" will be excluded from the PP Population. The final decision regarding classification of deviations and inclusion and exclusion

of subjects from the analysis populations will be based on a final listing of protocol deviations. Subject inclusion/exclusion in analysis populations will be determined during a blinded review meeting before study data are unblinded. Clinical and Biostatistics team members will provide input to the decision and the final composition of the analysis populations will be approved by the Sponsor.

Protocol deviations will be summarized by treatment group and overall subjects for the All Subjects population. Data will also be presented in a by-subject listing.

7.3. Demographics and Other Baseline Characteristics

Summary statistics for demographic and other baseline characteristics will be presented overall and by treatment group. Demographic variables will include age, sex, race, ethnicity, height, weight, and body mass index (BMI). Baseline variables will include HAM-A total score, ADNM total score, and IADQ total score. Demographic and baseline characteristic data will be summarized for the ITT and Safety populations.

Prior medications will be classified by ATC Class Level 2 and preferred term. The number and percentage of subjects taking each classification of medication will be summarized overall and by treatment group. The analysis will be conducted for the Safety population. Data will also be presented in a by-subject listing.

Medical and psychiatric history will be classified by system organ class (SOC) and preferred term. The number and percentage of subjects with each classification will be summarized overall and by treatment group. The analysis will be conducted for the Safety population. Data will also be presented in a by-subject listing.

Results from the Mini-International Neuropsychiatric Interview (MINI) and data on substance use will be presented in a by-subject listing.

7.4. Exposure and Compliance

Drug and placebo will be supplied in identical 10 mL amber glass vials with metered dose spray nozzle containing 8 mL of IP. Both drug and placebo nozzles will deliver 100 µL of IP. Each vial contains 40 doses of IP (8 mL/200 µL/dose = 40 doses). Subjects will be dispensed 2 vials of IP at Visit 2 (Baseline) and Visits 3 through 5. Vial weights will be recorded prior to dispensation. At Visits 3 through 6, the 3 vials dispensed at the previous visit will be returned. Weights of the returned vials will be recorded.

The difference in vial weight and doses missing will be computed for each subject and visit for which vials were returned (Visits 3 through 6). Details of these calculations are provided in Section 6.1.7.1. The calculation for doses missing does not differentiate between doses administered for priming purposes versus doses administered to the nasal cavity. It is assumed that priming practices are uniform across subjects and treatment groups. Differences in vial weight, differences in vial volume, and doses missing will be summarized by visit, overall and by treatment group for the Safety population.

8. Efficacy Analysis

8.1. Primary Efficacy Analysis

The primary endpoint will be tested for the following hypothesis:

H_{10}: Mean change in HAM-A total score from Visit 2 (Baseline) to Visit 6 does not differ between PH94B and placebo.

H_{11}: Mean change in HAM-A total score from Visit 2 (Baseline) to Visit 6 does differ between PH94B and placebo.

The estimand for the primary efficacy endpoint has the following components:

Table 4: Primary Efficacy Estimand

Attribute	Definition
Treatment	The treatment of interest is PH94B, 3.2 µg administered as an intranasal solution [redacted]. The active drug will be compared to a placebo control.
Population	The population of interest is adults with AjDA as defined by inclusion and exclusion criteria.
Variable of Interest	The variable of interest is change in subject reported severity of anxiety as measured by change from baseline in HAM-A total score using the SIGH-A, after 4 weeks of randomized treatment with study drug.
Intercurrent Events	Treatment discontinuation prior to the planned assessment time frame. Intercurrent events will be treated as described in Table 3.
Population Summary	The difference in change from baseline in mean HAM-A total score between PH94B-treated and placebo-treated subjects after 4 weeks of treatment.

Descriptive summaries of HAM-A total scores and change from baseline in HAM-A total scores will be provided for the primary endpoint by visit and by treatment group, based on the observed data.

An ANCOVA model with change from baseline to Visit 6 in HAM-A total scores as the outcome, treatment group as the factor, and baseline HAM-A as a covariate will be used to test the null hypothesis that there is no difference between PH94B- and placebo-treated subjects in mean change from baseline to Visit 6 in HAM-A total score. The analysis will be performed in the ITT population using SAS PROC MIXED. The following parameters will be presented: the change from baseline LS means and standard error (SE), 95% CI for the LS means, *p* value for testing if the LS mean is different than 0, LS mean difference between treatment groups (PH94B minus placebo) with SE, 95% CI for the LS mean difference, and *p* value for testing if the treatment LS means are equal.

If, for unanticipated reasons (intercurrent events), the fraction of subjects with missing change

from baseline to Visit 6 HAM-A total scores is greater than 0.05, change from baseline to Visit 6 HAM-A total scores will be imputed using the fully conditional specification approach to multiple imputation as described in Section 6.1.4. If the fraction of missing change scores is ≤0.05, missing change from baseline to Visit 6 HAM-A total scores will be imputed with treatment group mean change scores.

8.1.1. Sensitivity Analyses of the Primary Efficacy Endpoint

8.1.1.1. Complete Case Sensitivity Analysis

Should imputation of the primary endpoint be necessary, a complete case analysis will be performed in the ITT population. The complete case analysis will be exactly parallel to the planned primary efficacy analysis, except it will exclude any subjects with missing change from baseline to Visit 6 HAM-A total scores, using only observed responses. Descriptive summaries will be provided for the primary endpoint based on the complete-case data.

8.1.1.2. Control-Case Sensitivity Analysis

Should imputation of the primary endpoint be necessary, an additional sensitivity analysis will be performed assuming that subjects with missing HAM-A total scores at Visit 6 responded to treatment as if they had received placebo. Specifically, missing values for the HAM-A change from baseline to Visit 6 will be set to the mean change from baseline for the placebo group. The analysis will be otherwise parallel to that of the primary efficacy analysis with the exception that descriptive summaries will not be presented.

8.2. Secondary Efficacy Analyses

8.2.1. Analysis of Proportion of CGI-I Responders

The CGI-I secondary endpoint will be tested for the following hypothesis:

H_{20}: The proportion of CGI-I responders at Visit 6 does not differ between PH94B and placebo.

H_{21}: The proportion of CGI-I responders at Visit 6 does differ between PH94B and placebo.

The estimand for the CGI-I secondary efficacy endpoint includes the same population, treatment, and anticipated intercurrent events as the primary estimand. The variable of interest is the proportion of CGI-I responders at Visit 6. The proportion of CGI-I responders will be calculated as described in Section 6.1.7.3. The population-level summary measure is the difference in the proportion of CGI-I responders between PH94B-treated and placebo-treated subjects at Visit 6.

The PH94B and placebo proportions of CGI-I responders will be compared using a normal approximation (Wald) test for the difference between 2 binomial proportions. If expected cell sizes are less than 5, a Fisher's exact test will be used. The analysis will be performed using the ITT population. The following parameters will be presented: proportion of responders in each

treatment group, odds ratio and corresponding 95% CIs for PH49B responders versus placebo responders, and *P* value for the Wald test for equality of proportions will be presented.

Additionally, CGI-I scores and responder status will be summarized using frequencies and percentages by visit and by treatment group.

8.2.2. Analysis of the Proportion of PGI-C Responders

The PGI-C secondary endpoint will be tested for the following hypothesis:

H_{30}: The proportion of PGI-C responders at Visit 6 does not differ between PH94B and placebo.

H_{31}: The proportion of PGI-C responders at Visit 6 does differ between PH94B and placebo.

The estimand for the PGI-C secondary efficacy endpoint includes the same population, treatment, and anticipated intercurrent events as the primary estimand. The variable of interest is the proportion of PGI-C responders at Visit 6. The proportion of PGI-C responders will be calculated as described in Section 6.1.7.4. The population-level summary measure is the difference in the proportion of PGI-C responders between PH94B-treated and placebo-treated subjects at Visit 6.

The analysis for this endpoint will be exactly parallel to the one described for the CGI-I secondary endpoint in Section 8.2.1.

8.2.3. Secondary Efficacy Analysis of Change from Baseline in ADNM Total Score

The ADNM secondary endpoint will be tested for the following hypothesis:

H_{10}: Mean change in ADNM total score from Visit 2 (Baseline) to Visit 6 does not differ between PH94B and placebo.

H_{11}: Mean change in ADNM total score from Visit 2 (Baseline) to Visit 6 does differ between PH94B and placebo.

The estimand for the ADNM secondary efficacy endpoint is the same as that for the primary endpoint, except that it uses the ADNM total scores as the variable of interest. Change from baseline to Visit 6 in ADNM total score will be analyzed analogously to the primary endpoint. Multiple imputation will not be performed.

Descriptive summaries will be provided for observed ADNM total scores and changes from baseline by visit and by treatment group.

8.2.4. Secondary Efficacy Analysis of Change from Baseline in IADQ Total Score

The IADQ secondary endpoint will be tested for the following hypothesis:

H_{10}: Mean change in IADQ total score from Visit 2 (Baseline) to Visit 6 does not differ

between PH94B and placebo.

H_{11}: Mean change in IADQ total score from Visit 2 (Baseline) to Visit 6 does differ between PH94B and placebo.

The estimand for the IADQ secondary efficacy endpoint is the same as that for the primary endpoint, except that it uses the IADQ total scores as the variable of interest. Change from baseline to Visit 6 in IADQ total score will be analyzed analogously to the primary endpoint. Multiple imputation will not be performed.

Descriptive summaries will be provided for observed IADQ total scores and changes from baseline by visit and by treatment group.

8.3. Exploratory Efficacy Analysis

To evaluate the efficacy of PH94B over time, observed values and changes from baseline in HAM-A total scores will be summarized by visit and by treatment group. Summaries of CGI-I and PGI-C scores by visit and by treatment group will be displayed with the secondary efficacy analyses.

The differences in changes from baseline between the PH94B and placebo groups in HAM-A total scores at Visits 3, 4, and 5 will be assessed using the ANCOVA analysis described in Section 8.1 for the observed data.

The ADNM and IADQ observed subscores and changes from baseline will be displayed in by-subject listings.

9. Safety and Tolerability Analysis

Safety in this study will be evaluated based on data collected on AEs, clinical laboratory assessments, vital signs, 12-lead ECGs, and physical examinations including examination of the nasal passages, C-SSRS, MADRS scores, and PWC-20 scores.

All safety analysis reporting will be based on the Safety population (as defined in Section 5).

9.1. Adverse Events

Treatment emergent adverse events are defined as in Section 6.1.7.1. Missing and partially missing start dates will be imputed for the purpose of analysis as described in Section 6.1.8.

All AE data will be categorized as Severe > Moderate > Mild. Relationship of all AEs to IP will be categorized as related or not related. In the summaries showing severity and relationship to study drug, the event with the maximum severity or strongest relationship to study drug will be reported. If a particular event is missing the severity and/or relationship, then the strongest possible severity or relationship will be assumed for analysis (severity = severe, relationship = related).

An overall summary of TEAEs will be provided giving the number and percent of subjects who

reported at least 1 of the following: TEAE (including any TEAE, TEAEs categorized as severe, and related TEAEs), TEAE leading to discontinuation of the study drug, serious TEAEs, and TEAEs leading to death. The summary will be displayed overall and by treatment group.

In addition to the overall summary, summaries of the number and percentage of subjects with TEAEs will be displayed overall and for each treatment group by SOC and preferred term. Summaries of TEAEs by severity (Severe > Moderate > Mild) and relationship to IP (Related > Not Related) will also be provided. Treatment emergent AEs resulting in discontinuation of study drug will be summarized separately in a similar manner.

The AE summary tables will include counts of subjects. Therefore, if a subject experiences more than 1 episode of a particular AE, the subject will be counted only once for that event. If a subject has more than 1 AE that is coded to the same preferred term, the subject will be counted only once for that preferred term. Similarly, if a subject has more than 1 AE within an SOC, the subject will be counted only once in that SOC.

Subject listings of AEs will be produced. Adverse events that are treatment emergent will be flagged.

9.1.1. Adverse Events Leading to Discontinuation of Study Drug

A summary of incidence rates (frequencies and percentages) of TEAEs leading to discontinuation of study drug, overall and by treatment group, SOC, and preferred term will be prepared for the Safety population. No inferential statistical tests will be performed.

A data listing of AEs leading to discontinuation of study drug will also be provided, displaying details of the event(s) captured on the CRF.

9.1.2. Deaths and Serious Adverse Events

Serious adverse events will be displayed in a separate by-subject listing.

9.2. Clinical Laboratory Evaluations

Descriptive summaries of observed values and change from baseline values will be presented for continuous hematology, chemistry (also including prolactin and thyroid function parameters) for each treatment group and overall subjects at each study visit. Urinalysis results will be listed.

Laboratory values that are outside the normal range will also be flagged in the data listings and presented with the corresponding normal ranges. Any out-of-range hematology or clinical chemistry values that are identified by the investigator as being clinically significant will also be shown in a separate data listing.

Urine drug screen and pregnancy test results will be listed.

9.3. Vital Signs

Descriptive summaries of observed values and changes from baseline will be calculated for systolic blood pressure (mmHg), diastolic blood pressure (mmHg), heart rate (beats/min), respiratory rate (breaths/min), and temperature (°C), overall, by treatment group, and by study visit.

9.4. Electrocardiograms

The number and percentage of subjects with normal and abnormal 12-lead ECG findings will be summarized overall and by treatment group at each study visit. Abnormal results will be grouped as clinically significant and not clinically significant.

Descriptive summaries for the observed results and change from baseline will be presented for 12-lead ECG measures of RR interval (msec), PR interval (msec), QRS interval (msec), and heart rate (bpm) for each treatment group and overall subjects at each study visit. If triplicate reads are taken, the mean of the reads will serve as the observed value at the specific visit.

A comparison of QT results will be presented. Summary statistics for baseline values at Visit 1 (Screening) and Visit 6 will be displayed overall and by treatment group for QT interval (msec) and QT interval corrected for heart rate using Fridericia's formula (QTcF) (msec). In addition, the number and percent of subjects in each treatment group who experienced a change >30 msec or a change >60 msec will be presented.

9.5. Physical Examination

Physical examination findings will be listed. Abnormal results and clinically significant abnormal results will be flagged.

9.6. Concomitant Medication

The number and percentage of subjects taking each concomitant medication will be summarized by treatment group and overall subjects. Medications will be classified by ATC Class Level 2 and preferred term.

9.7. Columbia-Suicide Severity Rating Scale (C-SSRS)

The number and percentage of subjects reporting "Yes" for any of the 5 suicidal ideation questions (Categories 1 to 5) or any of the 5 suicidal behavior questions (Categories 6 to 10) will be displayed for each treatment group and overall subjects, along with the number and percentage reporting suicidal ideation OR behavior (Categories 1 to 10). The number and percentage of subjects with treatment emergent suicidal ideation, treatment emergent suicidal behavior, and treatment emergent suicidal ideation or behavior as defined in Section 6.1.7.9 will also be presented.

9.8. Montgomery-Asberg Depression Rating Scale (MADRS)

For each subject and visit, MADRS total scores will be derived as described in Section 6.1.7.8. Summaries of MADRS total scores and changes from baseline will be presented by visit, overall and by treatment group.

9.9. Physician Withdrawal Checklist (PWC-20)

Physician Withdrawal Checklist total scores and proportion of subjects with at least one symptom will be derived as described in Section 6.1.7.10. Mean PWC-20 total score will be compared between PH94B- and placebo-treated subjects using a 2-sample t-test. Summaries of PWC-20 total scores and frequency and percentage of subjects with withdrawal symptoms will be presented overall and by treatment group. The difference in total score means, SE of the difference, p-value and 95% confidence interval will be displayed.

10. Other Planned Analysis

No additional analyses are prospectively planned for this study.

10.1. Coronavirus 2019 (COVID-19) Impact

The SARS-CoV-2 virus and variants may still be a threat and safety precautions may still be in place during study enrollment. To assess the impact of the COVID-19 pandemic on study procedures, study staff will complete the COVID-19 Impact questionnaire. Should a study visit be affected by COVID-19, study staff will record how the visit was affected (missed, abbreviated, delayed, performed remotely, or otherwise deviating from the planned format in the protocol) and which procedures were impacted. All COVID-19 protocol deviations will be provided in a separate listing. This listing will include the subjects, affected visits, and affected assessments.

11. Changes from Planned Analysis

Study staff will complete the Coronavirus 2019 (COVID-19) Impact questionnaire to assess the impact of the COVID-19 pandemic on study procedures. The COVID-19 Impact questionnaire is described in Section 10.1. All COVID-19 protocol deviations will be provided in a separate listing.

The ADNM subscales exploratory endpoints analysis will not be completed as part of this SAP.

Physical examination and urinalysis results will not be summarized using descriptive statistics but will be listed.

The treatment failure sensitivity analysis will be replaced with a control-case sensitivity analysis that imputes the mean change from baseline to Week 6 in HAM-A total scores from the placebo group for missing change from baseline responses. This approach accounts for the potential for a

high placebo response.

12. References

ASA. (2018) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2018. http://www.amstat.org/about/ethicalguidelines.cfm

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ICH (1998). ICH Harmonised Tripartite Guideline. Statistical Principles for Clinical Trials E9; 1998. https://database.ich.org/sites/default/files/E9_Guideline.pdf

Little R and Rubin D. (1987). Statistical Analysis with Missing Data, New York: Wiley.

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13. Tables and Listings

All listings and tables will have a header showing the sponsor company name and protocol and a footer showing the version of SAS, the file name and path, and the source of the data (e.g., listing number).

The following are planned summary tables for protocol number PH94B-CL029. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

13.1. Demographic Data

Table 5: Demographic Data Summary Tables

Table Number	Population	Table Title/Summary
14.1 Demographic Data Summary Tables		
Table 14.1.1	All Subjects	Subject Disposition
Table 14.1.2	Safety	Protocol Deviations and Violations
Table 14.1.3.1	Safety	Demographics and Baseline Characteristics
Table 14.1.3.2	ITT	Demographics and Baseline Characteristics
Table 14.1.4	Safety	Medical and Psychiatric History by System Organ Class and Preferred Term

Table Number	Population	Table Title/Summary
Table 14.1.5	Safety	Prior Medications by ATC Class Level 2 and Preferred Term
Table 14.1.6	Safety	Exposure to Study Drug

13.2. Efficacy Data

Table 6: Efficacy Data

Table Number	Population	Table Title / Summary
Table 14.2. Efficacy Tables		
Table 14.2.1.1	ITT	ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Primary Analysis
Table 14.2.1.2	ITT	ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Sensitivity Analysis Using Complete Cases
Table 14.2.1.3	ITT	ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Control-Case Sensitivity Analysis
Table 14.2.2.1	ITT	Analysis of the Proportion CGI-I Responders – Secondary Analysis
Table 14.2.3.1	ITT	Analysis of the Proportion PGI-C Responders – Secondary Analysis
Table 14.2.4.1	ITT	ANCOVA Change from Baseline in ADNM Total Scores by Visit – Secondary Analysis
Table 14.2.5.1	ITT	ANCOVA Change from Baseline in IADQ Total Scores by Visit – Secondary Analysis
Table 14.2.6.1	ITT	ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Exploratory Endpoint

13.3. Safety Data

Table 7: Safety Data

Table Number	Population	Table Title / Summary
14.3.1 Displays of Adverse Events		
Table 14.3.1.1	Safety	Overall Summary of Treatment Emergent Adverse Events
Table 14.3.1.2.1	Safety	Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Table 14.3.1.2.2	Safety	Treatment Emergent Adverse Events by Preferred Term
Table 14.3.1.3	Safety	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Table 14.3.1.4	Safety	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Relationship to Study Drug

Table Number	Population	Table Title / Summary
14.3.2 Summary of Deaths, Other Serious and Significant Adverse Events		
Table 14.3.2.1	Safety	Treatment Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term
14.3.3 Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events		
Table 14.3.3.1	Safety	Subject Listing of Serious Adverse Events
Table 14.3.3.2	Safety	Subject Listing of Adverse Events Leading to Discontinuation of Study Drug
14.3.4 Abnormal Laboratory Values		
Table 14.3.4.1	Safety	Subject Listing of Clinically Significant Abnormal Laboratory Values: Hematology
Table 14.3.4.2	Safety	Subject Listing of Clinically Significant Abnormal Laboratory Values: Clinical Chemistry
14.3.5 Laboratory Data Summary Tables		
Table 14.3.5.1	Safety	Hematology: Observed Results and Change from Baseline by Visit
Table 14.3.5.2	Safety	Clinical Chemistry and Thyroid: Observed Results and Change from Baseline by Visit
14.3.6 Other Safety Data Summary Tables		
Table 14.3.6.1	Safety	Vital Signs: Observed Results and Change from Baseline by Visit
Table 14.3.6.2.1	Safety	12-Lead Electrocardiogram: Summary of Interpretation by Visit
Table 14.3.6.2.2	Safety	12-Lead Electrocardiogram: Observed Results and Change from Baseline by Visit
Table 14.3.6.2.3	Safety	12-Lead Electrocardiogram: Summary of QT and QTcF Results by Visit
Table 14.3.6.3	Safety	Summary of Concomitant Medications by ATC Class Level 2 and Preferred Term
Table 14.3.6.4	Safety	Summary of Columbia Suicide Severity Rating Scale (C-SSRS) by Visit
Table 14.3.6.5	Safety	Summary of Montgomery-Asberg Depression Rating Scale (MADRS) Total Score by Visit
Table 14.3.6.6	Safety	Summary of Physician Withdrawal Checklist (PWC-20)

13.4. Planned Listing Descriptions

The following are planned data and subject data listings for protocol number PH94B-CL029.

In general, 1 listing will be produced per eCRF domain. All listings will be sorted by treatment, site, and subject number. All calculated variables will be included in the listings.

In all listings a blank line will be placed between each subject. Within a data listing, if an item appears line after line (e.g., repetition of subject number), then only the first occurrence will be displayed.

In data listings, the information for 1 subject will be kept on 1 page, if at all possible, rather than splitting a subject's information across pages.

Table 8: Planned Listings

Listing Number	Population	Listing Title / Summary
16.2 Subject Data Listings		
16.2.1 Subject Discontinuations/Completions		
Listing 16.2.1.1	All Subjects	Subject Disposition
16.2.2 Protocol Deviations		
Listing 16.2.2.1	Screen Failures	Inclusion and Exclusion Criteria
Listing 16.2.2.2	All Subjects	Protocol Deviations
16.2.3 Subjects Excluded from the Efficacy Analyses		
Listing 16.2.3.1	All Subjects	Analysis Populations
16.2.4 Demographic Data and Other Baseline Characteristics		
Listing 16.2.4.1	All Subjects	Subject Consent and Demographics
Listing 16.2.4.2	All Subjects	Medical and Psychiatric History
Listing 16.2.4.3	All Subjects	Substance Use
Listing 16.2.4.4	All Subjects	Mini-International Neuropsychiatric Interview (MINI)
Listing 16.2.4.5	All Subjects	Liebowitz Social Anxiety Scale (LSAS)
16.2.5 Compliance Data		
Listing 16.2.5.1	All Subjects	Study Drug Dispensation
Listing 16.2.5.2	All Subjects	Study Drug Administration
16.2.6 Individual Efficacy Response Data		
Listing 16.2.6.1	All Subjects	Hamilton Anxiety Scale (HAM-A)
Listing 16.2.6.2	All Subjects	Adjustment Disorder New Module (ADNM)
Listing 16.2.6.3	All Subjects	International Adjustment Disorder Questionnaire (IADQ)
Listing 16.2.6.4	All Subjects	Clinical Global Impression – Improvement (CGI-I)
Listing 16.2.6.5	All Subjects	Patient Global Impression of Change (PGI-C)
16.2.7 Adverse Event Listings (by Subject)		
Listing 16.2.7.1	All Subjects	Adverse Events
16.2.8 Laboratory Values (by Subject)		

Listing Number	Population	Listing Title / Summary
16.2 Subject Data Listings		
Listing 16.2.8.1	All Subjects	Hematology Laboratory Evaluations
Listing 16.2.8.2	All Subjects	Clinical Chemistry and Thyroid Laboratory Evaluations
Listing 16.2.8.3	All Subjects	Urinalysis Laboratory Evaluations
Listing 16.2.8.4	All Enrolled Female Subjects	Pregnancy Test Results
Listing 16.2.8.5	All Subjects	Laboratory Results for Urine Drug Screen
16.2.9 Other Clinical Observations and Measurements (by Subject)		
Listing 16.2.9.1	All Subjects	Vital Signs
Listing 16.2.9.2	All Subjects	12-Lead Electrocardiogram Measurements
Listing 16.2.9.3	All Subjects	Physical Examination Including Nasal Passages Measurements
Listing 16.2.9.4	All Subjects	Prior and Concomitant Medications
Listing 16.2.9.5	All Subjects	Columbia Suicide Severity Rating Scale (C-SSRS)
Listing 16.2.9.6	All Subjects	Montgomery-Asberg Depression Rating Scale (MADRS)
Listing 16.2.9.7	All Subjects	Clinical Global Impression – Severity (CGI-S) Scale
Listing 16.2.9.8	All Subjects	Physician Withdrawal Checklist (PWC-20)
16.2.10 Other Study Measurements or Assessments (by Subject)		
Listing 16.2.10.1	All Subjects	COVID-19 Impact Assessment

14. PH94B-CL029Tables and Listing Shells

14.1. Standard Layout for all Tables and Listings

The following standard layout will be applied to all Tables and Listings in support of this study. Note that programming notes may be added if appropriate after each TLF shell.

Figure 1: Standardized Layout

VistaGen Therapeutics, Inc. Page xx of xx

Protocol: PH94B-CL029 Version

<Table, Listing, Figure> xx.x.x

<Title of Table Listing or Figure>

<Study Population and if applicable subgroup Description>

Body of Table, Listing or Figure

<Note: If directly Applicable>

Footnote 1 *<if applicable>* Recommendation is to keep footnotes to a minimum

Footnote 2 *<if applicable>*

Footnote n *<if applicable>*

Footnote n+1 *<pgm path and name>, <date>*

14.2. Planned Table Shells

See Figure 2 below.

[redacted]

Figure 2: Planned Table Shells

Table 14.1.1
Subject Disposition
All Subjects

Status Category	PH49B (N=XX)	Placebo (N=XX)	Overall (N=XX)
All Subjects Population [1]			
Screened for Eligibility			XX
Screen Failure at Visit 1 (Screening)			XX
Subject Failed to Return for Visit 2 (Baseline)			XX
Adverse Event			XX
Death			XX
Lost to Follow-Up			XX
Physician Decision			XX
Protocol Violation			XX
Withdrawal by Subject			XX
Study Terminated by Sponsor			XX
Disease Progression			XX
Other			XX
Screen Failure at Visit 2 (Baseline)			XX
Randomized	XX	XX	XX
Safety Population [1]	XX (XX.X%)	XX (XX.X%)	XX
ITT Population [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviation: ITT = intent-to-treat.
Note: Subjects are displayed by treatment received. Percentages are n/number of subjects in the Safety population within treatment received and overall subjects * 100.
[1] The All Subjects population includes all subjects who sign an informed consent, participate in Visit 1 (Screening), and are entered into the eCRF.
[2] The Safety population includes all subjects who were dispensed study drug and reported administering at least 1 dose.
[3] The ITT population includes all subjects who were randomized and had 1 documented dose of study drug at Visit 2 (Baseline).
Reference Listing: 16.2.1.1, 16.2.2.1, 16.2.3.1

Programming Note: *Subjects who discontinue due to "Screen Failure" should not be included as a "Discontinued Early" subject. The "Ongoing in Study" row will only be presented for pre-lock blinded dry run deliveries; upon lock, it will be removed.*

Table 14.1.1 (cont.)
Subject Disposition
All Subjects

Status Category	PH49B (N=xx)	Placebo (N=xx)	Overall (N=xx)
Completed Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ongoing in Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Discontinued Early	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for Discontinuation:	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Adverse Event	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Death	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lack of Efficacy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lost to Follow-Up	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Non-Compliance with Study Drug	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Physician Decision	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Protocol Violation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Withdrawal by Subject	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Study Terminated by Sponsor	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Disease Progression	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missed Two or More Consecutive Visits During 4-Week Treatment Period	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviation: ITT = intent-to-treat.
Note: Subjects are displayed by treatment received. Percentages are n/number of subjects in the Safety population within treatment received and overall subjects * 100.
[1] The All Subjects population includes all subjects who sign an informed consent, participate in Visit 1 (Screening), and are entered into the eCRF.
[2] The Safety population includes all subjects who were dispensed study drug and reported administering at least 1 dose.
[3] The ITT population includes all subjects who were randomized and had 1 documented dose of study drug at Visit 2 (Baseline).
Reference Listing: 16.2.1.1, 16.2.2.1, 16.2.3.1

Programming Note: *Subjects who discontinue due to "Screen Failure" should not be included as a "Discontinued Early" subject. The "Ongoing in Study" row will only be presented for pre-lock blinded dry run deliveries; upon lock, it will be removed.*

[redacted]

Table 14.1.2
Protocol Deviations and Violations
Safety Population

Category Protocol Deviation	PH94B (N=XXX)	Placebo (N=XXX)	Overall (N=XXX)
Subjects With Any Protocol Deviation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with Important Protocol Deviations	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with Non-Important Protocol Deviations	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXXXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. Subjects with one or more deviations within a type of protocol deviation were counted only once.
Reference Listing: 16.2.2.2

Programming note: *Protocol deviations will be presented as per the PD log.*

[redacted]

Table 14.1.3.1
Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Age (years) [1]			
n	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Age Category			
18 to 35 years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
36 to 55 years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
≥ 56 years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Sex			
Male	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Female	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ethnicity			
Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Reported	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Continue for Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, More than One Race, Not Reported), Height (cm), Weight (kg), BMI (kg/m2), Baseline HAM-A Total Score, Baseline ADNM Total Score, Baseline IADQ

Abbreviations: ADNM = Adjustment Disorder New Module; BMI = Body Mass Index; HAM-A = Hamilton Anxiety Scale; IADQ = International Adjustment Disorder Questionnaire; SD = standard deviation.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. Assessments are from the baseline visit as defined for the variable of interest.
[1] Age was calculated as the integer difference in years between the subject's date of informed consent and the date of birth.
Reference Listings: 16.2.4.1, 16.2.6.1, 16.2.6.2, 16.2.6.3

Programming Note: *If variable has missing values, then add "Missing" row for the specified variable. If there are no missing values, then missing row is not needed.*

Table 14.1.3.2
Demographics and Baseline Characteristics
ITT Population

Same shell as Table 14.1.3.1; Programming Note: *Update footnote to state "Percentages are n/Number of subjects in the ITT population within planned treatment and overall subjects * 100."*

Table 14.1.4
Medical and Psychiatric History by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Subjects with at least 1 Recorded Medical/Psychiatric History	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; SOC = system organ class.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. Medical/Psychiatric histories were coded using MedDRA version XX.X. Subjects were counted once for each SOC and once for each PT. Medical/Psychiatric history terms are displayed by descending frequency of SOC, then PT within SOC, and then alphabetically by PT.
Reference Listings: 16.2.4.2

Programming Note: *Replace "XX.X" in the footnote with the correct version of the MedDRA used for coding. For dry run delivery, use MedDRA version 24.1.*

Table 14.1.5
Prior Medications by ATC Class Level 2 and Preferred Term
Safety Population

ATC Class Level 2 Preferred Term	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Subjects with at Least 1 Prior Medication	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ATC Class 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: ATC = anatomical therapeutic chemical; PT = preferred term; WHO-DD = World Health Organization Drug Dictionary.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. Medications were coded using WHO-DD Global B3 version XX. All medications taken in the month prior to Visit 1 (Screening) or in the time interval between Visit 1 (Screening) and Visit 2 (Baseline) are considered prior medications, whether or not they were stopped before Visit 2 (Baseline). Medications are displayed by alphabetical order of ATC Level 2 classification, then descending frequency of PT within ATC, and then alphabetically by PT. Subjects were counted only once for each ATC and PT.
Reference Listings: 16.2.9.4

Programming Note: *ATC & PT text should be presented as is from the dataset. Replace "XX" in the footnote with the correct version of the WHO-DD used for coding. For dry run delivery, use WHO-DD Global B3 version Sep 2021.*

Table 14.1.6
Exposure to Study Drug
Safety Population

Study Visit [1] Parameter Statistic	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Visit 3			
Difference in Vial Weight			
n	XX	XX	XX
Mean (SD)	XX.XX (XX.XXX)	XX.XX (XX.XXX)	XX.XX (XX.XXX)
Median	XX.XX	XX.XX	XX.XX
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Doses Missing			
n	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
…			
Continue for Visit 4, Visit 5, and Visit 6 (End of Treatment/Early Termination).			

Note: Weights of the 2 vials dispensed or returned were summed to compute the total vial weight at each visit. Subjects with a protocol deviation due to missing vials are excluded from this table by visit. Difference in vial weight is calculated as the difference in the total vial weight returned at the visit minus the total vial weight dispensed at the previous visit. Doses missing is calculated as the absolute value of the difference in vial weight, divided by 0.2. The calculation for doses missing does not differentiate between doses administered for priming purposes versus doses administered to the nasal cavity. It is assumed that priming practices are uniform across subjects and treatment groups.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
Reference Listings: 16.2.5.1

Table 14.2.1.1
ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Primary Analysis
ITT Population

Study Visit [1]	PH94B (N=XX)		Placebo (N=XX)	
Statistic	Observed	CFB	Observed	CFB
Visit 1 (Screening)				
n	XX		XX	
Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)	
Median	XX.X		XX.X	
Min, Max	(XX, XX)		(XX, XX)	
Visit 2				
n	XX		XX	
Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)	
Median	XX.X		XX.X	
Min, Max	(XX, XX)		(XX, XX)	
Baseline				
n	XX		XX	
Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)	
Median	XX.X		XX.X	
Min, Max	(XX, XX)		(XX, XX)	

Abbreviations: ANCOVA = analysis of covariance; CFB = change from baseline; CI = confidence interval; HAM-A = Hamilton Anxiety Scale; LS = least-squares; SD = standard deviation; SE = standard error.
Note: Subjects are summarized by planned treatment. The HAM-A is a questionnaire used to assess anxiety and is completed by trained personnel. It consists of 14 items, each scored on a 5-point scale rating anxiety from "Not Present" to "Very severe". The HAM-A total score is the sum of the individual item scores. Baseline is defined as the HAM-A total score from Visit 2 (Baseline). Change from baseline is calculated as result – baseline result. Least squares mean, LS mean differences (treatment – placebo), 95% CIs, and P values were obtained from an ANCOVA model with change from baseline to Visit 6 in HAM-A total scores as the outcome, treatment group as a factor, and baseline HAM-A total score as a covariate.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
Reference Listing: 16.2.6.1

***Programming Note**: If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is >0.05 for the ITT population, then report the results of the multiple imputation analysis. Rate of missingness is computed as the number of ITT subjects missing change from baseline to Visit 6 HAM-A total scores divided by the total number of subjects in the ITT population. If reporting the results of the multiple imputation analysis, add the following text to the footnote before the sentence beginning with "Least squares mean…": "Multiple imputation was performed using conditional specification with baseline HAM-A total score, sex, age, LSAS total score, and analysis site. Twenty-five imputation datasets were created." If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is <=0.05 but greater than 0, then add the following text to the footnote: "Missing change from baseline in HAM-A total scores were imputed with treatment group mean change scores."*

Table 14.2.1.1 (cont.)
ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Primary Analysis
ITT Population

Study Visit [1]	PH94B (N=XX)		Placebo (N=XX)	
Statistic	Observed	CFB	Observed	CFB
Visit 3				
n	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)
Visit 4				
n	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)
Visit 5				
n	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)

Abbreviations: ANCOVA = analysis of covariance; CFB = change from baseline; CI = confidence interval; HAM-A = Hamilton Anxiety Scale; LS = least-squares; SD = standard deviation; SE = standard error.
Note: Subjects are summarized by planned treatment. The HAM-A is a questionnaire used to assess anxiety and is completed by trained personnel. It consists of 14 items, each scored on a 5-point scale rating anxiety from "Not Present" to "Very severe". The HAM-A total score is the sum of the individual item scores. Baseline is defined as the HAM-A total score from Visit 2 (Baseline). Change from baseline is calculated as result – baseline result. Least squares mean, LS mean differences (treatment – placebo), 95% CIs, and P values were obtained from an ANCOVA model with change from baseline to Visit 6 in HAM-A total scores as the outcome, treatment group as a factor, and baseline HAM-A total score as a covariate.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
Reference Listing: 16.2.6.1

***Programming Note**: If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is >0.05 for the ITT population, then report the results of the multiple imputation analysis. Rate of missingness is computed as the number of ITT subjects missing change from baseline to Visit 6 HAM-A total scores divided by the total number of subjects in the ITT population. If reporting the results of the multiple imputation analysis, add the following text to the footnote before the sentence beginning with "Least squares mean…": "Multiple imputation was performed using conditional specification with baseline HAM-A total score, sex, age, LSAS total score, and analysis site. Twenty-five imputation datasets were created." If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is <=0.05 but greater than 0, then add the following text to the footnote: "Missing change from baseline in HAM-A total scores were imputed with treatment group mean change scores."*

Table 14.2.1.1 (cont.)
ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Primary Analysis
ITT Population

Study Visit [1]	PH94B (N=XX)		Placebo (N=XX)	
Statistic	Observed	CFB	Observed	CFB
Visit 6 (End of Treatment/Early Termination)				
n	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)
LS Mean (SE)		XX.X (X.XX)		XX.X (X.XX)
95% CI for LS Mean CFB		(XX.X, XX.X)		(XX.X, XX.X)
P value for Difference from Baseline		X.XXXX		X.XXXX
LS Mean Difference from Placebo (SE)		XX.X (X.XX)		
95% CI for Difference from Placebo		(XX.X, XX.X)		
P value for Difference from Placebo		X.XXXX		

Abbreviations: ANCOVA = analysis of covariance; CFB = change from baseline; CI = confidence interval; HAM-A = Hamilton Anxiety Scale; LS = least-squares; SD = standard deviation; SE = standard error.
Note: Subjects are summarized by planned treatment. The HAM-A is a questionnaire used to assess anxiety and is completed by trained personnel. It consists of 14 items, each scored on a 5-point scale rating anxiety from "Not Present" to "Very severe". The HAM-A total score is the sum of the individual item scores. Baseline is defined as the HAM-A total score from Visit 2 (Baseline). Change from baseline is calculated as result – baseline result. Least squares mean, LS mean differences (treatment – placebo), 95% CIs, and P values were obtained from an ANCOVA model with change from baseline to Visit 6 in HAM-A total scores as the outcome, treatment group as a factor, and baseline HAM-A total score as a covariate.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Reference Listing: 16.2.6.1

***Programming Note**: If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is >0.05 for the ITT population, then report the results of the multiple imputation analysis. Rate of missingness is computed as the number of ITT subjects missing change from baseline to Visit 6 HAM-A total scores divided by the total number of subjects in the ITT population. If reporting the results of the multiple imputation analysis, add the following text to the footnote before the sentence beginning with "Least squares mean…": "Multiple imputation was performed using conditional specification with baseline HAM-A total score, sex, age, LSAS total score, and analysis site. Twenty-five imputation datasets were created." If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is <=0.05 but greater than 0, then add the following text to the footnote: "Missing change from baseline in HAM-A total scores were imputed with treatment group mean change scores."*

Table 14.2.1.1 (cont.)
ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Primary Analysis
ITT Population

Study Visit	PH94B (N=XX)		Placebo (N=XX)	
Statistic	Observed	CFB	Observed	CFB
Visit 7 (Follow-Up)				
n	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)

Abbreviations: ANCOVA = analysis of covariance; CFB = change from baseline; CI = confidence interval; HAM-A = Hamilton Anxiety Scale; LS = least-squares; SD = standard deviation; SE = standard error.
Note: Subjects are summarized by planned treatment. The HAM-A is a questionnaire used to assess anxiety and is completed by trained personnel. It consists of 14 items, each scored on a 5-point scale rating anxiety from "Not Present" to "Very severe". The HAM-A total score is the sum of the individual item scores. Baseline is defined as the HAM-A total score from Visit 2 (Baseline). Change from baseline is calculated as result – baseline result. Least squares mean, LS mean differences (treatment – placebo), 95% CIs, and P values were obtained from an ANCOVA model with change from baseline to Visit 6 in HAM-A total scores as the outcome, treatment group as a factor, and baseline HAM-A total score as a covariate.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Reference Listing: 16.2.6.1

***Programming Note**: If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is >0.05 for the ITT population, then report the results of the multiple imputation analysis. Rate of missingness is computed as the number of ITT subjects missing change from baseline to Visit 6 HAM-A total scores divided by the total number of subjects in the ITT population. If reporting the results of the multiple imputation analysis, add the following text to the footnote before the sentence beginning with "Least squares mean…": "Multiple imputation was performed using conditional specification with baseline HAM-A total score, sex, age, LSAS total score, and analysis site. Twenty-five imputation datasets were created." If the rate of missingness in change from baseline to Visit 6 HAM-A total scores is <=0.05 but greater than 0, then add the following text to the footnote: "Missing change from baseline in HAM-A total scores were imputed with treatment group mean change scores."*

Table 14.2.1.2
ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Sensitivity Analysis Using Complete Cases
ITT Population

Same Shell as 14.2.1.1; Programming Note: *Add the following text to the footnote before the sentence beginning with "Least squares mean…": "Subjects with missing change from baseline to Visit 6 HAM-A total scores were excluded from the analysis, including descriptive summaries."*

Table 14.2.1.3
ANCOVA Change from Baseline in HAM-A Total Scores – Control-Case Sensitivity Analysis
ITT Population

Same Shell as 14.2.1.1 but do not include descriptive summaries by visit, only include LS means results; Programming Note: *Add the following text to the footnote before the sentence beginning with "Least squares mean…": "For subjects with missing change from baseline to Visit 6 HAM-A total scores, change from baseline in HAM-A total scores was set to the mean change from baseline for the placebo group."*

Table 14.2.2.1
Analysis of the Proportion CGI-I Responders – Secondary Analysis
ITT Population

Study Visit [1] Variable Category	PH94B (N=XX)	Placebo (N=XX)
Visit 3		
CGI-I Score		
0 = Not Assessed	XX (XX.X%)	XX (XX.X%)
1 = Very Much Improved	XX (XX.X%)	XX (XX.X%)
2 = Much Improved	XX (XX.X%)	XX (XX.X%)
3 = Minimally Improved	XX (XX.X%)	XX (XX.X%)
4 = No Change	XX (XX.X%)	XX (XX.X%)
5 = Minimally Worse	XX (XX.X%)	XX (XX.X%)
6 = Much Worse	XX (XX.X%)	XX (XX.X%)
7 = Very Much Worse	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)
…		
	Continue for Visits 4, 5, and 6.	
CGI-I Responder [1]		
Responders	XX (XX.X%)	XX (XX.X%)
Non-Responders	XX (XX.X%)	XX (XX.X%)
PH94B vs. Placebo [2]		
Odds Ratio (95% CI) [3]	X.XX (X.XX, X.XX)	
P value	X.XXXX	

Abbreviations: CGI-I = Clinical Global Impression of Improvement; CI = confidence interval.
Note: Subjects are summarized by planned treatment. Percentages are n/Number of subjects in the ITT population within planned treatment * 100. The CGI-I is a 7-point categorical scale, where clinicians rate the subject's change in overall status compared to baseline.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] A subject with a score of 1 = "Very Much Improved" and 2 = "Much Improved" was categorized as a "Responder".
[3] P value and odds ratio were obtained from a Wald test or Fisher's exact test, whichever is appropriate, when comparing proportions of responders between treatment to placebo.
[4] The odds ratio is the estimate of the odds of having significant improvement for subjects treated with PH49B relative to the same response for subjects treated with placebo.
Reference Listing: 16.2.6.4

Table 14.2.3.1
Analysis of the Proportion PGI-C Responders – Secondary Analysis
ITT Population

Same Shell as 14.2.2.1 but replace all instances of "CGI-I" with "PGI-C"; Programming Note: *Update abbreviations to add PGI-C = Patient Global Impression of Change (in alphabetical order) and remove CGI-I = Clinical Global Impression of Improvement. Update the last sentence of "Note" to read: "The PGI-C is a 7-point categorical scale, where the subject rates their own change in overall status compared to baseline." Update Reference Listing to 16.2.6.5.*

Table 14.2.4.1
ANCOVA Change from Baseline in ADNM Total Scores by Visit – Secondary Analysis
ITT Population

Same Shell as 14.2.1.1; Programming Note: *Replace the entire footnote with the following:*

"Abbreviations: ANCOVA = analysis of covariance; CFB = change from baseline; CI = confidence interval; ADNM = Adjustment Disorder New Module; LS = least-squares; SD = standard deviation; SE = standard error.
Note: Subjects are summarized by planned treatment. The ADNM consists of an 18-item stressful life event checklist and a list of 20 statements about which reactions these types of events can trigger. Subjects are also asked to indicate how often statements apply to them on a 4-point scale. The ADNM total score is calculated as the sum of the 20 statement scores. Baseline is defined as the ADNM total score from Visit 2 (Baseline). Change from baseline is calculated as result – baseline result. Least squares mean, LS mean differences (treatment – placebo), 95% CIs, and P values were obtained from an ANCOVA with treatment group as a factor and baseline ADNM total score as a covariate.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
Reference Listing: 16.2.6.2"

Table 14.2.5.1
ANCOVA Change from Baseline in IADQ Total Scores by Visit – Secondary Analysis
ITT Population

Same Shell as 14.2.1.1; Programming Note: *Replace the entire footnote with the following:*

"Abbreviations: AjD = adjustment disorder; ANCOVA = analysis of covariance; CFB = change from baseline; CI = confidence interval; IADQ = International Adjustment Disorder Questionnaire; LS = least-squares; SD = standard deviation; SE = standard error.
Note: Subjects are summarized by planned treatment. The IADQ is a validated questionnaire to measure AjD. The subject completes a 9-item checklist of potential stressful events, and a 3-item list of potential problems suffered over the last month (Preoccupation subscale), a 3-item list of potential social impacts from the stressors (Failure to Adapt subscale), 1 item regarding timing of symptoms, and a 3-item list of potential functional impairments (Functional Impairment). The Preoccupation, Failure to Adapt, and Functional Impairment items are scored on a 5-point scale. The IADQ total score is calculated as the sum of the 6 Preoccupation and Failure to Adapt items (items 10 through 15. Baseline is defined as the IADQ total score from Visit 2 (Baseline). Change from baseline is calculated as result – baseline result. Least squares mean, LS mean differences (treatment – placebo), 95% CIs, and P values were obtained from an ANCOVA with treatment group as a factor and baseline IADQ total score as a covariate.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
Reference Listing: 16.2.6.3"

Table 14.2.6.1
ANCOVA Change from Baseline in HAM-A Total Scores by Visit – Exploratory Endpoint
ITT Population

Study Visit Statistic	PH94B (N=XX)	Placebo (N=XX)
Visit 3		
LS Mean (SE)	XX.X (X.XX)	XX.X (X.XX)
95% CI for LS Mean CFB	(XX.X, XX.X)	(XX.X, XX.X)
P value for Difference from Baseline	X.XXXX	X.XXXX
LS Mean Difference from Placebo (SE)	XX.X (X.XX)	
95% CI for Difference from Placebo	(XX.X, XX.X)	
P value for Difference from Placebo	X.XXXX	
Repeat for Visits 4 and 5.		

Abbreviations: ANCOVA = analysis of covariance; CFB = change from baseline; CI = confidence interval; HAM-A = Hamilton Anxiety Scale; LS = least-squares; SD = standard deviation; SE = standard error.
Note: Subjects are summarized by planned treatment. The HAM-A is a questionnaire used to assess anxiety and is completed by trained personnel. It consists of 14 items, each scored on a 5-point scale rating anxiety from "Not Present" to "Very severe". The HAM-A total score is the sum of the individual item scores. Baseline is defined as the HAM-A total score from Visit 2 (Baseline). Change from baseline is calculated as result – baseline result. Least squares mean, LS mean differences (treatment – placebo), 95% CIs, and P values were obtained from an ANCOVA with change from baseline in HAM-A total scores as the outcome, treatment group as a factor, and baseline HAM-A total score as a covariate.
Reference Listing: 16.2.6.1

Table 14.3.1.1
Overall Summary of Treatment Emergent Adverse Events
Safety Population

Category	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Subjects with at Least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with at Least 1 TEAE by Severity [1]			
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with at Least 1 Related TEAE [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with a TEAE Leading to Discontinuation of Study Drug	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subject with a TEAE Leading to Discontinuation of Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with at Least 1 Serious TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects with a Serious TEAE Leading to Death	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: AE = adverse event; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population within actual treatment and overall subjects * 100. A treatment emergent adverse event is defined as an adverse event with onset at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up), or an adverse event starting prior to the start of treatment but increasing in severity or relationship at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up).
[1] Subjects are counted only once at the worst severity. If a severity designation is missing, it will be considered as severe.
[2] Subjects are counted only once at the strongest possible relationship. If a relationship designation is missing, the AE will be considered as related.
Reference Listing: 16.2.7.1

Table 14.3.1.2.1
Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Subjects with at Least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1			
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 2			
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received and overall subjects * 100. AEs were coded using MedDRA version XX.X. A TEAE is defined as an AE with onset at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up), or an AE starting prior to the start of treatment but increasing in severity or relationship at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up). Subjects were counted once for each SOC and once for each PT. AEs are displayed by descending frequency of SOC, then PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.7.1

Programming Note: *Replace "XX.X" in the footnote with the correct version of the MedDRA used for coding. For dry run delivery, use MedDRA version 24.1.*

Table 14.3.1.2.2
Treatment Emergent Adverse Events by Preferred Term
Safety Population

System Organ Class Preferred Term	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Subjects with at Least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
...			

Abbreviations: AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received and overall subjects * 100. AEs were coded using MedDRA version XX.X. A TEAE is defined as an AE with onset at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up), or an AE starting prior to the start of treatment but increasing in severity or relationship at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up). Subjects were counted once for each PT. AEs are displayed by descending frequency of PT and then alphabetically by PT.
Reference Listing: 16.2.7.1

Programming Note: *Replace "XX.X" in the footnote with the correct version of the MedDRA used for coding. For dry run delivery, use MedDRA version 24.1.*

Table 14.3.1.3
Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population

System Organ Class Preferred Term Severity	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Subjects with at Least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1			
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1			
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…			

Abbreviations: AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received and overall subjects * 100. AEs were coded using MedDRA version XX.X. A TEAE is defined as an AE with onset at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up), or an AE starting prior to the start of treatment but increasing in severity or relationship at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up). Subjects are counted once for each SOC and once for each PT. The severity shown is the greatest severity reported for a particular subject (Severe > Moderate > Mild). AEs with a missing severity were counted as Severe. AEs are displayed by descending frequency of SOC, then PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.7.1

Programming Note: *Replace "XX.X" in the footnote with the correct version of the MedDRA used for coding. For dry run delivery, use MedDRA version 24.1.*

Table 14.3.1.4
Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Relationship to Study Drug
Safety Population

System Organ Class Preferred Term Relationship	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Subjects with at Least 1 TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1			
Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1			
Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Related	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
...			

Abbreviations: AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population within treatment received and overall subjects * 100. AEs were coded using MedDRA version XX.X A TEAE is defined as an AE with onset at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up), or an AE starting prior to the start of treatment but increasing in severity or relationship at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up). Subjects were counted once for each SOC and once for each PT. The relationship shown is the greatest relationship reported for a particular subject (Related > Not Related). AEs with a missing relationship were counted as Related. AEs are displayed by descending frequency of SOC, then PT within SOC, and then alphabetically by PT.
Reference Listing: 16.2.7.1

Programming Note: *Replace "XX.X" in the footnote with the correct version of the MedDRA used for coding. For dry run delivery, use MedDRA version 24.1.*

Table 14.3.2.1
Treatment Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term
Safety Population

Same as shell 14.3.1.2 except replace "Subjects with at Least 1 TEAE" with "Subjects with at Least 1 TEAE Leading to Discontinuation of Study Drug".

Table 14.3.3.1
Subject Listing of Serious Adverse Events
Safety Population

Actual Treatment: XXXX

Subject ID	TEAE? [1]	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship	Serious?/ Criteria Met	Caused Discontinuation from Study?	Outcome/ Study Drug Action Taken
XXXX	Yes	XXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH:MM (XX)/ DDMMMYYYY/HH:MM (XX)	Mild/ Related	Yes/ Persistent or significant disability/incapacity	Yes	Recovering/Resolving/ Dose Not Changed
XXXX	Yes	XXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH:MM (-XX)/ DDMMMYYYY/HH:MM (XX)	Severe/ Not Related	Yes/ Life-threatening event	No	Recovered/Resolved/ Dose Reduced

Abbreviations: AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment emergent AE.
Note: Study day is calculated relative to the date of first dose of study drug. AEs were coded using MedDRA version XX.X.
[1] A TEAE is defined as an AE with onset at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up), or an AE starting prior to the start of treatment but increasing in severity or relationship at the time of or following the start of treatment with study drug through Visit 7 (Follow-Up).

Programming Note: *If no events meet the criteria for display, present "No events are reported." If "Serious" is "Yes", concatenate all serious criteria marked as "Yes" with a semicolon. Replace "XX.X" in the footnote with the correct version of the MedDRA used for coding. For dry run delivery, use MedDRA version 24.1.*

Table 14.3.3.2
Subject Listing of Adverse Events Leading to Discontinuation of Study Drug
Safety Population

Same as shell 14.3.3.1.

Table 14.3.4.1
Subject Listing of Clinically Significant Abnormal Laboratory Values: Hematology
Safety Population

Actual Treatment: XXXXXX

Subject ID	Parameter (unit)	Study Visit [1]	Sample Collected?/ Reason Not Collected	Collection Date/Time (Study Day)	Result	Baseline Flag [2]	Change from Baseline [3]	Reference Range	Reference Range Flag/ Clinically Significant
XXXXXX	XXXXXX (unit)	Visit 1 (Screening)	XX/ XXXXXXXX						
XXXXXX	XXXXXX (unit)	Visit 1 (Screening)	Yes	DDMMMYYYY/HH:MM (XX)	XX			XX – YY	High
		Visit 2 (Baseline)	Yes	DDMMMYYYY/HH:MM (XX)	XX	Yes		XX – YY	High/ Yes
		Visit 3	Yes	DDMMMYYYY/HH:MM (XX)	XX		XX	XX – YY	Low
		Visit 4	Yes	DDMMMYYYY/HH:MM (XX)	XX		XX	XX – YY	High
		Visit 5	Yes	DDMMMYYYY/HH:MM (XX)	XX		XX	XX – YY	Low
		Visit 6 (End of Treatment/ Early Termination)	Yes	DDMMMYYYY/HH:MM (XX)	XX		XX	XX – YY	Low
	XXXXXX (unit)	XXXXX		DDMMMYYYY/HH:MM (XX)	XX			XX – YY	High
		XXXXX		DDMMMYYYY/HH:MM (XX)	XX	XXX	XX	XX – YY	Low/ Yes

Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline).
[3] Change from baseline is the difference between the baseline assessment and the current visit's assessment.

Programming Note: *If sample was not collected, concatenate with reason. If assay is clinically significant, concatenate Reference Range Flag with "Yes".*

[redacted]

Table 14.3.4.2
Subject Listing of Clinically Significant Abnormal Laboratory Values: Clinical Chemistry
Safety Population

Same as shell 14.3.4.1.

Table 14.3.5.1
Hematology: Observed Results and Change from Baseline by Visit
Safety Population

Parameter (unit) Study Visit [1] Statistics	PH94B (N=XX) Observed	 CFB	Placebo (N=XX) Observed	 CFB	Overall (N=XXX) Observed	 CFB
Parameter (unit)						
Visit 1 (Screening)						
n	XX		XX		XXX	
Mean (SD)	XXX.X (XX.XX)		XXX.X (XX.XX)		XXX.X (XX.XX)	
Median	XXX.X		XXX.X		XXX.X	
Min, Max	XXX, XXX		XXX, XXX		XXX, XXX	
Visit 2						
n	XX		XX		XXX	
Mean (SD)	XXX.X (XX.XX)		XXX.X (XX.XX)		XXX.X (XX.XX)	
Median	XXX.X		XXX.X		XXX.X	
Min, Max	XXX, XXX		XXX, XXX		XXX, XXX	
Baseline						
n	XX		XX		XXX	
Mean (SD)	XXX.X (XX.XX)		XXX.X (XX.XX)		XXX.X (XX.XX)	
Median	XXX.X		XXX.X		XXX.X	
Min, Max	XXX, XXX		XXX, XXX		XXX, XXX	
Visit 6 (End of Treatment/ Early Termination)						
n	XX	XX	XX	XX	XXX	XX
Mean (SD)	XXX.X (XX.XX)	XXX.X (XX.XX)	XXX.X (XX.XX)	XXX.X (XX.XX)	XXX.X (XX.XX)	XXX.X (XX.XX)
Median	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
Min, Max	XXX, XXX	XXX, XXX	XXX, XXX	XXX, XXX	XXX, XXX	XXX, XXX

Abbreviations: CFB = change from baseline, SD = standard deviation.
Note: Baseline is defined as the last non-missing assessment before receiving the first dose of study drug. Change from baseline is calculated as result – baseline result.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
Reference Listing: 16.2.8.1

Table 14.3.5.2
Clinical Chemistry and Thyroid: Observed Results and Change from Baseline by Visit
Safety Population

Same as shell 14.3.5.1; Programming Note: *Update Reference Listing to Listing 16.2.8.2.*

Table 14.3.6.1
Vital Signs: Observed Results and Change from Baseline by Visit
Safety Population

Same shell as 14.3.5.1; Programming note: *Summaries should be presented for the following visits: Visit 1 (Screening), Visit 2, Baseline, Visit 3, Visit 4, Visit 5, Visit 6 (End of Treatment/Early Termination), Visit 7 (Follow-Up). Parameters include systolic blood pressure (mmHg), diastolic blood pressure (mmHg), heart rate (beats/min), respiratory rate (breaths/min), and temperature (°C). Update Reference Listing to Listing 16.2.9.1.*

[redacted]

Table 14.3.6.2.1
12-Lead Electrocardiogram: Summary of Interpretation by Visit
Safety Population

Study Visit [1] Category	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Visit 1 (Screening)			
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal – Not Clinically Significant	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal – Clinically Significant	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Baseline [2]			
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal – Not Clinically Significant	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal – Clinically Significant	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Visit 6 (End of Treatment/Early Termination)			
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal – Not Clinically Significant	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal – Clinically Significant	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before receiving the first dose of study drug.
Reference Listing: 16.2.9.2

Table 14.3.6.2.2
12-Lead Electrocardiogram: Observed Results and Change from Baseline by Visit
Safety Population

Same shell as 14.3.5.1; Programming Note: *Visits include Baseline, Visit 6 (End of Treatment), and Visit 6 (Early Termination). Parameters include PR interval (msec), QRS interval (msec), and heart rate (bpm). Update Reference Listing to Listing 16.2.9.2.*

Table 14.3.6.2.3
12-Lead Electrocardiogram: Summary of QT and QTcF Results by Visit
Safety Population

ECG Parameter Study Visit [1] Category	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
QT Interval (msec)			
Visit 1 (Screening)			
n	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Min, Max	(XX, XX)	(XX, XX)	(XX, XX)
Baseline [2]			
n	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX.X	XX.X	XX.X
Change from Baseline > 30 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Change from Baseline > 60 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Visit 6 (End of Treatment/Early Termination)			
n	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX.X	XX.X	XX.X
Change from Baseline > 30 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Change from Baseline > 60 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Repeat for QTcF parameter.			

Abbreviations: ECG = electrocardiogram; QTcF = QT interval, Fridericia's correction.
Note: Percentages are n/Number of subjects in the Safety population at each study visit within treatment received and overall subjects * 100. Change from baseline is calculated as result – baseline result.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before receiving the first dose of study drug.
Reference Listing: 16.2.9.2

Table 14.3.6.3
Summary of Concomitant Medications by ATC Class Level 2 and Preferred Term
Safety Population

Same shell as 14.1.5 except first row text is "Subjects with at least 1 Concomitant Medication"; Programming Note: *Update note to read: "Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. Concomitant medications are any medications starting or continuing after Visit 2 (Baseline). Medications were coded using WHO-DD Global B3 version XX. At each level of summarization (ATC Level 2 or PT), subjects who reported more than one medication were only counted once. Medications are displayed by alphabetical order of ATC Level 2 classification, then descending frequency of PT within ATC, and then alphabetically by PT. Subjects were counted only once for each ATC and PT." Update Reference Listing to Listing 16.2.9.4. Replace "XX" in the footnote with the correct version of the WHO-DD used for coding. For dry run delivery, use WHO-DD Global B3 version Sep 2021.*

Table 14.3.6.4
Summary of Columbia Suicide Severity Rating Scale (C-SSRS) by Visit
Safety Population

Study Visit [1] C-SSRS Section C-SSRS Item / Statistic	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Visit 1 (Screening)			
Suicidal Ideation: Last 6 Months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Wish to be Dead	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Non-Specific Active Suicidal Thoughts	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Any Methods	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Some Intent	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Specific Plan	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal Behavior: Lifetime	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Actual Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Interrupted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Aborted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preparatory Acts or Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal Ideation or Behavior			
Subject Engaged in Non-Suicidal Self-Injurious Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. The number and percent of subjects who experience the event at least once during treatment are summarized. Subjects were counted once for each C-SSRS section and once for each C-SSRS item answered "Yes" during treatment period. "Baseline/Screening" version was used for Visit 1 (Screening) and "Since Last Visit" was used for all other visits.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Subjects are considered to have treatment emergent suicidal ideation if their maximum suicidal ideation score increased from a previous visit to the next visit after treatment with study drug.
[3] Subjects are considered to have treatment emergent suicidal behavior if they did not have suicidal behavior prior to treatment with study drug but did have suicidal behavior at any visit after treatment with study drug.
Reference Listings: 16.2.9.5

Programming Note: *Display summaries for all visits, including Visit 1 (Screening), Visit 2 (Baseline), Visit 3, Visit 4, Visit 5, Visit 6 (End of Treatment/Early Termination), Visit 7 (Follow-Up). Present treatment emergent counts and percentages as the last lines in the table after Visit 7 (Follow-Up).*

Table 14.3.6.4 (cont.)
Summary of Columbia Suicide Severity Rating Scale (C-SSRS) by Visit
Safety Population

Study Visit [1] C-SSRS Section C-SSRS Item / Statistic	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Visit 2 (Baseline)			
Suicidal Ideation: Since Last Visit	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Wish to be Dead	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Non-Specific Active Suicidal Thoughts	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Any Methods	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Some Intent	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Specific Plan	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal Behavior: Since Last Visit	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Completed Suicide	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Actual Attempt			
Interrupted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Aborted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preparatory Acts or Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal Ideation or Behavior			
Subject Engaged in Non-Suicidal Self-Injurious Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. The number and percent of subjects who experience the event at least once are summarized. Subjects were counted once for each C-SSRS section and once for each C-SSRS item answered "Yes" during treatment period. "Baseline/Screening" version was used for Visit 1 (Screening) and "Since Last Visit" was used for all other visits.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Subjects are considered to have treatment emergent suicidal ideation if their maximum suicidal ideation score increased from a previous visit to the next visit after treatment with study drug.
[3] Subjects are considered to have treatment emergent suicidal behavior if they did not have suicidal behavior prior to treatment with study drug but did have suicidal behavior at any visit after treatment with study drug.
Reference Listings: 16.2.9.5

Programming Note: *Display summaries for all visits, including Visit 1 (Screening), Visit 2 (Baseline), Visit 3, Visit 4, Visit 5, Visit 6 (End of Treatment/Early Termination), Visit 7 (Follow-Up). Present treatment emergent counts and percentages as the last lines in the table after Visit 7 (Follow-Up).*

Table 14.3.6.4 (cont.)
Summary of Columbia Suicide Severity Rating Scale (C-SSRS) by Visit
Safety Population

Study Visit [1] C-SSRS Section C-SSRS Item / Statistic	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Visit 7 (Follow-Up)			
Suicidal Ideation: Since Last Visit	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Wish to be Dead	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Non-Specific Active Suicidal Thoughts	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Any Methods	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Some Intent	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Specific Plan	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal Behavior: Since Last Visit	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Completed Suicide	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Actual Attempt			
Interrupted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Aborted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preparatory Acts or Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal Ideation or Behavior			
Subject Engaged in Non-Suicidal Self-Injurious Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Treatment Emergent Suicidal Ideation [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Treatment Emergent Suicidal Behavior [3]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Treatment Emergent Suicidal Ideation or Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. The number and percent of subjects who experience the event at least once are summarized. Subjects were counted once for each C-SSRS section and once for each C-SSRS item answered "Yes" during treatment period. "Baseline/Screening" version was used for Visit 1 (Screening) and "Since Last Visit" was used for all other visits.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Subjects are considered to have treatment emergent suicidal ideation if their maximum suicidal ideation score increased from a previous visit to the next visit after treatment with study drug.
[3] Subjects are considered to have treatment emergent suicidal behavior if they did not have suicidal behavior prior to treatment with study drug but did have suicidal behavior at any visit after treatment with study drug.
Reference Listings: 16.2.9.5

Programming Note: *Display summaries for all visits, including Visit 1 (Screening), Visit 2 (Baseline), Visit 3, Visit 4, Visit 5, Visit 6 (End of Treatment/Early Termination), Visit 7 (Follow-Up). Present treatment emergent counts and percentages as the last lines in the table after Visit 7 (Follow-Up).*

Table 14.3.6.5
Summary of Montgomery-Asberg Depression Rating Scale (MADRS) Total Score by Visit
Safety Population

Study Visit [1]	PH94B (N=XX)		Placebo (N=XX)		Overall (N=XX)	
Statistic	Observed	CFB	Observed	CFB	Observed	CFB
Visit 1 (Screening)						
n	XX		XX		XX	
Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
Median	XX.X		XX.X		XX.X	
Min, Max	(XX, XX)		(XX, XX)		(XX, XX)	
Visit 2						
n	XX		XX		XX	
Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
Median	XX.X		XX.X		XX.X	
Min, Max	(XX, XX)		(XX, XX)		(XX, XX)	
Baseline [1]						
n	XX		XX		XX	
Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
Median	XX.X		XX.X		XX.X	
Min, Max	(XX, XX)		(XX, XX)		(XX, XX)	
Visit 6 (End of Treatment/Early Termination)						
n	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
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)

Abbreviations: CFB = change from baseline; CI = confidence interval; MADRS = Montgomery-Asberg Depression Rating Scale; SD = standard deviation.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. The MADRS is a validated instrument used to measure the severity of depressive episodes. The MADRS includes 10 items and uses a 0 to 6 severity scale. The MADRS total score is calculated as the sum of the 10 items with higher scores indicating more severe depression. Change from baseline is calculated as result – baseline result.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before receiving the first dose of study drug.
Reference Listing: 16.2.9.6

Table 14.3.6.6
Summary of Physician Withdrawal Checklist (PWC-20)
Safety Population

Variable Statistic or Category	PH94B (N=XX)	Placebo (N=XX)	Overall (N=XX)
Presence of Symptom			
Loss of appetite	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Nausea—Vomiting	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Diarrhea	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…			
Proportion Subjects with at Least 1 Symptom	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PWC-20 Total Score			
n	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Min, Max	(XX, XX)	(XX, XX)	(XX, XX)
PWC-20 Total Score Mean Difference from Placebo (SE)	XX.X (X.XX)		
95% CI for Difference from Placebo	(XX.X, XX.X)		
P value for Difference from Placebo [1]	X.XXXX		

Abbreviations: CI = confidence interval; PWC-20 = Physician Withdrawal Checklist; SD = standard deviation; SE = standard error.
Note: Percentages are n/Number of subjects in the Safety population within treatment received and overall subjects * 100. The PWC-20 is a 20-item instrument for assessing anxiolytic discontinuation symptoms. Subjects with any score >0 were categorized as having a withdrawal symptom. The proportion of subjects with withdrawal symptoms was calculated as the number of subjects with any score >0 divided by the total number of subjects in the population of interest.
[1] P value was obtained from a two-sample t-test comparing PWC-20 total score in PH94B and Placebo treated subjects.
Reference Listing: 16.2.9.8

[redacted]

14.3. Planned Listing Shells

See Figure 3 below.

Figure 3: Planned Listing Shells

Listing 16.2.1.1
Subject Disposition
All Subjects

Actual Treatment: XXXXXXXXXXXXXXXX

Subject ID	Site ID/ Analysis Site ID	Subject Status	Date of Completion /Discontinuation (Study Day)	Reason for Discontinuation	If Death, Date of Death (Study Day)/ Cause of Death	If Lost to Follow-Up, Date of Last Contact (Study Day)/ Comment	Treatment Unblinded?/ Date (Study Day)/ Reason
XXXXX	XXX/ XXX	Discontinued	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	Adverse Event: XXXXX			
XXXXX	XXX/ XXX	Completed	DDMMMYYYY (XX)/ DDMMMYYYY (XX)				XXX/ DDMMMYYYY (XX)/ XXXXXXX
XXXXX	XXX/ XXX	XXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXXXXXXXX	DDMMMYYYY (XX)/ XXXXXXXXXX		
XXXXX	XXX/ XXX	XXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXXXXXXXX		DDMMMYYYY (XX)/ XXXXXXXXXX	

Note: Study day is calculated relative to the date of first dose of study drug.

Programming Note: *If reason for discontinuation is AE, physician decision, protocol violation, or other, concatenate reason for discontinuation with specify text, e.g., "Adverse Event: XXXXXXX." For Analysis Site ID, use the numeric pooled site ID and include leading zeroes so that it is 3 digits. If pooling was not necessary for the study (i.e., analysis site ID is missing), header should be displayed as only "Site ID" and analysis site ID should not be included in the listing.*

Listing 16.2.2.1
Inclusion and Exclusion Criteria
Screen Failures

Subject ID	Date Screened	Visit	Met All Eligibility Criteria?/ Criteria Not Met
XXXXXX	DDMMMYYYY	Visit 1 (Screening)	No/ XXXXXXXXXXX
XXXXXX	DDMMMYYYY	Visit 1 (Screening)	No/ XXXXXXXXXXX
XXXXXX	DDMMMYYYY	Visit 2 (Baseline)	No/ XXXXXXXXXXX

Note: H

Programming note: *If "Met All Eligibility Criteria" is "No", concatenate criterion not met.*

[redacted]

Listing 16.2.2.2
Protocol Deviations
All Subjects

Actual Treatment: XXXXXXXXXXX

Subject ID	Date of Protocol Violation Collection (Study Day)	Event Type	Violation Level	Description
XXXXXX	DDMMMYYYY (XX)	XXXXXXXXXXX	IMPORTANT	XXXXXXX
	DDMMMYYYY (XX)	XXXXXXXXXXXXX	NON-IMPORTANT	XXXXXXXXXXXXXX
XXXXXX	DDMMMYYYY (XX)	XXXXXXXXXXX	NON-IMPORTANT	XXXXXXXXXXXXXXXXXX
	DDMMMYYYY (XXX)	XXXXXXXXXXXXXX	NON-IMPORTANT	XXXXXXXXXX
XXXXXX	DDMMMYYYY (X)	XXXXXXXXXXX	IMPORTANT	XXXXXXXXXXXXXXXXXXX

Note: Study day is calculated relative to the date of first dose of study drug.

Listing 16.2.3.1
Analysis Populations
All Subjects

Planned Treatment: XXXXXXXX

	Randomization			Actual	Analysis Populations		
Subject ID	Date (Study Day)	Number	Treatment	Treatment	Safety [1]	ITT [2]	Primary Reason(s) for Exclusion
XXXXXX	DDMMMYYYY (XX)	XXXX	XXXXX	XXXXX	Yes	No	ITT: Subject was not randomized and/or did not administer at least one dose of IP at Visit 2 (Baseline).
XXXXXX	DDMMMYYYY (XX)	XXXX	XXXXX	XXXXX	Yes	Yes	
XXXXXX	DDMMMYYYY (XX)	XXXX	XXXXX	XXXXX	Yes	Yes	
XXXXXX	DDMMMYYYY (XX)	XXXX	XXXXX	XXXXX	No	No	Safety: Subject did not administer at least one dose of IP.

Abbreviations: IP = investigational product; ITT = intent-to-treat.
Note: Study day is calculated relative to the date of first dose of study drug. Subjects were randomized 1:1 to receive 4 weeks of either PH94B or placebo 4 times daily.
[1] The Safety Population includes all subjects who were dispensed IP and reported administering at least 1 dose of IP.
[2] The ITT Population includes all subjects who were randomized and had 1 documented dose of IP at Visit 2 (Baseline).

Programming note: *Concatenate reasons for exclusion with a semi-colon. Sort by planned treatment and subject ID. Add abbreviations as needed depending on what is displayed.*

Listing 16.2.4.1
Subject Consent and Demographics
All Subjects

Actual Treatment: XXXXXXXXXXX

Subject ID	Date Informed Consent Signed/ Protocol Version	Date of Birth	Age (years)	Sex	Child-Bearing Potential?	Date of Last Menstrual Period Known?	Date of Last Menstrual Period	Ethnicity	Race	Weight (kg)	Height (cm)	BMI (kg/m^2)
XXXXXX	DDMMMYYYY/ XXXXXXXXXXX	DDMMMYYYY	XX	Male				XXXXXX	XXXXXXX	XX.X	XX	XX
XXXXXX	DDMMMYYYY/ XXXXXXXXXXX	DDMMMYYYY	XX	Female	Yes	Yes	DDMMMYYYY	XXXXXX	XXXXXX	XX.X	XX	XX
XXXXXX	DDMMMYYYY/ XXXXXXXXXXX	DDMMMYYYY	XX	Male				XXXXXX	XXXXX	XX.X	XX	XX
XXXXXX	DDMMMYYYY/ XXXXXXXXXXX	DDMMMYYYY	XX	Female	No	No		XXXXXX	XXXXXX	XX.X	XX	XX
XXXXXX	DDMMMYYYY/ XXXXXXXXXXX	DDMMMYYYY	XX	Female	Yes	Yes	DDMMMYYYY	XXXXXX	XXXXXX	XX.X	XX	XX

Abbreviation: BMI = Body Mass Index.

Programming Note: *Concatenate if multiple races selected (e.g., Multiple: XXXX, XXXX). If Asian is selected, concatenate with any selected Asian subcategories (e.g., Asian: XXXX, XXXX).*

Listing 16.2.4.2
Medical and Psychiatric History
All Subjects

Actual Treatment: XXXXXXXXX

Subject ID	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)
XXXXXX	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)
	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	--MMMYYYY / Ongoing
XXXXXX	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)
	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (XX) / Ongoing
	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	----YYYY (XX) / Ongoing

Abbreviation: MedDRA = Medical Dictionary for Regulatory Activities.
Note: Medical/Psychiatric history was coded using MedDRA version XX.X. Study day is calculated relative to the date of first dose of study drug.

Programming Note: *If medical/psychiatric history is ongoing, denote with "Ongoing" rather than the end date. Replace "XX.X" in the footnote with the correct version of the MedDRA used for coding. For dry run delivery, use MedDRA version 24.1.*

Listing 16.2.4.3
Substance Use
All Subjects

Actual Treatment: XXXXXXXX

Subject ID	Substance	Use?/ Start Date (Study Day)/ End Date (Study Day)	Type or Route	Amount Consumed	Frequency
XXXXX	Nicotine	Former/ DDMMMYYYY (-XX)/ DDMMMYYYY (XX)	Pipe	XX	Daily
	Alcohol	Current/ --MMMYYYY/ Ongoing	Spirits	XX	Weekly
	Cannabis	Never			
XXXXX	Nicotine	Former/ DDMMMYYYY (-XX)/ DDMMMYYYY (-XX)	Cigar	XX	Monthly
	Alcohol	Never	Spirits	XX	Weekly
	Cannabis	Former/ --MMMYYYY/ --MMMYYYY	Other: XXXXXX		Daily

Note: Study day is calculated relative to the date of first dose of study drug.

Programming Note: *If substance use is ongoing, denote with "Ongoing" rather than the end date. For cannabis use, if route is "Other", concatenate with "Other route, specify" (e.g., Other: XXXXX).*

Listing 16.2.4.4
Mini-International Neuropsychiatric Interview (MINI)
All Subjects

Actual Treatment: XXXXXXXXXXXXXXX

Subject ID	Study Visit	MINI Completed?/ Reason Not Completed	Date of Interview (Study Day)	Assessment	Result
XXXXX	Visit 1 (Screening)	No/ XXXXXXX			
XXXXX	Visit 1 (Screening)	Yes	DDMMMYYYY (XX)	Major Depressive Episode: Current (2 Weeks)	XXX
				Major Depressive Episode: Past	XXX
				Major Depressive Episode: Recurrent	XXX
				Major Depressive Disorder: Current (2 Weeks)	XXX
				Major Depressive Disorder: Past	XXX
				Major Depressive Disorder: Recurrent	XXX
				Suicidality	XXX
				Suicidality: Current (Past Month)	XXX
				Suicidality: Lifetime Attempt	XXXXXXX
				Suicide Behavior Disorder: Current	XXX
				Suicide Behavior Disorder: In Early Remission	XXX
				Manic Episode: Current	XXX
				Manic Episode: Past	XXX
				Hypomanic Episode: Current	XXX
				Hypomanic Episode: Past	XXX
				Bipolar I Disorder: Current	XXX
				Bipolar I Disorder: Past	XXX
				Bipolar II Disorder: Current	XXX
				Bipolar II Disorder : Past	XXX
				Other Specified Bipolar and Related Disorder: Current	XXX
				Other Specified Bipolar and Related Disorder: Past	XXX

Abbreviations: DSM = Diagnostic and Statistical Manual of Mental Disorder; MINI = Mini International Neuropsychiatric Interview, SAD = Social Anxiety Disorder.
Note: Study day is calculated relative to the date of first dose of study drug.

Programming Note: *If MINI was not conducted, concatenate reason. Continue for remaining assessments. Do not include rater initials.*

Listing 16.2.4.4 (cont.)
Mini-International Neuropsychiatric Interview (MINI)
All Subjects

Actual Treatment: XXXXXXXXXXXXXXX

Subject ID	Study Visit	MINI Completed?/ Reason Not Completed	Date of Interview (Study Day)	Assessment	Result
XXXXX	XXXX	Yes	DDMMMYYYY (XX)	Panic Disorder: Current (Past Month)	XXX
				Panic Disorder: Lifetime	XXX
				Agoraphobia: Current	XXX
				Social Anxiety Disorder (Social Phobia): Current (Past Month)	XXX
				Obsessive-Compulsive Disorder: Current (Past Month)	XXX
				Posttraumatic Stress Disorder: Current	XXX
				Alcohol Use Disorder: Past 12 Months	XXX
				Substance Use Disorder (Non-alcohol): Past 12 Months	XXX
				Any Psychotic Disorders: Current	XXX
				Any Psychotic Disorders: Lifetime	XXX
				Major Depressive Disorder with Psychotic Features: Current	XXX
				Major Depressive Disorder with Psychotic Features: Past	XXX
				Bipolar I Disorder with Psychotic Features: Current	XXX
				Bipolar I Disorder with Psychotic Features: Past	XXX
				Anorexia Nervosa: Current (Past 3 Months)	XXX
				Bulimia Nervosa: Current (Past 3 Months)	XXX
				Binge-Eating Disorder: Current (Past 3 Months)	XXX
				Generalized Anxiety Disorder: Current (Past 6 Months)	XXX
				Medical, Organic, Drug Cause Ruled Out	XXX
				Antisocial Personality Disorder: Lifetime	XXX
				Adjustment Disorder: Current	XXX
				Identify the Primary Diagnosis	XXXXXXXXXXXXXXXXXXXXXX

Abbreviations: DSM = Diagnostic and Statistical Manual of Mental Disorder; MINI = Mini International Neuropsychiatric Interview, SAD = Social Anxiety Disorder.
Note: Study day is calculated relative to the date of first dose of study drug. The MINI was only collected at Visit 1 (Screening).

Programming Note: *If MINI was not conducted, concatenate reason. Continue for remaining assessments. Do not include rater initials.*

Listing 16.2.4.5
Liebowitz Social Anxiety Scale (LSAS)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit	LSAS Completed/ Reason Not Completed	Date/Time of Assessment (Study Day)	Score or Question	Result
XXXXX	Visit 1 (Screening)	No/ XXXXXX			
XXXXX	Visit 1 (Screening)	Yes	DDMMMYYYY:HHMM (XX)	Total LSAS Score	XXX
				Total Fear or Anxiety Subscore	XXX
				Fear or Anxiety Total Performance Subscore	XXX
				Fear or Anxiety Total Social Subscore	XXX
				Total Avoidance Subscore	XXX
				Avoidance Total Performance Subscore	XXX
				Avoidance Total Social Subscore	XXX
				Total Performance Subscore	XXX
				Total Social Subscore	XXX
				1. Telephoning in public: Fear or Anxiety	X = XXXXXXXXXXXX
				1. Telephoning in public: Avoidance	X = XXXXXXXXXXXX
				2. Participating in small groups: Fear or Anxiety	X = XXXXXXXXXXXX
				2. Participating in small groups: Avoidance	X = XXXXXXXXXXXX
				3. Eating in public places: Fear or Anxiety	X = XXXXXXXXXXXX
				3. Eating in public places: Avoidance	X = XXXXXXXXXXXX
				4. Drinking with others in public places: Fear or Anxiety	X = XXXXXXXXXXXX
				4. Drinking with others in public places: Avoidance	X = XXXXXXXXXXXX
				5. Talking to people in authority: Fear or Anxiety	X = XXXXXXXXXXXX
				5. Talking to people in authority: Avoidance	X = XXXXXXXXXXXX
				6. Acting, performing or giving a talk in front of an audience: Fear or Anxiety	X = XXXXXXXXXXXX
				6. Acting, performing or giving a talk in front of an audience: Avoidance	X = XXXXXXXXXXXX
				7. Going to a party: Fear or Anxiety	X = XXXXXXXXXXXX
				7. Going to a party: Avoidance	X = XXXXXXXXXXXX

Abbreviations: LSAS = Liebowitz Social Anxiety Scale.
Note: Study day is calculated relative to the date of first dose of study drug.

Programming Note: *If LSAS not completed, concatenate reason.*

Listing 16.2.4.5 (cont.)
Liebowitz Social Anxiety Scale (LSAS)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	LSAS Completed/ Reason Not Completed	Date/Time of Assessment (Study Day)	Score or Question	Result
XXXXX	Yes	DDMMMYYYY:HHMM (XX)	8. Working while being observed: Fear or Anxiety	X = XXXXXXXXXXXX
			8. Working while being observed: Avoidance	X = XXXXXXXXXXXX
			9. Writing while being observed: Fear or Anxiety	X = XXXXXXXXXXXX
			9. Writing while being observed: Avoidance	X = XXXXXXXXXXXX
			10. Calling someone you don't know very well: Fear or Anxiety	X = XXXXXXXXXXXX
			10. Calling someone you don't know very well: Avoidance	X = XXXXXXXXXXXX
			11. Talking with people you don't know very well: Fear or Anxiety	X = XXXXXXXXXXXX
			11. Talking with people you don't know very well: Avoidance	X = XXXXXXXXXXXX
			12. Meeting strangers: Fear or Anxiety	X = XXXXXXXXXXXX
			12. Meeting strangers: Avoidance	X = XXXXXXXXXXXX
			13. Urinating in a public bathroom: Fear or Anxiety	X = XXXXXXXXXXXX
			13. Urinating in a public bathroom: Avoidance	X = XXXXXXXXXXXX
			14. Entering a room when others are already seated: Fear or Anxiety	X = XXXXXXXXXXXX
			14. Entering a room when others are already seated: Avoidance	X = XXXXXXXXXXXX
			15. Being the center of attention: Fear or Anxiety	X = XXXXXXXXXXXX
			15. Being the center of attention: Avoidance	X = XXXXXXXXXXXX
			16. Speaking up at a meeting: Fear or Anxiety	X = XXXXXXXXXXXX
			16. Speaking up at a meeting: Avoidance	X = XXXXXXXXXXXX
			17. Taking a test: Fear or Anxiety	X = XXXXXXXXXXXX
			17. Taking a test: Avoidance	X = XXXXXXXXXXXX
			18. Expressing disagreement or disapproval to people you don't know very well: Fear or Anxiety	X = XXXXXXXXXXXX
			18. Expressing disagreement or disapproval to people you don't know very well: Avoidance	X = XXXXXXXXXXXX
			19. Looking at people you don't know very well in the eyes: Fear or Anxiety	X = XXXXXXXXXXXX
			19. Looking at people you don't know very well in the eyes: Avoidance	X = XXXXXXXXXXXX

Abbreviations: LSAS = Liebowitz Social Anxiety Scale.
Note: Study day is calculated relative to the date of first dose of study drug. The LSAS was only collected at Visit 1 (Screening).

Programming Note: *If LSAS not completed, concatenate reason.*

Listing 16.2.4.5 (cont.)
Liebowitz Social Anxiety Scale (LSAS)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	LSAS Completed/ Reason Not Completed	Date/Time of Assessment (Study Day)	Score or Question	Result
XXXXX	Yes	DDMMMYYYY:HHMM (XX)	20. Giving a report to a group: Fear or Anxiety	X = XXXXXXXXXXXX
			20. Giving a report to a group: Avoidance	X = XXXXXXXXXXXX
			21. Trying to pick up someone: Fear or Anxiety	X = XXXXXXXXXXXX
			21. Trying to pick up someone: Avoidance	X = XXXXXXXXXXXX
			22. Returning good to a store: Fear or Anxiety	X = XXXXXXXXXXXX
			22. Returning good to a store: Avoidance	X = XXXXXXXXXXXX
			23. Giving a party: Fear or Anxiety	X = XXXXXXXXXXXX
			23. Giving a party: Avoidance	X = XXXXXXXXXXXX
			24. Resisting a high pressure salesperson: Fear or Anxiety	X = XXXXXXXXXXXX
			24. Resisting a high pressure salesperson: Avoidance	X = XXXXXXXXXXXX

Abbreviations: LSAS = Liebowitz Social Anxiety Scale.
Note: Study day is calculated relative to the date of first dose of study drug. The LSAS was only collected at Visit 1 (Screening).

Programming Note: *If LSAS not completed, concatenate reason.*

[redacted]

Listing 16.2.5.1
Study Drug Dispensation
All Subjects

Actual Treatment: XXXXXXX

		Dispensing				Returning			
Subject ID	Study Visit [1]	Date/Time (Study Day)	Dispensed?/ Reason Not Dispensed	Vial 1 Dispensed?/ Kit Number/ Weight (g)	Vial 2 Dispensed?/ Kit Number/ Weight (g)	Date/Time (Study Day)	Returned?/ Reason Not Returned	Vial 1 Returned?/ Kit Number/ Weight (g)	Vial 2 Returned?/ Kit Number/ Weight (g)
XXXXX	XXXX	DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX				
	XXXX	DDMMMYYYY:HHMM (XX)	XX/ XXXXXXXX			DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX
XXXXX	Visit 2 (Baseline)	DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XX/ XXXXXXX/ XX				
	Visit 3	DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX	DDMMMYYYY:HHMM (XX)	XX/ XXXXXXXX	XX	XXX/ XXXXXXX/ XX
	Visit 4	DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX	DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX
	Visit 5	DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX	DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX
	Visit 6 (End of Treatment/Early Termination)					DDMMMYYYY:HHMM (XX)	XXX	XXX/ XXXXXXX/ XX	XXX/ XXXXXXX/ XX

Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If study drug was not dispensed, concatenate reason.*

[redacted]

Listing 16.2.5.2
Study Drug Administration
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Subject Instructed?	Subject Self-Administer First Dose?/ Reason Not Administered	Date/Time (Study Day) of Administration
XXXXX	XXX	XXX	DDMMMYYYY:HHMM (XX)
XXXXX	XXX	XX/ XXXXXXXXXXX	DDMMMYYYY:HHMM (XX)
XXXXX	XXX	XXX	DDMMMYYYY:HHMM (XX)
XXXXX	XXX	XXX	DDMMMYYYY:HHMM (XX)

Note: Study day is calculated relative to the date of first dose of study drug.

Listing 16.2.6.1
Hamilton Anxiety Scale (HAM-A)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	HAM-A Completed?/ Reason Not Completed	Date/Time of Assessment (Study Day)	Assessment	Result	Baseline Flag [2]
XXXXX	Visit 1 (Screening)	XX/ XXXXXXX				
XXXXX	Visit 2 (Baseline)	XXX	DDMMMYYYY/HH:MM (XX)	Anxious mood	X = XXXXXXXX	
				Tension	X = XXXXXXXX	
				Fears	X = XXXXXXXX	
				Insomnia	X = XXXXXXXX	
				Intellectual	X = XXXXXXXX	
				Depressed mood	X = XXXXXXXX	
				Somatic (muscular)	X = XXXXXXXX	
				Somatic (sensory)	X = XXXXXXXX	
				Cardiovascular symptoms	X = XXXXXXXX	
				Respiratory symptoms	X = XXXXXXXX	
				Gastrointestinal symptoms	X = XXXXXXXX	
				Genitourinary symptoms	X = XXXXXXXX	
				Autonomic symptoms	X = XXXXXXXX	
				Total Score	XX	Yes

Abbreviation: CFB = change from baseline; HAM-A = Hamilton Anxiety Scale.
Note: Study day is calculated relative to the date of first dose of study drug. The HAM-A total score is the sum of the individual item scores. CFB is calculated as the difference between the baseline score and the score at the current visit.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline).

Programming Note: *If HAM-A was not completed, concatenate reason. Baseline flag is only indicated for the Total Score row. CFB Total Score is only displayed for Visit 3 or later.*

Listing 16.2.6.1 (cont.)
Hamilton Anxiety Scale (HAM-A)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	HAM-A Completed?/ Reason Not Completed	Date/Time of Assessment (Study Day)	Assessment	Result	Baseline Flag [2]
XXXXX	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY/HH:MM (XX)	Anxious mood	X = XXXXXXXX	
				Tension	X = XXXXXXXX	
				Fears	X = XXXXXXXX	
				Insomnia	X = XXXXXXXX	
				Intellectual	X = XXXXXXXX	
				Depressed mood	X = XXXXXXXX	
				Somatic (muscular)	X = XXXXXXXX	
				Somatic (sensory)	X = XXXXXXXX	
				Cardiovascular symptoms	X = XXXXXXXX	
				Respiratory symptoms	X = XXXXXXXX	
				Gastrointestinal symptoms	X = XXXXXXXX	
				Genitourinary symptoms	X = XXXXXXXX	
				Autonomic symptoms	X = XXXXXXXX	
				Total Score	XX	
				CFB Total Score	XX	

Abbreviation: CFB = change from baseline; HAM-A = Hamilton Anxiety Scale.
Note: Study day is calculated relative to the date of first dose of study drug. The HAM-A total score is the sum of the individual item scores. CFB is calculated as the difference between the baseline score and the score at the current visit.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline).

Programming Note: *If HAM-A was not completed, concatenate reason. Baseline flag is only indicated for the Total Score row. CFB Total Score is only displayed for Visit 3 or later.*

Listing 16.2.6.2
Adjustment Disorder New Module (ADNM)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	ADNM Completed?/ Reason Not Completed	Date of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 2 (Baseline)	XX/ XXXXXXX			
XXXXX	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY (XX)	1. Divorce / separation	YES
				2. Family conflicts	YES
				3. Conflicts in working life	
				4. Conflicts with neighbors	YES
				5. Illness of a loved one	
				6. Death of a loved one	YES
				7. Adjustment due to retirement	YES
				8. Unemployment	
				9. Too much/too little work	YES
				10. Pressure to meet deadlines / time pressure	YES
				11. Moving to a new home	YES
				12. Financial problems	
				13. Own serious illness	YES
				14. Serious accident	
				15. Assault	
				16. Termination of an important leisure activity	
				17. Any other stressful event	YES
				Other stressful event, specify	XXXXXXXXXX

Abbreviation: ADNM = Adjustment Disorder New Module; CFB = change from baseline.
Note: Study day is calculated relative to the date of first dose of study drug. Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline). The ADNM total score was calculated as the sum of the 20 reaction frequency scores. The subscores were calculated as the sum of the reaction frequency scores as follows. Preoccupation subscore is the sum of items 2, 4, 13, and 15; Failure to Adapt subscore the sum of items 10, 17, 19, and 20; Avoidance subscore is the sum of items 3, 7, 11, and 14; Depressed Mood Subscore is the sum of items 1, 5, and 18; Anxiety subscore is the sum of items 6 and 16; Impulse Disturbance subscore is the sum of items 8, 9, and 12. CFB is calculated as the difference between the baseline score and the Visit 6 (End of Treatment/Early Termination) score.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If ADNM was not completed, concatenate reason. Note that CFB scores are only displayed at Visit 6 (End of Treatment/Early Termination).*

Listing 16.2.6.2 (cont.)
Adjustment Disorder New Module (ADNM)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	ADNM Completed?/ Reason Not Completed	Date of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY (XX)	Most straining event	XXXXXXXXXX
				Most straining event start date	DDMMMYYYY
				Most straining event ongoing	NO
				Most straining event end date	DDMMMYYYY
				1. Since the stressful problem, I feel low and sad: Frequency	X = XXXXXX
				1. Since the stressful problem, I feel low and sad: Duration	XXXXXX
				2. I have to think about the stressful situation repeatedly: Frequency	X = XXXXXX
				2. I have to think about the stressful situation repeatedly: Duration	XXXXXX
				3. I try to avoid talking about the stressful situation wherever possible: Frequency	X = XXXXXX
				3. I try to avoid talking about the stressful situation wherever possible: Duration	XXXXXX
				4. I keep having to think about the stressful situation and this is a great burden to me: Frequency	X = XXXXXX
				4. I keep having to think about the stressful situation and this is a great burden to me: Duration	XXXXXX
				5. Nowadays, I do those activities which I used to enjoy much more rarely: Frequency	X = XXXXXX
				5. Nowadays, I do those activities which I used to enjoy much more rarely: Duration	XXXXXX
				6. If think about the stressful situation, I find myself in a real state of anxiety: Frequency	X = XXXXXX
				6. If think about the stressful situation, I find myself in a real state of anxiety: Duration	XXXXXX
				7. I avoid certain things that might remind me of the stressful situation: Frequency	X = XXXXXX
				7. I avoid certain things that might remind me of the stressful situation: Duration	XXXXXX
				8. I am nervous and restless since the stressful situation: Frequency	X = XXXXXX
				8. I am nervous and restless since the stressful situation: Duration	XXXXXX

Abbreviation: ADNM = Adjustment Disorder New Module; CFB = change from baseline.
Note: Study day is calculated relative to the date of first dose of study drug. Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline). The ADNM total score was calculated as the sum of the 20 reaction frequency scores. The subscores are calculated as the sum of the reaction frequency scores as follows. Preoccupation subscore is the sum of items 2, 4, 13, and 15; Failure to Adapt subscore the sum of items 10, 17, 19, and 20; Avoidance subscore is the sum of items 3, 7, 11, and 14; Depressed Mood Subscore is the sum of items 1, 5, and 18; Anxiety subscore is the sum of items 6 and 16; Impulse Disturbance subscore is the sum of items 8, 9, and 12. CFB is calculated as the difference between the baseline score and the Visit 6 (End of Treatment/Early Termination) score.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If ADNM was not completed, concatenate reason. Note that CFB scores are only displayed at Visit 6 (End of Treatment/Early Termination).*

Listing 16.2.6.2 (cont.)
Adjustment Disorder New Module (ADNM)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	ADNM Completed?/ Reason Not Completed	Date of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY (XX)	9. Since the stressful situation, I am much quicker to lose my temper: Frequency	X = XXXXXX
				9. Since the stressful situation, I am much quicker to lose my temper: Duration	XXXXXX
				10. Since the stressful situation, I can only concentrate on certain things with difficulty: Frequency	X = XXXXXX
				10. Since the stressful situation, I can only concentrate on certain things with difficulty: Duration	XXXXXX
				11. I try to abolish the stressful situation from my memory: Frequency	X = XXXXXX
				11. I try to abolish the stressful situation from my memory: Duration	XXXXXX
				12. I have noticed that I am becoming more irritable due to the stressful situation: Frequency	X = XXXXXX
				12. I have noticed that I am becoming more irritable due to the stressful situation: Duration	XXXXXX
				13. I get constant memories of the stressful situation and can't do anything to stop them: Frequency	X = XXXXXX
				13. I get constant memories of the stressful situation and can't do anything to stop them: Duration	XXXXXX
				14. I try to suppress my feelings because they are a burden to me: Frequency	X = XXXXXX
				14. I try to suppress my feelings because they are a burden to me: Duration	XXXXXX
				15. My thoughts revolve around anything to do with the stressful situation: Frequency	X = XXXXXX
				15. My thoughts revolve around anything to do with the stressful situation: Duration	XXXXXX
				16. Since the stressful situation, I am scared of doing certain things: Frequency	X = XXXXXX
				16. Since the stressful situation, I am scared of doing certain things: Duration	XXXXXX
				17. Since the stressful situation, I don't like going to work or carrying out the necessary tasks in everyday life: Frequency	X = XXXXXX
				17. Since the stressful situation, I don't like going to work or carrying out the necessary tasks in everyday life: Duration	XXXXXX
				18. I have been feeling dispirited since the stressful situation and have little hope for the future: Frequency	X = XXXXXX

Abbreviation: ADNM = Adjustment Disorder New Module; CFB = change from baseline.
Note: Study day is calculated relative to the date of first dose of study drug. Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline). The ADNM total score was calculated as the sum of the 20 reaction frequency scores. The subscores are calculated as the sum of the reaction frequency scores as follows. Preoccupation subscore is the sum of items 2, 4, 13, and 15; Failure to Adapt subscore the sum of items 10, 17, 19, and 20; Avoidance subscore is the sum of items 3, 7, 11, and 14; Depressed Mood Subscore is the sum of items 1, 5, and 18; Anxiety subscore is the sum of items 6 and 16; Impulse Disturbance subscore is the sum of items 8, 9, and 12. CFB is calculated as the difference between the baseline score and the Visit 6 (End of Treatment/Early Termination) score.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If ADNM was not completed, concatenate reason. Note that CFB scores are only displayed at Visit 6 (End of Treatment/Early Termination).*

Listing 16.2.6.2 (cont.)
Adjustment Disorder New Module (ADNM)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	ADNM Completed?/ Reason Not Completed	Date of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY (XX)	18. I have been feeling dispirited since the stressful situation and have little hope for the future: Duration	XXXXXX
				19. Since the stressful situation, I can no longer sleep properly: Frequency	X = XXXXXX
				19. Since the stressful situation, I can no longer sleep properly: Duration	XXXXXX
				20. Overall, the situation affected me strongly in my personal relationships, my leisure activities, or other important areas of life: Frequency	X = XXXXXX
				20. Overall, the situation affected me strongly in my personal relationships, my leisure activities, or other important areas of life: Duration	XXXXXX
				Preoccupation Subscore	XX
				CFB Preoccupation Subscore	XX
				Failure to Adapt Subscore	XX
				CFB Failure to Adapt Subscore	XX
				Avoidance Subscore	XX
				CFB Avoidance Subscore	XX
				Depressed Mood Subscore	XX
				CFB Depressed Mood Subscore	XX
				Anxiety Subscore	XX
				CFB Anxiety Subscore	XX
				Impulse Disturbance Subscore	XX
				CFB Impulse Disturbance	XX
				Total Score	XX
				CFB Total Score	XX

Abbreviation: ADNM = Adjustment Disorder New Module; CFB = change from baseline.
Note: Study day is calculated relative to the date of first dose of study drug. Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline). The ADNM total score was calculated as the sum of the 20 reaction frequency scores. The subscores are calculated as the sum of the reaction frequency scores as follows. Preoccupation subscore is the sum of items 2, 4, 13, and 15; Failure to Adapt subscore the sum of items 10, 17, 19, and 20; Avoidance subscore is the sum of items 3, 7, 11, and 14; Depressed Mood Subscore is the sum of items 1, 5, and 18; Anxiety subscore is the sum of items 6 and 16; Impulse Disturbance subscore is the sum of items 8, 9, and 12. CFB is calculated as the difference between the baseline score and the Visit 6 (End of Treatment/Early Termination) score.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If ADNM was not completed, concatenate reason. Note that CFB scores are only displayed at Visit 6 (End of Treatment/Early Termination).*

Listing 16.2.6.3
International Adjustment Disorder Questionnaire (IADQ)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	IADQ Completed?/ Reason Not Completed	Date/Time of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 2 (Baseline)	No/ XXXXXXXXX			
XXXXX	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY:HHMM (XX)	1. Financial problems	No
				2. Work problems	Yes
				3. Educational problems	Yes
				4. Housing problems	Yes
				5. Relationship problems	No
				6. My own health problems	Yes
				7. A loved one's health problems	No
				8. Caregiving problems	Yes
				9. Some other problem	No
				10. I worry a lot about stressful event(s)	X = XXXXXXXX
				11. I can't stop thinking about stressful event(s)	X = XXXXXXXX
				12. I often feel afraid about what might happen in the future since the stressful event(s)	X = XXXXXXXX
				13. I find it difficult to adapt to life since the stressful event(s)	X = XXXXXXXX
				14. I find it difficult to relax and feel calm since the stressful event(s)	X = XXXXXXXX
				15. I find it difficult to achieve a state of inner peace since the stressful event(s)	X = XXXXXXXX

Abbreviation: IADQ = International Adjustment Disorder Questionnaire.
Note: Study day is calculated relative to the date of first dose of study drug. Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline). The IADQ total score was calculated as the sum items 10 through 15. The Preoccupation, Failure to Adapt, and Functional Impairment subscale scores were calculated as the sums of the individual scores for items 10, 11, and 12 (Preoccupation); 13, 14, and 15 (Failure to Adapt); and 17, 18, and 19 (Functional Impairment). CFB is calculated as the difference between the baseline score and the Visit 6 (End of Treatment/Early Termination) score.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If IADQ was not completed, concatenate reason. CFB Total Score is only displayed for Visit 6 (End of Treatment/Early Termination).*

Listing 16.2.6.3 (cont.)
International Adjustment Disorder Questionnaire (IADQ)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	IADQ Completed?/ Reason Not Completed	Date/Time of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY:HHMM (XX)	16. Did these problems start within one month of the stressful event(s)?	X = XXXXXXXX
				17. Affected your relationships or social life?	X = XXXXXXXX
				18. Affected your ability to work or your educational life?	X = XXXXXXXX
				19. Affected any other important part of your life?	X = XXXXXXXX
				Preoccupation Subscore	XX
				CFB Preoccupation Subscore	XX
				Failure to Adapt Subscore	XX
				CFB Failure to Adapt Subscore	XX
				Functional Impairment Subscore	XX
				CFB Functional Impairment Subscore	XX
				Total Score	XX
				CFB Total Score	XX

Abbreviation: IADQ = International Adjustment Disorder Questionnaire.
Note: Study day is calculated relative to the date of first dose of study drug. Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline). The IADQ total score was calculated as the sum items 10 through 15. The Preoccupation, Failure to Adapt, and Functional Impairment subscale scores were calculated as the sums of the individual scores for items 10, 11, and 12 (Preoccupation); 13, 14, and 15 (Failure to Adapt); and 17, 18, and 19 (Functional Impairment). CFB is calculated as the difference between the baseline score and the Visit 6 (End of Treatment/Early Termination) score.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If IADQ was not completed, concatenate reason. CFB Total Score is only displayed for Visit 6 (End of Treatment/Early Termination).*

Listing 16.2.6.4
Clinical Global Impression - Improvement (CGI-I)
All Subjects

Actual Treatment: XXXXXXX

Subject ID	Study Visit [1]	CGI-I Completed?/ Reason Not Completed	Date/Time of Assessment (Study Day)	CGI-I Score
XXXXX	Visit 3	XXX/ XXXXXXXXXX		
XXXXX	Visit 3	XXX	DDMMMYYYY/HH:MM (XX)	X = XXXXXXXXXXXXX
	Visit 4	XXX	DDMMMYYYY/HH:MM (XX)	X = XXXXXXXXXXXXX
	Visit 5	XXX	DDMMMYYYY/HH:MM (XX)	X = XXXXXXXXXXXXX
	Visit 6 (End of Treatment/Early Termination)	XXX	DDMMMYYYY/HH:MM (XX)	X = XXXXXXXXXXXXX
XXXXX	XXXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	X = XXXXXXXXXXXXX

Abbreviation: CGI-I = Clinical Global Impression – Improvement.
Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If CGI-I was not completed, concatenate reason.*

[redacted]

Listing 16.2.6.5
Patient Global Impression of Change (PGI-C)
All Subjects

Same shell as Listing 16.2.6.4 but replace any references to CGI-I with PGI-C; Programming Note: *In the abbreviations list, remove CGI-I and replace with "PGI-C = Patient Global Impression of Change".*

[redacted]

Listing 16.2.7.1
Adverse Events
All Subjects

Same as shell 14.3.3.1.

Listing 16.2.8.1
Hematology Laboratory Evaluations
All Subjects

Same as shell 14.3.4.1

Listing 16.2.8.2
Clinical Chemistry and Thyroid Laboratory Evaluations
All Subjects

Same as shell 14.3.4.1

Listing 16.2.8.3
Urinalysis Laboratory Evaluations
All Subjects

Same as shell 14.3.4.1

Listing 16.2.8.4
Pregnancy Test Results
Female Subjects

Actual Treatment: XXXXXXXXXXXXXX

Subject ID	Study Visit [1]	Test Type	Pregnancy Test Performed or Sample Collected?/ Reason Not Performed or Collected	Date/Time of Assessment (Study Day)	Result
XXXXX	Visit 1 (Screening)	Serum	Yes	DDMMMYYYY/HH:MM (XX)	Negative
		Urine	Yes	DDMMMYYYY/HH:MM (XX)	Negative
	Visit 2 (Baseline)	Serum	Yes	DDMMMYYYY/HH:MM (XX)	Negative
		Urine	Yes	DDMMMYYYY/HH:MM (XX)	Negative
	Visit 6 (End of Treatment/ Early Termination)	Serum	Yes	DDMMMYYYY/HH:MM (XX)	Negative
		Urine	Yes	DDMMMYYYY/HH:MM (XX)	Negative
XXXXX	XXXXXX	Serum	Yes	DDMMMYYYY/HH:MM (XX)	Negative
		Urine	Yes	DDMMMYYYY/HH:MM (XX)	Negative
	XXXXXX	Serum	Yes	DDMMMYYYY/HH:MM (XX)	Positive
		Urine	Yes	DDMMMYYYY/HH:MM (XX)	Positive
XXXXX	XXXXXX	Serum	No/ XXXXXXXXXXXXXX		

Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If pregnancy test was not performed, concatenate with reason.*

Listing 16.2.8.5
Laboratory Results for Urine Drug Screen
All Subjects

Actual Treatment: XXXXXXXXXXXXXXX

Subject ID	Study Visit [1]	Urine Drug Screen Performed?/ Reason Not Performed	Date/Time Performed (Study Day)	Result	Substances found
XXXXX	Visit 1 (Screening)	Yes	DDMMMYYYY/HH:MM (XX)	Negative	
	Visit 2 (Baseline)	XXX	DDMMMYYYY/HH:MM (XX)	Positive	XXXXX; XXXX; XXXXX
	Visit 6 (End of Treatment/ Early Termination)	XXX	DDMMMYYYY/HH:MM (XX)	Negative	
XXXXX	XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	XXXXXXXXX	XXX
	XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	XXXXXXXXX	XXX
	XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	XXXXXXXXX	XXX
XXXXX	XXXXXX	No/ XXXXXXXX			

Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming note: *If more than 1 substance, concatenate substances with semi-colons. Substances can be Tricyclic Antidepressants, Opiates, Cocaine, Benzodiazepines, Amphetamines, Barbiturates, Cannabinoids, Methadone, Phencyclidine, Propoxyphene, Buprenorphine, 3,4-methylenedioxymethamphetamine (MDMA), Oxycodone, and Methamphetamine. If urine drug screen was not performed, concatenate with reason.*

Listing 16.2.9.1
Vital Signs
All Subjects

Actual Treatment: XXXXXXXXXXXXX

Subject ID	Parameter (unit)	Study Visit [1]	Vital Signs Collected/ Reason Not Collected	Subject Rested 5 Mins Prior?	Date/Time Collected (Study Day)	Results	Baseline Flag [2]	Change from Baseline [3]	Normal Range	Normal Range Flag
XXXXX	XXXXXX	Visit 1 (Screening)	Yes	Yes	DDMMMYYYY/HH:MM (XX)	XX			XX - YY	Normal
		Visit 2 (Baseline)	XXX	No	DDMMMYYYY/HH:MM (XX)	XX	Yes		XX - YY	Normal
		Visit 3	XXX	XXX	DDMMMYYYY/HH:MM (XX)	XX		XX	XX - YY	Below
		Visit 4				XX		XX	XX - YY	Normal
		Visit 5	XXX	XXX	DDMMMYYYY/HH:MM (XX)	XX		XX	XX - YY	Normal
		Visit 6 (End of Treatment/ Early Termination)	XXX	XX	DDMMMYYYY/HH:MM (XX)	XX		XX	XX - YY	Above
		Visit 7 (Follow-Up)	XXX	XX	DDMMMYYYY/HH:MM (XX)	XX		XX	XX - YY	Normal
	XXXXXX	XXXXXX	XXX	XXX	DDMMMYYYY/HH:MM (XX)	XX				Normal
	XXXXXX	XXXXXX	XXX	XXX	DDMMMYYYY/HH:MM (XX)	XX	Yes		XX - YY	Normal
	XXXXXX	XXXXXX	XXX	XXX	DDMMMYYYY/HH:MM (XX)	XX		XX	XX - YY	Normal
	XXXXXX	XXXXXX	XXX	XXX	DDMMMYYYY/HH:MM (XX)	XX		XX	XX - YY	Normal
XXXXX	XXXXXX	XXXXXX	No/ XXXXXXXXXX							

Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline).
[3] Change from baseline is the difference between the baseline assessment and the current visit's assessment.

Programming note: *Parameters will be Temperature (°C), Heart Rate (beats/min), Respiratory Rate (breaths/min), Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg). If vital signs were not collected, concatenate with reason.*

Listing 16.2.9.2
12-Lead Electrocardiogram Measurements
All Subjects

Actual Treatment: XXXXXXXXXXXXXXXXX

Subject ID	Parameter (unit)	Study Visit [1]	Was ECG Performed?/ Reason Not Performed	Date/Time of ECG (Study Day)	Result	Baseline Flag [2]	Change from Baseline [3]
XXXXX	XXXXX (XXX)	Visit 1 (Screening) Visit 6 (End of Treatment/ Early Termination)	Yes No/ XXXXX	DDMMMYYYY/HH:MM (XX)	XX	Yes	
	XXXXX (XXX)	XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	XX	Yes	
		XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	XX		XX
	Interpretation	XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	Abnormal, not clinically significant/ XXXXXXXXXX		
		XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	Abnormal, clinically significant/ XXXXXXXXXX		
XXXXX	XXXXX (XXX)	XXXXXX	XXX	DDMMMYYYY/HH:MM (XX)	XX	XXX	
			XXX	DDMMMYYYY/HH:MM (XX)	XX		XX

Abbreviations: ECG = electrocardiogram; QTc = QT interval corrected for heart rate using default formula; QTcF = QT interval corrected for heart rate using Fridericia's formula.
Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.
[2] Baseline is defined as the last non-missing assessment before the first dose of study drug at Visit 2 (Baseline).
[3] Change from baseline is the difference between the baseline assessment and the current visit's assessment.

Programming note: *Parameters will be Ventricular Rate (beats/min), RR Interval (msec), PR Interval (msec), QRS Interval (msec), QT Interval (msec), QTc Interval (msec), QTcF Interval (msec), Interpretation. If ECG was not performed, concatenate with reason. Concatenate "ECG results" and "Please describe the finding" together in the "Results" column.*

Listing 16.2.9.3
Physical Examination Including Nasal Passages Measurements
All Subjects

Actual Treatment: XXXXXXXXXXX

Subject ID	Study Visit [1]	Was Physical Exam Performed?/ Reason Not Performed	Exam Date/Time (Study Day)	Body System	Result	Abnormal Findings	Clinically Significant?
XXXXXX	Visit 1 (Screening)	No/ XXXXXX					
XXXXXX	Visit 1 (Screening)	Yes	DDMMMYYYY/HH:MM (XX)	Abdomen	Normal		
				Cardiovascular	Abnormal	XXXXXXXX	Yes
				Extremities	Normal		
				General Appearance	Normal		
				Genitourinary	Normal		
				Head, Ears, Eyes, Nose, Throat	Normal		
				Integumentary	Normal		
				Lymphatic	Normal		
				Musculoskeletal	Normal		
				Nasal Passages	Normal		
				Neck/Thyroid	Normal		
				Nervous System	Normal		
				Respiratory	Normal		
	Visit 3	Yes	DDMMMYYYY/HH:MM (XX)	Nasal Passages	Normal		
	Visit 4	Yes	DDMMMYYYY/HH:MM (XX)	Nasal Passages	Normal		
	Visit 5	Yes	DDMMMYYYY/HH:MM (XX)	Nasal Passages	Normal		
	Visit 6	Yes	DDMMMYYYY/HH:MM (XX)	Abdomen	Normal		
				Cardiovascular	Normal		
				Extremities	Normal		
				General Appearance	Normal		
				Genitourinary	Abnormal	XXXXXXXX	No
				Head, Ears, Eyes, Nose, Throat	Normal		
				Integumentary	Normal		
				...			

Note: Study day is calculated relative to the date of first dose of study drug.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming note: *If physical examination was not performed, concatenate with reason. Note that only the nasal passages are examined at Visits 3, 4, and 5.*

Listing 16.2.9.4
Prior and Concomitant Medications
All Subjects

Actual Treatment: XXXXXXXXXXX

Subject ID	Prior or Concomitant [1]	ATC Class (Level 2)/ Preferred Term/ Medication or Therapy	Indication	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Dose (unit)	Route/ Frequency
XXXXXX	XXX	XXXXX/ XXXXXXXXX/ XXXXXXXXXX	XXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXX (XXX)	XXXXXXXX/ XXXXXXX
		XXXXX/ XXXXXXXXX/ XXXXXXXXXX	XXXXX	--MMMYYYY/ Ongoing	XXX (XXX)	XXXXXXXX/ XXXXXXX
		XXXXX/ XXXXXXXXX/ XXXXXXXXXX	XXXXX	DDMMMYYYY (XX)/ -----YYYY (XX)	XXX (XXX)	XXXXXXXX/ XXXXXXX

Abbreviations: ATC = Anatomical Therapeutic Chemical; WHO-DD = World Health Organization Drug Dictionary.
Note: Study day is calculated relative to the date of first dose of study drug. Medications were coded using WHO-DD Global B3 Version XX.
[1] All medications taken in the month prior to Visit 1 (Screening) or in the time interval between Visit 1 (Screening) and Visit 2 (Baseline) are considered prior medications, whether or not they were stopped before Visit 2 (Baseline). Any medications continuing or starting after Visit 2 (Baseline) are considered concomitant. If a medication starts before Visit 2 (Baseline) and continues after Visit 2 (Baseline) it is considered both prior and concomitant.

Programming note: *If Dose Unit, Route or Frequency is Other, display other specify text only (i.e., do not display "Other: XXXXXX" but just "XXXXXX "). Sort by subject, start date/, end date, ATC level 2 & PT. Replace "XX" in the footnote with the correct version of the WHO-DD used for coding. For dry run delivery, use WHO-DD Global B3 version Sep 2021.*

Listing 16.2.9.5
Columbia Suicide Severity Rating Scale (C-SSRS)
All Subjects

Actual Treatment: XXXXXXXXXX

Subject ID	Study Visit [1]	C-SSRS Completed?/ Reason Not Completed	Date (Study Day)	Category	Assessment	Result
XXXXX	XXXXXXX	XX/ XXXXX				
XXXXX	Visit 1 (Screening)	XXX	DDMMMYYYY (XX)	Suicidal Ideation	1. Wish to be dead (lifetime)	No
					1. Wish to be dead (past 6 months)	Yes
					If yes, describe	XXXXXX
					2. Non-Specific Active Suicidal Thoughts (lifetime)	XXX
					2. Non-Specific Active Suicidal Thoughts (past 6 months)	XXX
					If yes, describe	XXXXXX
					3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act (lifetime)	XXX
					3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act (past 6 months)	XXX
					If yes, describe	XXXXXX
					4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan (lifetime)	XXX
					4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan (past 6 months)	XXX
					If yes, describe	XXXXXX
					5. Active Suicidal Ideation with Specific Plan and Intent (lifetime)	XXX
					5. Active Suicidal Ideation with Specific Plan and Intent (past 6 months)	XXX
					If yes, describe:	XXXXXX

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale
Note: Study day is calculated relative to the date of first dose of study drug.
[1] The C-SSRS has two versions: C-SSRS (Long Term/Recent) and C-SSRS (Since Last Visit). The C-SSRS (Long Term/Recent) version is used at Visit 1 (Screening), while the C-SSRS (Since Last Visit) version is used at all other study visits. Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If C-SSRS was not conducted, concatenate reason.*

Listing 16.2.9.5 (cont.)
Columbia Suicide Severity Rating Scale (C-SSRS)
All Subjects

Actual Treatment: XXXXXXXXXX

Subject ID	Study Visit [1]	C-SSRS Completed?/ Reason Not Completed	Date (Study Day)	Category	Assessment	Result
XXXXX	Visit 1 (Screening)	XXX	DDMMMYYYY (XX)	Intensity of Ideation	Most Severe Ideation Type # (1-5) (lifetime)	X
					Description of Ideation (lifetime)	XXXXXX
					Most Severe Ideation Type # (1-5) (past 6 months)	X
					Description of Ideation (past 6 months)	XXXXXX
					Frequency (lifetime)	X = XXXXX
					Frequency (past 6 months)	X = XXXXX
					Duration (lifetime)	X = XXXXX
					Duration (past 6 months)	X = XXXXX
					Controllability (lifetime)	X = XXXXX
					Controllability (past 6 months)	X = XXXXX
					Deterrents (lifetime)	X = XXXXX
					Deterrents (past 6 months)	X = XXXXX
					Reasons for Ideation (lifetime)	X = XXXXX
					Reasons for Ideation (past 6 months)	X = XXXXX
				Suicidal Behavior	Actual Attempt (lifetime)	XXX
					Total # of Attempts (lifetime)	XXXX
					Actual Attempt (past 2 years)	XXX
					Total # of Attempts (past 2 years)	XXXX
					If yes, describe:	XXXXXXXXXXX
					Non-Suicidal Self-Injurious Behavior (lifetime)	XXX
					Non-Suicidal Self-Injurious Behavior (past 2 years)	XXX
					Interrupted Attempt (lifetime)	XXX
					Total # of interrupted (lifetime)	XXXX
					Interrupted Attempt (past 2 years)	XXX
					Total # of interrupted (past 2 years)	XXXX

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale
Note: Study day is calculated relative to the date of first dose of study drug.
[1] The C-SSRS has two versions: C-SSRS (Long Term/Recent) and C-SSRS (Since Last Visit). The C-SSRS (Long Term/Recent) version is used at Visit 1 (Screening), while the C-SSRS (Since Last Visit) version is used at all other study visits. Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If C-SSRS was not conducted, concatenate reason.*

Listing 16.2.9.5 (cont.)
Columbia Suicide Severity Rating Scale (C-SSRS)
All Subjects

Actual Treatment: XXXXXXXXXX

Subject ID	Study Visit [1]	C-SSRS Completed?/ Reason Not Completed	Date (Study Day)	Category	Assessment	Result
XXXXX	Visit 1 (Screening)	XXX	DDMMMYYYY (XX)	Suicidal Behavior	If yes, describe:	XXXXXXXXXXX
					Aborted Attempt (lifetime)	XXX
					Total # of aborted (lifetime)	XXXX
					Aborted Attempt (past 2 years)	XXX
					Total # of aborted (past 2 years)	XXXX
					If yes, describe	XXXXXXXXXXX
					Preparatory Acts or Behavior (lifetime)	XXX
					Preparatory Acts or Behavior (past 2 years)	XXX
					If yes, describe	XXXXXXXXXXX
					Suicidal Behavior (lifetime)	XXX
					Suicidal Behavior (past 2 years)	XXX
					Most Recent Attempt Date	DDMMMYYYY
					Actual Lethality – Most Recent Attempt Code	X = XXXXXXXXX
					Potential Lethality – Most Recent Attempt Code	X = XXXXXXXXX
					Most Lethal Attempt Date	DDMMMYYYY
					Actual Lethality – Most Lethal Attempt Code	X = XXXXXXXXX
					Potential Lethality – Most Lethal Attempt Code	X = XXXXXXXXX
					Initial/First Attempt Date	DDMMMYYYY
					Actual Lethality – Initial/First Attempt Code	X = XXXXXXXXX
					Potential Lethality – Initial/First Attempt Code	X = XXXXXXXXX

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale
Note: Study day is calculated relative to the date of first dose of study drug.
[1] The C-SSRS has two versions: C-SSRS (Long Term/Recent) and C-SSRS (Since Last Visit). The C-SSRS (Long Term/Recent) version is used at Visit 1 (Screening), while the C-SSRS (Since Last Visit) version is used at all other study visits. Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If C-SSRS was not conducted, concatenate reason.*

Listing 16.2.9.5 (cont.)
Columbia Suicide Severity Rating Scale (C-SSRS)
All Subjects

Actual Treatment: XXXXXXXXXX

Subject ID	Study Visit [1]	C-SSRS Completed?/ Reason Not Completed	Date (Study Day)	Category	Assessment	Result
XXXXX	Visit 2 (Baseline)	XXX	DDMMMYYYY (XX)	Suicidal Ideation	1. Wish to be dead	XXX
					If yes, describe	XXXXXX
					2. Non-Specific Active Suicidal Thoughts	XXX
					If yes, describe	XXXXXX
					3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act	XXX
					If yes, describe	XXXXXX
					4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan	XXX
					If yes, describe	XXXXXX
					5. Active Suicidal Ideation with Specific Plan and Intent	XXX
					If yes, describe:	XXXXXX
				Intensity of Ideation	Most Severe Ideation Type # (1-5)	X
					Description of Ideation	XXXXXX
					Frequency	X = XXXXX
					Duration	X = XXXXX
					Controllability	X = XXXXX
					Deterrents	X = XXXXX
					Reasons for Ideation	X = XXXXX

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale
Note: Study day is calculated relative to the date of first dose of study drug.
[1] The C-SSRS has two versions: C-SSRS (Long Term/Recent) and C-SSRS (Since Last Visit). The C-SSRS (Long Term/Recent) version is used at Visit 1 (Screening), while the C-SSRS (Since Last Visit) version is used at all other study visits. Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If C-SSRS was not conducted, concatenate reason.*

Listing 16.2.9.5 (cont.)
Columbia Suicide Severity Rating Scale (C-SSRS)
All Subjects

Actual Treatment: XXXXXXXXXX

Subject ID	Study Visit [1]	C-SSRS Completed?/ Reason Not Completed	Date (Study Day)	Category	Assessment	Result
XXXXX	Visit 2 (Baseline)	XXX	DDMMMYYYY (XX)	Suicidal Behavior	Actual Attempt	XXX
					Total # of Attempts	XXXX
					If yes, describe:	XXXXXXXXXXX
					Non-Suicidal Self-Injurious Behavior	XXX
					Interrupted Attempt	XXX
					Total # of interrupted	XXXX
					If yes, describe:	XXXXXXXXXXX
					Aborted Attempt	XXX
					Total # of aborted	XXXX
					If yes, describe	XXXXXXXXXXX
					Preparatory Acts or Behavior	XXX
					If yes, describe:	XXXXXXXXXXX
					Suicidal Behavior	XXX
					Suicide	XXX
					Most Recent Attempt Date	DDMMMYYYY
					Actual Lethality – Most Recent Attempt Code	X = XXXXXXXXX
					Potential Lethality – Most Recent Attempt Code	X = XXXXXXXXX

Abbreviation: C-SSRS = Columbia Suicide Severity Rating Scale
Note: Study day is calculated relative to the date of first dose of study drug.
[1] The C-SSRS has two versions: C-SSRS (Long Term/Recent) and C-SSRS (Since Last Visit). The C-SSRS (Long Term/Recent) version is used at Visit 1 (Screening), while the C-SSRS (Since Last Visit) version is used at all other study visits. Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If C-SSRS was not conducted, concatenate reason.*

Listing 16.2.9.6
Montgomery-Asberg Depression Rating Scale (MADRS)
All Subjects

Actual Treatment: XXXXXXXXXX

Subject ID	Study Visit [1]	MADRS Completed?/ Reason Not Completed	Date/Time of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 1 (Screening)	Yes	DDMMMYYYY/HH:MM (XX)	1. Apparent sadness	0 = No sadness
				2. Reported sadness	XXXXXXXX
				3. Inner tension	XXXXXXX
				4. Reduced sleep	XXXXX
				5. Reduced appetite	XXXXXXX
				6. Concentration difficulties	XXXXXX
				7. Lassitude	XXXXXX
				8. Inability to feel	XXXXXX
				9. Pessimistic thoughts	XXXXXX
				10. Suicidal thoughts	XXXXXX
				Total Score	XX
XXXXX	Visit 6 (End of Treatment/ Early Termination)	No/ XXXXXXXXXXX			

Abbreviation: MADRS = Montgomery-Asberg Depression Rating Scale.
Note: Study day is calculated relative to the date of first dose of study drug. The MADRS total score was calculated as the sum of the 10 items.
[1] Visit 6 (End of Treatment/Early Termination) includes data from subjects who either completed Visit 6 (End of Treatment) or who discontinued from the study and completed an early termination visit.

Programming Note: *If MADRS was not completed, concatenate reason.*

Listing 16.2.6.7
Clinical Global Impression – Severity (CGI-S)
All Subjects

Same as shell 16.2.6.4 except replace all mentions of CGI-I with CGI-S; Programming Note: *Update abbreviations to include "CGI-S = Clinical Global Impression – Severity" and remove the CGI-I abbreviation. If CGI-S was not completed, concatenate reason. Note that the CGI-S assessments will be displayed for Visit 1 (Screening) through Visit 6 (End of Treatment/Early Termination).*

Listing 16.2.9.8
Physician Withdrawal Checklist (PWC-20)
All Subjects

Actual Treatment: XXXXXXXXXX

Subject ID	Study Visit	PWC-20 Completed?/ Reason Not Completed	Date of Assessment (Study Day)	Assessment	Result
XXXXX	Visit 7 (Follow-Up)	No/ XXXXXXXXX			
XXXXX	Visit 7 (Follow-Up)	XXX	DDMMMYYYY (XX)	Did the subject manifest or describe any of the following symptoms since the last visit?	Yes
				Loss of appetite	1 = Mild
				Nausea-vomiting	X = XXXXXXX
				Diarrhea	X = XXXXXXX
				Anxiety-Nervousness	X = XXXXXXX
				Irritability	X = XXXXXXX
				Dysphonic mood-Depression	X = XXXXXXX
				Insomnia	X = XXXXXXX
				Fatigue-Lethargy-Lack of energy	X = XXXXXXX
				Poor coordination	X = XXXXXXX
				Restlessness-Agitation	X = XXXXXXX
				Diaphoresis	X = XXXXXXX
				Tremor-Tremulousness	X = XXXXXXX
				Dizziness-Lightheadedness	X = XXXXXXX
				Headaches	X = XXXXXXX
				Muscle aches or stiffness	X = XXXXXXX
				Weakness	X = XXXXXXX
				Increased acuity for sound, smell, touch, or pain	X = XXXXXXX
				Paresthesias	X = XXXXXXX
				Difficulty concentrating, remembering	X = XXXXXXX
				Depersonalization-derealization	X = XXXXXXX
				Total Score [1]	XX

Abbreviation: PWC-20 = Physician Withdrawal Checklist.
Note: Study day is calculated relative to the date of first dose of study drug. The PWC-20 total score was calculated as the sum of the 20 items.

Programming Note: *If PWC-20 was not conducted, concatenate reason.*

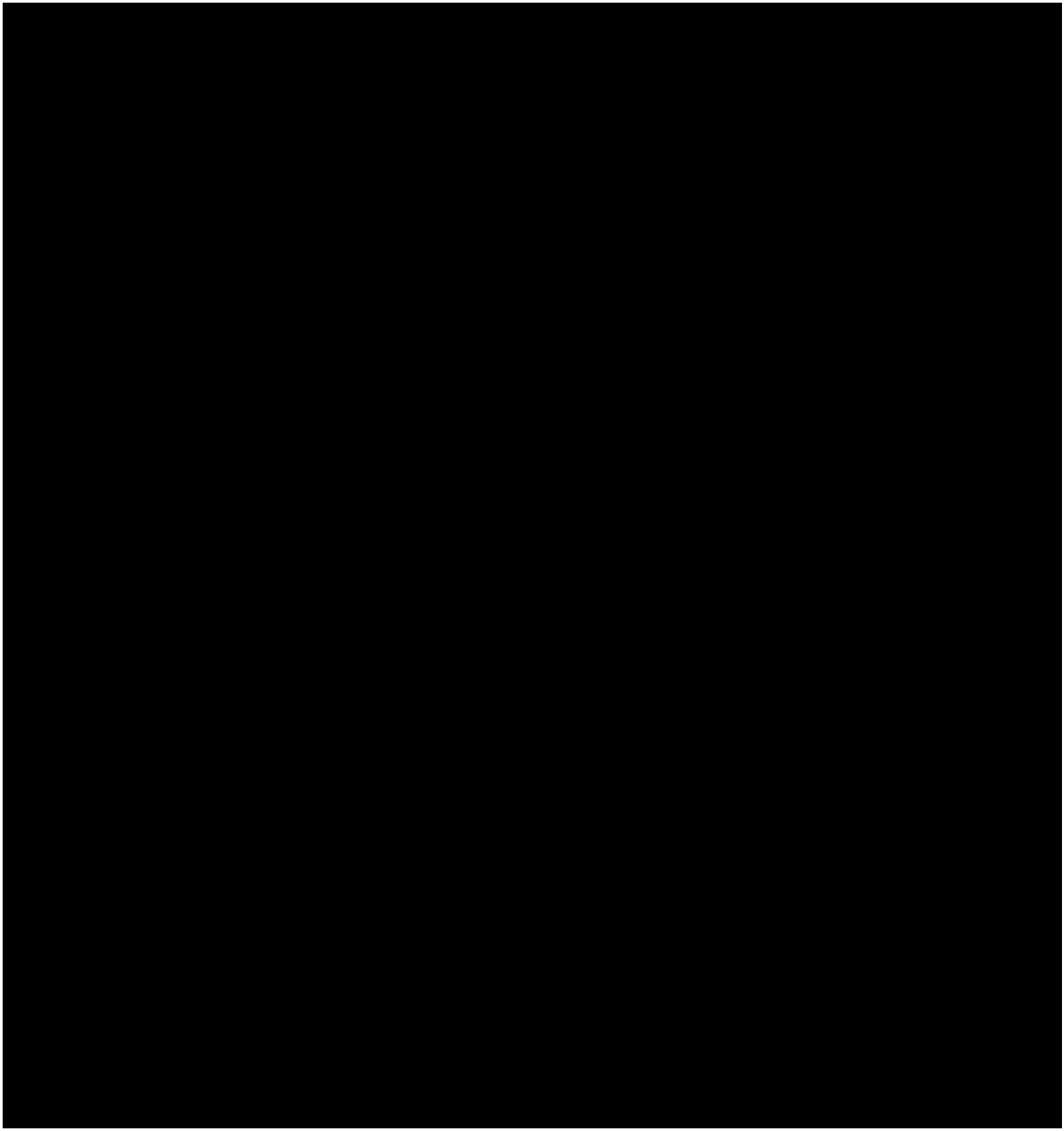
Listing 16.2.10.1
COVID-19 Impact Assessment
All Subjects

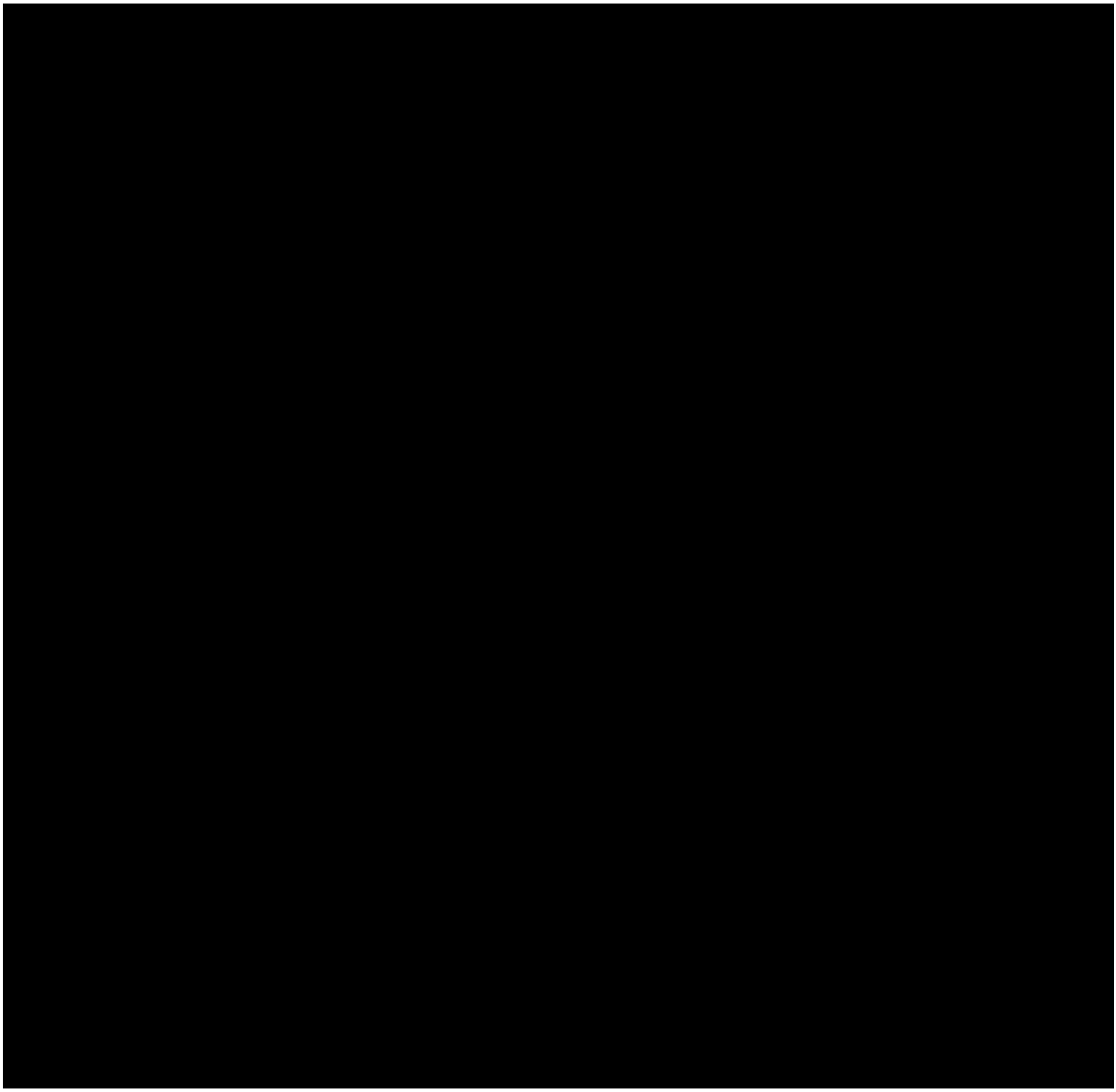
Actual Treatment: XXXXXXXXXXX

Subject ID	Subject Affected by COVID-19?	Visit Impacted/ Visit Type Adjustment	Visit Date (Study Day)	Efficacy Assessments Missed?/ Safety Assessments Missed?	Early Termination Reason/ Comments	IP Impact/ Start Date (Study Day)/ End Date (Study Day)	Study Drug Dispensation Change/ Study Drug Administration Change	IP Impact Comments
XXXXX	Yes	Visit 1 (Screening)/ XXXXXXXXXX; XXXXX	DDMMMYYYY (XX)	Yes/ No	SUBJECT INFECTED WITH COVID-19/ XXXXXXXXX	DOSING INTERRUPTION/ DDMMMYYYY (XX)/ DDMMMYYYY(XX)	SHIPPED VIA COURIER/ ADMINISTERED VIA HOME HEALTHCARE	XXXXXXX
XXXXX	Yes	Visit 3/ XXXXX	DDMMMYYYY (XX)	No/ No	TRAVEL RESTRICTIONS/ XXXXXXXXXXXXX	SUBJECT DECISION/ DDMMMYYYY (XX)/ DDMMMYYYY(XX)	DISPENSED VIA HOME HEALTHCARE/ SELF-ADMINISTERED	XXXXXXX

Abbreviations: COVID-19 = novel coronavirus disease-2019; IP = investigational product.
Note: Study day is calculated relative to the date of first dose of study drug.

Programming note: *If more than 1 visit type adjustment, concatenate. If visit type adjustment, early termination reason, IP impact, study drug dispensation change, or study drug administration change is "Other", display other specify text only (i.e., do not display "Other: XXXXXX" but just "XXXXXX").*





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