STATISTICAL ANALYSIS PLAN
PHASE 2

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STUDY DRUG:

NBI-98854

PROTOCOL NUMBER:

NBI-98854-1601

STUDY TITLE:

An Open-Label, Safety and Tolerability Study of NBI-98854 for the Treatment of Subjects with Tourette Syndrome

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1. LIST OF ABBREVIATIONS

Table 1: List of Abbreviations

Abbreviation	Term
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body mass index
CDRS-R	Children's Depression Rating Scale-Revised
CGI-Tics-Severity	Clinical Global Impression of Tics-Severity
CGI-TS	Clinical Global Impression of Improvement-Tourette Syndrome
CSR	Clinical study report
C-SSRS	Columbia Suicide Severity Rating Scale
CY-BOCS	Children's Yale-Brown Obsessive-Compulsive Scale
ECG	Electrocardiogram
eCRF	Electronic case report form
ESRS-A	Extrapyramidal Symptom Rating Scale-Abbreviated
GGT	Gamma-glutamyl transferase
GTS-QOL	Giles de la Tourette Syndrome-Quality of Life Scale
HBsAg	Hepatitis B surface antigen
HCV-Ab	Hepatitis C virus antibody
MedDRA	Medical Dictionary for Regulatory Activities
NBI	Neurocrine Biosciences, Inc.
PedsQL	Pediatric Quality of Life Inventory
PGIC-TS	Patient Global Impression of Change-Tourette Syndrome
PK	Pharmacokinetic(s)
PUTS	Premonitory Urge for Tics Scale
QTcF	Corrected QT interval using Fridericia's formula
RTRS	Rush Video-based Tic Rating Scale
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SIGH-D-17	Structured Interview Guide for the Hamilton Depression Rating Scale
TEAE	Treatment-emergent adverse event

TS	Tourette syndrome
TTS	Total tic score
UDS	Urine drug screen
ULN	Upper limit of normal
VAS	Visual analog scale
WHO	World Health Organization
Y-BOCS	Yale-Brown Obsessive-Compulsive Scale
YGTSS	Yale Global Tic Severity Scale

2. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and data displays to be included in the clinical study report (CSR) for protocol NBI-98854-1601.

This SAP provides details on analysis sets and on how analysis variables will be derived and missing data will be handled, and describes the statistical methods to be used to summarize the pharmacodynamic (PD), pharmacokinetic (PK), and safety data for the CSR.

Deviations from the final approved SAP will be documented in the CSR.

3. STUDY OBJECTIVE

The objective of this clinical study is to evaluate the safety and tolerability of NBI-98854 (titrated from 10 mg to 20 mg in children, 20 mg to 40 mg in adolescents, and 40 mg to 80 mg in adults) administered once daily for up to 24 weeks for the treatment of Tourette syndrome (TS).

4. STUDY DESIGN

4.1. Summary of Study Design

This is a Phase 2, open-label, fixed-dose titration study to evaluate the safety and tolerability of NBI-98854 administered once daily for a total of 24 weeks in children, adolescents, and adults with TS. NBI-98854 doses will be titrated from 10 mg to 20 mg in children (6 to 11 years of age), 20 mg to 40 mg in adolescents (12 to 17 years of age), and 40 mg to 80 mg in adults (18 to 64 years of age). Up to 180 male and female subjects (up to 90 pediatric subjects [ie, children and adolescents] and up to 90 adult subjects) with a clinical diagnosis of TS will be enrolled. The study will include approximately 60 study sites in the United States.

Subjects who have their final Phase 2 study (NBI-98854-1501 or NBI-98854-1505) visit >30 days prior to anticipated baseline (Day -1) require screening. These subjects will be screened to determine eligibility within 20 days (Days -21 to -2) before baseline (Day -1).

Subjects can have their final Phase 2 study (NBI-98854-1501 or NBI-98854-1505) visit on the same day as baseline (Day -1) for this study provided that the NBI-98854-1601 informed

consent, and assent (if applicable), is obtained before the final NBI-98854-1501 or NBI 98854 1505 visit. This will allow certain PD and safety assessments to be used for both the previous study and the current study. The PD assessments that can apply to both the previous study and the current study include the Yale Global Tic Severity Score (YGTSS), RTRS, Premonitory Urge for Tics Scale (PUTS), and Clinical Global Impression (CGI) of Tics Severity. The safety assessment results that can apply to both the previous study and the current study include physical examinations (including weight), vital signs, electrocardiograms (ECG), Extrapyramidal Symptom Rating Scale-Abbreviated (ESRS-A), Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS; pediatric subjects only), Children's Depression Rating Scale - Revised (CDRS-R; pediatric subjects only), Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; adult subjects only), and the Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D-17; adult subjects only). All other Day -1 assessments (including safety labs) must be collected for the current study (even if the subject is completing the final visit for the previous study).

On Day -1, all subjects will have baseline study assessments conducted and be assessed for eligibility. Eligible subjects will receive a supply of NBI-98854 (10, 20, or 40 mg, based on their age group) for the first 4 weeks of treatment. Beginning on Day 1, subjects will take study drug once daily at home at approximately the same time each day (under the supervision of the subject's parent/legal guardian for pediatric subjects) throughout the 24-week treatment period.

At the end of Week 4, the investigator may escalate the NBI-98854 dose from 10 to 20 mg in children, from 20 to 40 mg in adolescents, and from 40 to 80 mg in adults, or continue with the subject's current dose for the remainder of the treatment period. A dose escalation will be allowed if (1) the investigator or designee's assessment of the Clinical Global Impression of Improvement -Tourette Syndrome (CGI-TS) is "minimally improved", "not changed", "minimally worse", "much worse", or "very much worse", and (2) the safety and tolerability of the current dose is acceptable as determined by a physician. The subject will then continue at this dose until the end of the treatment period (ie, the end of Week 24).

At any time after dose escalation, the investigator may modify the timing of study drug dosing (eg, qam to qhs) and/or decrease a subject's dose (to 10 mg for children, 20 mg for adolescents, or 40 mg for adults) if the subject is unable to tolerate the dose increase. Subjects who are unable to tolerate the starting dose of 10 mg for children, 20 mg for adolescents, 40 mg for adults, or the resumption of the 10 mg, 20 mg, or 40 mg dose after the dose escalation at Week 4, will be discontinued from the study.

Subjects will return to the study site every 4 weeks during the treatment period, at the end of Weeks 4, 8, 12, 16, 20, and 24.

A follow-up visit will be performed at the end of Week 28 (4 weeks after the last dose of study drug) or early termination. Subjects who withdraw from the study will be asked to complete an early termination visit within 4 weeks. Safety, PD, and PK will be assessed at scheduled times throughout the study. The treatment period visits (end of Weeks 4, 8, 12, 16, 20, and 24) and the follow-up visit (end of Week 28) will have a visit window of ±6 days.

4.2. Sample Size Considerations

The sample size for this study is based on practical considerations and not on a statistical power calculation.

4.3. Randomization

Subjects are not randomized to treatment in this study.

4.4. Clinical Assessments

Pharmacodynamics: The following PD assessments will be administered at baseline (Day -1), at the end of Weeks 4, 8, 12, 16, 20, and 24, and at the follow-up visit (the end of Week 28, or early termination):

All subjects:

- YGTSS
- RTRS
- PUTS
- CGI-Tics Severity

Pediatric subjects only:

- Pediatric Quality of Life Inventory (PedsQL)

Adult subjects only:

- Gilles de la Tourette Syndrome-Quality of Life (GTS-QOL)

The CGI-TS (assessed by the investigator) and Patient Global Impression of Change-Tourette Syndrome (PGIC-TS) scales will be administered at the end of Weeks 4, 8, 12, 16, 20, and 24, and at the follow-up visit (the end of Week 28 or upon early termination) in all subjects.

Plasma Drug Exposure: Blood samples to evaluate plasma concentrations of NBI-98854 and the metabolite NBI-98782 will be collected during the treatment period (end of Weeks 4, 8, 12, 16, 20, and 24), and at the follow-up visit (end of Week 28, or early termination).

Safety: Safety and tolerability will be monitored throughout the study and will include the following assessments:

All subjects:

- Adverse events (AEs)
- Clinical laboratory tests (hematology, clinical chemistry, and urinalysis)
- Serum prolactin
- Hemoglobin A1c
- Vital signs (including orthostatic blood pressures and pulse, respiratory rate, and oral body temperature)
- Physical examinations (including height and weight)
- 12-lead ECGs
- Columbia Suicide Severity Rating Scale (C-SSRS) (pediatric version will be used for pediatric subjects)

- ESRS-A

Pediatric subjects only:

- CDRS-R, CY-BOCS, and Attention-Deficit Hyperactivity Disorder (ADHD) Rating Scale 5: Home Version

Adult subjects only:

- Y-BOCS and SIGH-D-17

5. PLANNED ANALYSES

5.1. Interim Analyses

An interim analysis is not planned for this study.

5.2. Final Analyses

A single, final analysis will be performed after the study database has been locked.

6. STATISTICAL ANALYSES

6.1. General Statistical Considerations

Descriptive statistical methods will be used to summarize the data from this study. The term "descriptive statistics" refers to the number of subjects (n), mean, median, standard deviation (SD), standard error of the mean (SEM), minimum, and maximum for continuous variables; and refers to the number and/or percentage of subjects (or events) for categorical variables.

Unless stated otherwise, each table of descriptive statistics and associated figures will summarize data according to the following treatment groups:

Children:

NBI-98854 10 mg (subjects whose dose is not escalated to 20 mg at Week 4)

NBI-98854 20 mg (subjects whose dose is escalated to 20 mg at Week 4 and maintained at that dose for the duration of the treatment period)

NBI-98854 20/10 mg (subjects whose dose is escalated to 20 mg at Week 4 and subsequently reduced to 10 mg at any time during the treatment period)

Adolescents:

NBI-98854 20 mg (subjects whose dose is not escalated to 40 mg at Week 4)

NBI-98854 40 mg (subjects whose dose is escalated to 40 mg at Week 4 and maintained at that dose for the duration of the treatment period)

NBI-98854 40/20 mg (subjects whose dose is escalated to 40 mg at Week 4 and subsequently reduced to 20 mg at any time during the treatment period)

Adults:

NBI-98854 40 mg (subjects whose dose is not escalated to 80 mg at Week 4)

NBI-98854 80 mg (subjects whose dose is escalated to 80 mg at Week 4 and maintained at that dose for the duration of the treatment period)

NBI-98854 80/40 mg (subjects whose dose is escalated to 80 mg at Week 4 and subsequently reduced to 40 mg at any time during the treatment period)

Note that subjects who discontinue from the study prior to the Week 4 dose escalation visit will be included in the treatment group corresponding to the starting dose for their age group. In addition, it should be noted that while the data at Week 4 will be summarized by treatment group as described above, all subjects will have received only the starting dose for their age group up to that timepoint.

A comprehensive set of data listings including all enrolled subjects will be provided. These listings will include both measured (as reported) and derived values. Observations in data listings will typically be sorted by age group, subject, and timepoint (if applicable).

The derived variable "study day" is used in calculations for data summaries and listings. This variable is calculated as the number of days after a subject's Day -1 visit. Study Day 1, then, is the day after the Day -1 visit.

Summary statistics will be presented using a significant figure rule: the median, minimum, and maximum will have the same number of significant figures as the data; the mean will have one more significant figure than the data being summarized; the SD and SEM will have the same number of significant figures as the mean; and the sample size (N) will be reported as an integer. This rule may be modified if warranted, based on practical considerations.

6.2. Definition of Baseline

The term "baseline" as used in this SAP normally refers to the baseline visit (Day -1), and baseline values will therefore be those reported at Day -1. However, there may be cases where a value is reported after the nominal Day -1 timepoint (but prior to the first dose of study drug) or a Day -1 value is missing but a screening value is available. For purposes of analysis, the value of an analyte or measurement closest to (and prior to) the first dose of study drug will be used as "baseline" in summary tables and figures.

6.3. Pooling of Sites

With the exception of the summary of subject enrollment by site, study sites will be pooled in all tables and graphs, as the majority of sites in this study are expected to enroll a small number of subjects.

6.4. Handling of Early Termination Visit Data

An early termination (ET) visit occurs when a subject discontinues from the study prior to completing the scheduled Week 28 visit. The data collected at ET visits will be included in summary tables and figures in accordance with the ET visit mapping scheme described in this section.

An ET visit will be mapped to Week 4 if it occurs within 7 days prior to and 6 days after the expected study day of the Week 4 visit (but only if the subject has not completed a scheduled Week 4 visit). For study visits after Week 4, an ET visit will be mapped to the next scheduled study visit if it occurs within 14 days prior to and 13 days after the expected study day of the visit (note that, for Week 28, only the lower bound of the study day range is applicable). If an ET visit falls outside the allowable study day range (see table below) for the next scheduled visit that follows a scheduled visit which was completed by the subject, the ET visit will not be mapped. An ET visit also will not be mapped to a visit during the treatment period if the ET visit does not occur within one week of the subject's last dose of study drug (note that dates for both the ET visit and the last dose of study drug must be present in the database for this to be confirmed).

Early termination visit data that are not mapped to a scheduled visit will be displayed in data listings but not included in by-visit summaries.

Table 2 displays the allowable study day range for each scheduled visit for ET visit mapping purposes.

Table 2: Allowable Study Day Range for Early Termination Visit Mapping

Scheduled Visit	Target Study Day	Time Interval (Study Day Range)
Week 4	28	21-34
Week 8	56	42-69
Week 12	84	70-97
Week 16	112	98-125
Week 20	140	126-153
Week 24	168	154-181
Week 28	196	182 +

6.5. Handling of Missing Data

Missing values for outcome measures will not be replaced with imputed values except as noted above for the ET visit data mapped to scheduled visits for data summary purposes.

Missing and incomplete ("partial") dates for AEs and concomitant medications will be imputed only to estimate the time of the event or medication usage in relationship to study treatment periods (eg, pretreatment period vs. treatment period); however, all data listings will display the original dates as reported on the eCRF.

The imputation rules for AE start dates are as follows:

- If the date is completely missing, the date will be imputed as the date of the first dose of study drug;
- If only the day component is missing from the date, the date will be imputed as the date of the first dose of study drug if the date is in the same month and year as the first dose of study drug; otherwise, the missing day component will be imputed as the first day of the month;

- If both the day and month components are missing from the date, the date will be imputed as the date of the first dose of study drug if the date is in the same year as the first dose; otherwise, the missing components will be imputed as 01 January;
- If any of the above imputations result in a start date that is later than an existing complete (not imputed) end date for the event, the start date will be set equal to the end date.

The imputation rules for concomitant medication start dates are as follows:

- If the date is completely missing, the date will be imputed as 01 January in the year of the subject's screening vital signs assessment;
- If only the day component is missing from the date, the date will be imputed as the date of the first dose of study drug if the date is in the same month and year as the first dose of study drug; otherwise, the missing day component will be imputed as the first day of the month;
- If both the day and month components are missing from the date, the date will be imputed as the date of the first dose of study drug if the date is in the same year as the first dose; otherwise, the missing components will be imputed as 01 January;
- If any of the above imputations result in a start date which is later than an existing complete (not imputed) medication stop date, the start date will be set equal to the stop date.

6.6. Coding Dictionaries

Medical history and AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, version 12.0). Prior and concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary.

6.7. Analysis Sets

The safety analysis set will be the single analysis set used for this study. The safety analysis set will include all enrolled subjects who take at least one dose of study drug and have any data collected after the initial dose of study drug. However, if it is unknown whether the subject took at least one dose of study drug but the subject has postbaseline data in the study database, the subject will be included in the safety analysis set.

A summary of the number and percentage of subjects included in (and excluded from, as applicable) the safety analysis set will be provided for each treatment group by age group (ie, a separate summary table will be presented for each age group). The number and percentage of subjects excluded from the safety analysis set by reason for exclusion will also be provided.

Summaries of subject enrollment and disposition, enrollment by study site, and analysis set inclusion/exclusion status will include all enrolled subjects. All other summaries will be based on the safety analysis set.

6.8. Subject Enrollment and Disposition

Subject enrollment and disposition will be summarized for each age group and for the overall study population (ie, with age groups combined).

The summary for each age group will display, by treatment group and overall (ie, "all subjects"), the number and percentage of subjects who enrolled in the study, discontinued from the study prior to or at the Week 4 visit, discontinued from the study early, and completed the study (ie, completed their scheduled Week 28 visit). The summary will also present the number and percentage of subjects who discontinued from the study early according to the reason for discontinuation as per the eCRF.

A separate summary of enrollment and disposition will be presented with age groups combined. This table will not include treatment group but will otherwise provide the same information displayed in the by-age group summary tables.

A summary of enrollment by study site will be presented for each age group. This summary will display the number of subjects enrolled at each site, by treatment group and for all subjects.

An additional table will be presented for each age group that displays the number of subjects in each treatment group (and overall) who completed each study visit. This summary is based on the safety analysis set rather than all enrolled subjects.

6.9. Protocol Deviations

Important protocol deviations (IPDs) are protocol deviations that might significantly affect the completeness, accuracy and/or reliability of the study data or that might significantly affect a subject's rights, safety, or well-being. An assessment of which protocol deviations are considered IPDs will be performed by a committee composed of NBI Clinical Development project team members. Important protocol deviations may include, but are not limited to the following:

- Failure to obtain informed consent from the subject prior to performing any study procedures
- Deviations from key inclusion/exclusion criteria
- Use of prohibited concomitant medications
- Error in drug dispensing which results in a subject not receiving intended treatment
- Significant deviation from protocol-specified dosing regimen

The number and percentage of subjects with IPDs will be summarized for each age group by deviation category, treatment group, and for all subjects.

6.10. Demographics

The following demographic data will be summarized with descriptive statistics for each age group by treatment group and for all subjects:

- Age
- Gender
- Race
- Ethnicity

6.11. Baseline Subject Characteristics

The following baseline subject characteristics will be summarized with descriptive statistics for each age group by treatment group and for all subjects:

- Weight (in units of pounds and kilograms)
- Weight percentile (pediatric subjects only)
- Height
- Body mass index
- Age at TS diagnosis
- CYP2D6 genotype classification
- Baseline YGTSS total tic score (TTS)

6.12. Medical History

Medical history will be summarized for each age group in frequency tables (number and percentage of subjects) by MedDRA System Organ Class (SOC) and Preferred Term (PT) by treatment group and for all subjects.

6.13. Study Drug Dosing

6.13.1. Study Drug Dosing Compliance

Study drug dosing compliance (defined as the subject having taken at least 80% of doses since their previous visit as captured on the eCRF) will be summarized by visit (beginning with Week 4). The number and percentage of subjects who were dose compliant will be summarized for each age group by treatment group and for all subjects.

6.13.2. Dose Escalation at Week 4

The number and percentage of subjects whose dose was increased from the starting dose level to the higher dose level (eg, from 10 mg to 20 mg for children) will be summarized for each age group and for age groups combined. The reason for dose maintenance at Week 4 (adverse event, clinical impression of TS, or "other") will also be summarized (number and percentage of subjects in each category). Note that this summary is not "by treatment group".

6.13.3. Dose Reductions after Week 4

The dose reduction summary will present the number of subjects with a dose reduction at any time after Week 4 during the treatment period for each age group and for age groups combined. The number of subjects with a dose reduction will be displayed by dose reduction reason category (adverse event, clinical impression of TS, or "other").

Note that this summary is not "by treatment group".

6.14. Pharmacokinetic Data

The plasma concentrations of NBI-98854 and its metabolite NBI-98782 will be summarized with descriptive statistics for each age group by visit (Weeks 4, 8, 12, 16, 20, 24, and 28) and the most recent NBI-98854 dose level received by a subject prior to that visit.

Concentrations below the lower limit of quantification (BLQ) will be set equal to zero for all plasma concentration summaries. The lower limits of quantification are as follows: (a) NBI-98854: 1.00 ng/mL and (b) NBI 98782: 0.100 ng/mL.

The following additional descriptive statistics will be included in the plasma concentration summary tables: (a) the number of plasma concentration values greater than or equal to the lower limit of quantification, (b) the geometric mean, and (c) the geometric coefficient of variation (%).

6.15. Pharmacodynamic Assessments

6.15.1. Yale Global Tic Severity Scale (YGTSS)

The following three analysis variables are based on the YGTSS: (a) the TTS, (b) the Impairment score, and (c) the Global Tic Severity score.

The TTS is defined as the sum of the YGTSS motor tic severity score and phonic (vocal) tic severity score. The motor tic severity score is calculated as the sum of the scores for the 5 motor tic items (number, frequency, intensity, complexity, and interference). The score for each item can range from 0 to 5, for a maximum total score of 25. The vocal (phonic) tic severity score is calculated similarly. If any one of the 5 items for the motor or vocal tic severity score is not scored (ie, has a missing value), the associated severity score will be set equal to missing. If any of these items has a missing value at a given subject visit, the TTS value for the subject visit will also be set equal to missing. The TTS value can range from 0 to 50.

The YGTSS Impairment score is captured directly in the eCRF. This score can range in value from 0 to 50.

The YGTSS Global Tic Severity score is the sum of the TTS and the Impairment score. The YGTSS Global Tic Severity score at a given subject visit will be set equal to missing if either of the TTS or Impairment scores are missing. The YGTSS Global Tic Severity score value can range from 0 to 100.

For each of these three variables, descriptive statistics will be presented for the observed values at each visit and for the changes from baseline to each postbaseline visit. These summaries will be presented for each age group by treatment group and for all subjects.

Figures will also be presented for the TTS observed values and changes from baseline (mean values ± SEM) for each age group by treatment group.

6.15.2. Rush Video-Based Tic Rating Scale (RTRS)

The RTRS videos recorded during the study were to be scored by a blinded central rater; however, the scoring was not performed. Therefore, no summaries will be presented for the RTRS.

6.15.3. Premonitory Urge for Tics Scale (PUTS)

The PUTS consists of 9 items, each of which is scored on a 4-point scale (1=not at all true, 2=a little true, 3=pretty much true, 4=very much true). The PUTS total score is calculated as the sum

of the scores for the 9 items. The maximum possible total score is 36. If any one of the 9 items is not scored (ie, has a missing value), the PUTS total score will be set equal to missing.

Descriptive statistics will be presented for the PUTS total score observed values at each visit and for the changes from baseline to each postbaseline visit. These summaries will be presented for each age group by treatment group and for all subjects.

6.15.4. Clinical Global Impression of Tics-Severity (CGI-Tics-Severity)

Each of the CGI-Tics-Severity response categories will be assigned a numerical score as follows:

- Normal, not at all ill = 1
- Borderline ill = 2
- Mildly ill = 3
- Moderately ill = 4
- Markedly ill = 5
- Severely ill = 6
- Among the most extremely ill patient = 7

Descriptive statistics (including both frequency counts [using response categories] and continuous variable statistics [based on numerical scores]) will be presented for each age group by treatment group and for all subjects for the CGI-Tics-Severity data at each visit. Changes from baseline to each postbaseline visit will be summarized also for the numerical scores with continuous variable descriptive statistics.

6.15.5. Clinical Global Impression of Improvement-Tourette Syndrome (CGI-TS)

Each of the CGI-TS response categories will be assigned a numerical score as follows:

- Very much improved = 1
- Much improved = 2
- Minimally improved = 3
- Not changed = 4
- Minimally worse = 5
- Much worse = 6
- Very much worse = 7

Descriptive statistics (including both frequency counts [using response categories] and continuous variable statistics [based on numerical scores]) will be presented for each age group by treatment group and for all subjects for the CGI-TS data at each visit.

6.15.6. Patient Global Impression of Change-Tourette Syndrome (PGIC-TS)

Each of the PGIC-TS response categories will be assigned a numerical score as follows:

- Very much improved = 1
- Much improved = 2
- Minimally improved = 3
- Not changed = 4
- Minimally worse = 5

- Much worse = 6
- Very much worse = 7

Descriptive statistics (including both frequency counts [using response categories] and continuous variable statistics [based on numerical scores]) will be presented for each age group by treatment group and for all subjects for the PGIC-TS data at each visit.

6.15.7. Pediatric Quality of Life Inventory (PedsQL; Pediatric Subjects Only)

Three age-specific versions of the PedsQL were used in this study: one for young children (age 5 through 7), one for older children (age 8 through 12), and one for teens (age 13 through 18). Each version consists of 23 items across 4 domains, with each item scored on a 3-point scale for young children (0=not at all true, 2=sometimes, 4=a lot) and a 5-point scale for older children and teens (0=never, 1=almost never, 2=sometimes, 3=often, 4=almost always). The PedsQL total score is calculated as the sum of the scores for the 23 items. The maximum possible total score is 92. If any one of the 23 items is not scored (ie, has a missing value), the PedsQL total score will be set equal to missing.

In addition to the total score, the scores for each domain (physical functioning, emotional functioning, social functioning, and school functioning) will be calculated in a similar manner as the sum of the scores for the items within each domain.

Descriptive statistics will be presented for the PedsQL total score and each domain score observed values at each visit and for the changes from baseline to each postbaseline visit. These summaries will be presented for each pediatric age group by treatment group and for all subjects.

6.15.8. Gilles de la Tourette Syndrome-Quality of Life Scale (GTS-QOL; Adult Subjects Only)

The GTS-QOL has two parts: (1) a 27-item scale which includes 4 factors (subscales), with each of the 27 items scored on a 5-point scale (0=no problem, 1=slight problem, 2=moderate problem, 3=marked problem, 4=extreme problem) and (2) a visual analog scale (VAS) which ranges in value from 0 to 100. The GTS-QOL total score is calculated as the sum of the scores for the 27 items and is then normalized to value which can range from 0 to 100 by the following formula:

(100 x [(observed score – minimum possible score) / (maximum possible score -minimum possible score)])

If any one of the 27 items is not scored (ie, has a missing value), the total score will be set equal to missing.

Scores will be calculated (and normalized to a 0 to 100 range using the formula above) for each of the 4 GTS-QOL factors in a similar fashion. These factors and the items included in each factor are as follows (item numbers are displayed):

- Psychological (16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27)
- Physical and activities of daily living (1, 2, 3, 4, 5, 6, 26)
- Obsessive-compulsive (7, 8, 9, 10, 15)
- Cognitive (11, 12, 13, 14)

Descriptive statistics will be presented for the GTS-QOL total score, each factor score, and the VAS score observed values at each visit and for the changes from baseline to each postbaseline visit. These summaries will be presented by treatment group and for all subjects.

6.16. Safety Assessments

6.16.1. Adverse Events

6.16.1.1. Treatment-Emergent Adverse Event Frequency Tables

A treatment-emergent adverse event (TEAE) is an adverse event (AE) not present prior to the initiation of study drug dosing, or is an already present event that worsens either in intensity or frequency following the initiation of study drug dosing. The determination of whether an AE is treatment emergent is based on the AE onset date relative to the date of the subject's first dose of study drug. If the AE onset date and date of the first dose of study drug are the same, or if the AE onset date is unknown, it will be assumed that the AE is a TEAE.

TEAEs, categorized by MedDRA (Version 12.0) system organ class (SOC) and preferred term (PT), will be summarized in frequency tables. In these tables, SOCs and PTs within each SOC will be sorted alphabetically. TEAEs categorized by PT only will be presented also. Unless stated otherwise, the frequency tables will include the number of events reported, and the number and percentage of unique subjects experiencing each event one or more times during the study interval summarized in the table. A description of each summary table is provided below. All TEAE summary tables will be presented for each age group separately.

Adverse events with an onset date prior to the date of the first dose of study drug will be presented only in a data listing.

TEAEs Reported through Week 4 Visit

TEAEs with an onset date during the first 4 weeks of the study (through the Week 4 visit) will be summarized separately from TEAEs with an onset date after the Week 4 visit, as all subjects receive the same dose (within an age group) during the first 4 weeks of treatment. These tables will therefore not be "by treatment" and will summarize data for all subjects within each age group.

In addition to the summaries that include all TEAEs, summaries will be presented for TEAEs considered to be possibly or definitely related to study drug ("treatment related") and for TEAEs categorized according to the maximum intensity reported for a given subject. For these additional summaries, TEAEs will be presented by PT only (ie, not by SOC), with PTs sorted according to decreasing frequency of subjects reporting each event.

TEAEs Reported after Week 4 Visit

TEAEs with an onset date after the Week 4 visit will be summarized by treatment group and for all subjects.

Similar tables will be presented including only TEAEs considered to be possibly or definitely related to study drug and categorizing TEAEs according to the maximum intensity reported for a given subject. In these summaries, TEAEs will be presented by PT only, based on the "all subjects" column.

TEAEs Reported during Posttreatment Period

TEAEs with an onset date after the Week 24 visit will be summarized by treatment group and for all subjects.

TEAEs Reported at Any Time During Study

TEAEs reported at any time during the study will be summarized for all subjects (ie, without regard to treatment group).

6.16.1.2. Adverse Event Overall Summaries

Overall summary tables will be presented which summarize the number and percentage of subjects with any TEAE, any treatment-related TEAE (ie, possibly or definitely related per electronic case report form [eCRF]), any severe TEAE, any TEAE leading to study discontinuation, any serious TEAE, and any TEAE resulting in death. An overall summary table will be presented for each of the study intervals described above and will include the same treatment group columns as in the frequency tables.

6.16.1.3. Adverse Events Resulting in a Study Drug Dose Reduction

A summary of TEAEs resulting in a study drug dose reduction in subjects with a dose escalation at Week 4 will be presented. The summary table for each age group will display the PTs for the TEAEs resulting in a dose reduction, with the PTs sorted in order of decreasing frequency (based on number of subjects). The first line of the table will display the total number of subjects with a dose reduction.

A listing of TEAEs resulting in a study drug dose reduction will be included in the study report (this listing will include data for all three age groups and will be sorted by age group). The listing will include age group, subject, study day of the dose reduction, and both the PT and reported term for all TEAEs that resulted in the dose reduction

6.16.1.4. Adverse Events Resulting in Premature Study Discontinuation

A summary table of TEAEs resulting in premature study discontinuation will be presented for each age group for the following study periods:

- Through Week 4 visit
- After Week 4 visit

These summary tables will include both the SOC and PT, with data summarized by treatment group (for TEAEs occurring after Week 4) and for all subjects. Note that the onset date of the TEAE(s) resulting in study discontinuation (not the date of discontinuation) will be the basis for determining the study period assignment.

A listing of TEAEs resulting in premature study discontinuation will be presented in the study report, sorted by age group and subject. The listing will include age group, subject, treatment group, study period when the TEAE which resulted in study discontinuation occurred, study day of the TEAE onset, and both the PT and reported (verbatim) term for all TEAEs that resulted in the premature study discontinuation (note that this is determined from the AE eCRF “action taken” field).

6.16.1.5. Deaths and Other Serious Adverse Events

The frequency of SAEs will be summarized in tables using the approach described above for TEAEs resulting in premature study discontinuation. The table formats (which include both the SOC and PT) for the SAE tables will match those used for the TEAE premature study discontinuation tables. Deaths will be presented in a listing only.

Listings of SAEs and deaths will be presented in the study report, with each listing sorted by age group and subject. These listings will include age group, subject, treatment group, study period when the death or SAE occurred, study day of the death or SAE, and all other AE-specific information reported on the AE eCRF.

6.16.2. Clinical Laboratory Data

The hematology, clinical chemistry, hemoglobin A1c, and serum prolactin data at each visit will be summarized for each age group with descriptive statistics by treatment group and for all subjects. Both observed values and changes from baseline will be summarized.

The prolactin data will be summarized for each gender separately in addition to the summary described above.

Shift tables for each age group will be presented for selected clinical laboratory variables based on the reference ("normal") range-based categories of "Low," "Normal," or "High." A clinical laboratory variable value will be assigned to one of these three categories according to the reference ranges provided by the central clinical laboratory.

Each shift table will have three rows and three columns, with rows reflecting the reference range category at baseline, and columns reflecting the reference range category at the subject's final study visit. Subjects with missing data for a clinical laboratory variable at either timepoint will not be included in tables for that variable. The shift tables will be presented for each treatment group and for all subjects.

Shift tables will be displayed for the following clinical laboratory variables: aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), total bilirubin, creatine kinase, creatinine, BUN, prolactin, hemoglobin A1c, white blood cell count, absolute neutrophil count, hemoglobin, and platelet count.

Summaries of sponsor-defined potentially clinically significant (PCS) values will be presented by age group for the following clinical laboratory variables: ALT, AST, creatinine kinase, GGT, total bilirubin, white blood cell count, neutrophil count, creatinine, and BUN. The number and percentage of subjects with one or more PCS values at any time after baseline will be summarized by treatment group and for all subjects. Note that data collected at both scheduled and unscheduled study visits will be included in this assessment. The criteria for identifying PCS values are provided in Table 3.

Table 3: Potentially Clinically Significant Criteria for Selected Clinical Laboratory Variables

Variable	PCS Threshold
ALT	>3 x ULN (upper limit of normal)

Variable	PCS Threshold
AST	>3 x ULN
Creatine kinase	>5 x ULN
GGT	>3 x ULN
Total bilirubin	>1.5 x ULN
White blood cell count	≤2.8 x 1000/µL
Absolute Neutrophil count	<1.5 x 1000/µL
Creatinine	>1.5 x Day -1 value or > 1.5 x ULN
BUN	>30 mg/dL (> 10.71 mmol/L)

A listing of all subjects with any PCS value will be presented in the study report. This listing will include the values of the clinical laboratory variables in Table 3 at all study visits for each subject with one or more PCS values. The listing will be sorted by age group and subject, and will include age group, subject, treatment group, visit, study day of visit, and all laboratory results for the analytes with a PCS value. Values that meet the PCS criteria will be flagged with an asterisk in the listing.

Scatter plots for prolactin will be created for each age group which display the subjects' final study visit values vs. baseline values. Each plot will include a 45-degree ("y=x") reference line. A separate plot will be generated for each treatment group and for all subjects.

The clinical laboratory data listings will include associated normal/reference ranges (if provided). In addition, values outside the normal range will be flagged as "L" if below the lower limit of normal and as "H" if above the upper limit of normal. There will also be a flag for clinical significance based on the investigator's assessment of out-of-range values. The urinalysis data will be presented in data listings only.

Repeat clinical laboratory samples may be collected at any time during this study due to either missing or abnormal results. The general rule of thumb for summarizing these data is to include the original sample results in summary tables and graphs (subject to the definition of "baseline" as per Section 6.2. All sample results (original and repeat) will be included in data listings.

6.16.3. Physical Examination and Weight

Clinically significant physical examination findings will be presented in a data listing in the study report. The listing will include age group, subject, treatment group, visit at which the finding was reported, study day of the visit, and the clinically significant finding.

Body weight, which is measured during the physical examination, will be summarized in units of kilograms with descriptive statistics (both observed values and changes from baseline) for each age group at each visit by treatment group and for all subjects.

6.16.4. Vital Signs

The vital signs data, including orthostatic blood pressures and heart rate (calculated as standing value minus supine value), will be summarized with descriptive statistics for each age group at each visit by treatment group and for all subjects. Both observed values and changes from baseline will be summarized.

Sponsor-defined PCS values for systolic blood pressure, diastolic blood pressure, and heart rate will be summarized for each age group by treatment group and for all subjects. The number and percentage of subjects with one or more PCS values at any time after baseline will be summarized. Note that data collected at both scheduled and unscheduled study visits will be included in this assessment. The criteria for identifying PCS values are provided in Table 4.

Table 4: Potentially Clinically Significant Criteria for Selected Vital Signs

Variable Name	PCS – Low if:		PCS – High if:	
	Observed Value is: **AND**	**Decrease from Baseline is:**	**Observed Value is:** **AND**	**Increase from Baseline is:**
Systolic Blood Pressure	<90 mmHg	≥20 mmHg	>180 mmHg	≥20 mmHg
Diastolic Blood Pressure	<50 mmHg	≥10 mmHg	>105 mmHg	≥15 mmHg
Heart Rate	<50 bpm	≥15 bpm	>120 bpm	≥15 bpm

Note that both supine and standing values of blood pressures and heart rate will be included in the identification and summary of PCS values.

A listing of all subjects with a PCS value will be presented in the study report. This listing will include vital signs data at all study visits for each subject with one or more PCS values. The listing will be sorted by age group, subject, and visit, and will include age group, subject, treatment group, visit, study day of visit, systolic blood pressure (supine and standing), diastolic blood pressure (supine and standing), and heart rate (supine and standing). Values that meet the PCS criteria will be flagged with an asterisk in the listing.

6.16.5. Electrocardiogram

The triplicate values of the quantitative ECG variables (heart rate, PR interval, QRS duration, QT interval, and Fridericia's correction of QT interval [QTcF]) measured at each visit will be averaged for the purpose of analysis. For the overall assessment categorical variable (the investigator's assessment of the ECG as Normal, Abnormal not Clinically Significant, or Abnormal Clinically Significant), which is also reported in triplicate, the value that represents the greatest degree of abnormality will be used in all summary tables.

The ECG variables will be summarized with descriptive statistics (frequency tables for the overall assessment categorical variable) for each age group at each visit by treatment group and for all subjects. Both observed values and changes from baseline will be summarized (for the overall categorical assessment, only observed values will be summarized).

Categorical summaries will be presented for the QT and QTcF interval data. For these summaries, a subject's highest reported postbaseline value (including assessments at both scheduled and unscheduled study visits) will be used to determine in which category(s) the subject will be counted.

Two categorical summaries will be presented by age group for the QT and QTcF intervals (each interval will be summarized separately). For the first summary, the number and percentage of subjects in each treatment group (and for all subjects) whose highest reported postbaseline QT/QTcF value meets the following thresholds will be summarized:

- Greater than 450 msec
- Greater than 480 msec
- Greater than 500 msec

The second categorical summary will display the number and percentage of subjects in each treatment group (and for all subjects) whose largest QT/QTcF increase from their baseline value meets the following thresholds:

- Greater than 30 msec
- Greater than 60 msec

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

The C-SSRS data will be summarized for each age group as follows:

- Screening/baseline lifetime assessment by treatment group and for all subjects
- Screening/baseline "past 1 year" assessment by treatment group and for all subjects
- All postbaseline assessments (after Day -1 through final visit) by treatment group and for all subjects

Note that the screening/baseline assessments are completed at the screening visit for subjects who have a screening visit and at the Day -1 visit for subjects who do not have a screening visit.

Each summary will display the number and percentage of subjects who report "Yes" to specific C-SSRS items or categories of items (a category is assigned a "Yes" value if a "Yes" is reported for any item in the category). These C-SSRS items and categories are as follows:

- Suicidal Ideation Items
  - (1) Wish to be dead
  - (2) Non-specific active suicidal thoughts
  - (3) Active suicidal ideation with any methods (not plan) without intent to act
  - (4) Active suicidal ideation with some intent to act, without specific plan
  - (5) Active suicidal ideation with specific plan and intent
- Suicidal Ideation Category: Any of items (1) through (5)
- Suicidal Behavior Items
  - (6) Preparatory acts or behavior
  - (7) Aborted attempt
  - (8) Interrupted attempt
  - (9) Non-fatal suicide attempt

(10) Completed suicide

- Suicidal Behavior Category: Any of items (6) through (10)
- Suicidal Ideation or Behavior Category: Any of items (1) through (10)

For the postbaseline period, the C-SSRS responses for all assessments for a subject (including both scheduled and unscheduled visits) will be evaluated, and a "Yes" response for any assessment will be considered as a "Yes" for the subject.

In addition to the summaries described above, shift tables comparing postbaseline suicidal ideation scores to the "past 1 year" assessment scores will be presented. The shift table scores are defined as the following:

0=No suicidal ideation
1=Wish to be dead
2=Non-specific active suicidal thoughts
3=Active suicidal ideation with any methods (not plan) without intent to act
4=Active suicidal ideation with some intent to act, without specific plan
5=Active suicidal ideation with specific plan and intent

The shift tables will display, for each age group, the number and percentage of subjects within each cell of a 6 x 6 table for each treatment group and for all subjects, with the rows representing the "past 1 year" score and the columns representing the maximum score recorded during the postbaseline period (across all visits, including unscheduled visits). Subjects missing either a "past 1 year" score or all postbaseline scores will not be included in the shift tables.

A summary listing of individual subject data will be presented for the C-SSRS data and will be provided in the study report. This summary will list subjects with a positive response for suicidal ideation, suicidal behavior, or self-injurious behavior without suicidal intent at any time after Day -1. The listing will be in the form of a table, with each row representing a subject visit (including treatment group and study day for that visit), and a column for each suicidal ideation item (1 – 5), each suicidal behavior item (6 – 10), and a final column for self-injurious behavior without suicidal intent. The cells of the table will be populated with "Y" or "N," representing either a positive or negative response, respectively, for each item in the table (ie, for each column of the table). A separate table will be presented for each age group.

6.16.7. Extrapyramidal Symptom Rating Scale-Abbreviated (ESRS-A)

The ESRS-A assesses 4 types of movement disorders: parkinsonism, dystonia, akathisia, and tardive dyskinesia. The ESRS-A consists of four subscales, one for each type of movement disorder. The ESRS-A contains 10 items to evaluate parkinsonism, 6 items to evaluate dystonia, 6 items to evaluate dyskinesia, and 2 items to evaluate akathisia. Each item score can range from 0 to 5, for a maximum possible parkinsonism score of 50, maximum possible dystonia score of 30, maximum possible dyskinesia score of 30, and maximum possible akathisia score of 10. A Clinical Global Impression of Severity (CGI-S) is also completed for each type of movement disorder, and is also is scored on a 0 to 5 scale.

The subscale scores for each type of movement disorder (parkinsonism, akathisia, dystonia, and tardive dyskinesia) will be calculated as the sum of the scores of the individual items comprising each subscale. The overall total score will be calculated as the sum of each of the subscale

scores. If any one of the items is not scored (ie, has a missing value), the associated subscale score and total score will be set equal to missing. The CGI-S scores will be summarized separately from the subscale scores.

For each of the subscale scores for parkinsonism, akathisia, dystonia, and tardive dyskinesia, the overall total score, and the CGI-S score for each subscale, descriptive statistics will be presented for the observed values at each visit and for the changes from baseline to each postbaseline visit. These summaries will be presented for each age group by treatment group and for all subjects.

6.16.8. Children's Depression Rating Scale, Revised (CDRS-R)

The CDRS-R is a 17-item, semi-structured interview to determine the severity of depression in children. The CDRS-R total score is calculated as the sum of the 17 items making up the CDRS-R. Each item score ranges from 1 to 7 except for items 4, 5, and 16, which range from 1 to 5. The maximum possible total score is 113. If any one of the 17 items is not scored (ie, has a missing value), the total score will be set equal to missing.

The total score observed values at each visit and changes from baseline to each postbaseline visit will be summarized for the children and adolescent age groups with descriptive statistics by treatment group and for all subjects.

6.16.9. Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)

The CY BOCS is a semi-structured interview designed to rate the severity of obsessive and compulsive symptoms in children.

The CY-BOCS obsession subtotal score is calculated as the sum of the scores for items 1 through 5 of the CY-BOCS scale (excluding item 1b), and the CY-BOCS compulsion subtotal score is calculated as the sum of the scores for items 6 through 10 of the CY-BOCS scale (excluding item 6b). The CY-BOCS total score is the sum of the obsession and compulsion subtotal scores. Each item score ranges from 0 to 4, with a maximum possible obsession subtotal score of 20, a maximum possible compulsion subtotal score of 20, and a maximum possible total score of 40. If any one of these 10 items is not scored (ie, has a missing value), the associated subtotal score and total score will be set equal to missing.

The observed values of the total score and subtotal scores for obsession and compulsion at each visit and changes from baseline to each postbaseline visit will be summarized for the children and adolescent age groups with descriptive statistics by treatment group and for all subjects.

6.16.10. Attention-Deficit Hyperactivity Disorder (ADHD) Rating Scale 5: Home Version

The ADHD Rating Scale 5: Home Version will be used to determine the frequency and severity of ADHD symptoms and impairments over the past month in children. The 30-item scale consists of 2 subscales: Inattention (the sum of the scores for items 1 through 9) and Hyperactivity-Impulsivity (the sum of the scores for items 16 through 24), as well as a Total Scale raw score defined as the sum of the Inattention and Hyperactivity-Impulsivity subscale scores. Each item score ranges from 0 to 3, for a maximum possible Inattention score of 27, a maximum possible Hyperactivity-Impulsivity score of 27, and a maximum possible Total Scale raw score of 54. If any one of the 18 items is not scored (ie, has a missing value), the affected subscale score(s) and Total Scale raw score will be set equal to missing.

The ADHD Rating Scale 5: Home version also includes 6 domains of impairment associated with each of the 2 subscales described above (items 10 through 15 for Inattention and items 25 through 30 for Hyperactivity-Impulsivity). These domains will be included in data listings but will not be summarized in tables.

The observed values of the Total Scale raw score and the Inattention and Hyperactivity-Impulsivity subscale scores at each visit and changes from baseline to each postbaseline visit will be summarized for children and adolescent age groups with descriptive statistics by treatment group and for all subjects.

6.16.11. Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

The Y-BOCS is a semi-structured interview designed to rate the severity of obsessive and compulsive symptoms in adults.

The Y-BOCS obsession subtotal score is calculated as the sum of the scores for items 1 through 5 of the Y-BOCS scale (excluding item 1b), and the Y-BOCS compulsion subtotal score is calculated as the sum of the scores for items 6 through 10 of the Y-BOCS scale (excluding item 6b). The Y-BOCS total score is the sum of the obsession and compulsion subtotal scores. Each item score ranges from 0 to 4, with a maximum possible obsession subtotal score of 20, a maximum possible compulsion subtotal score of 20, and a maximum possible total score of 40. If any one of these 10 items is not scored (ie, has a missing value), the associated subtotal score and total score will be set equal to missing.

The observed values of the total score and subtotal scores for obsession and compulsion at each visit and changes from baseline to each postbaseline visit will summarized with descriptive statistics for the adult age group by treatment group and for all subjects.

6.16.12. Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D-17)

The SIGH-D-17 is a 17-item, semi-structured questionnaire for rating depression in adults. The SIGH-D-17 total score is calculated as the sum of the 17 items making up the SIGH-D-17. Each item is scored on a 3, 4, or 5-point scale. The maximum possible total score is 53. If any one of the 17 items is not scored (ie, has a missing value), the total score will be set equal to missing. Note that a score of 3 for Item 8 (loss of weight) represents “not assessed”, and should be ignored in calculating the total score.

The observed values of the total score at each visit and changes from baseline to each postbaseline visit will summarized with descriptive statistics for the adult age group by treatment group and for all subjects

6.16.13. Prior and Concomitant Medications

The number and percentage of subjects using prior medications (taken within the 30 days prior to Day -1 [and including Day -1]) and concomitant medications (taken during the study after Day -1) classified by WHO Drug Anatomical Therapeutic Chemical Classification (ATC) Level 3 category (or Level 2 if there is not an applicable Level 3 category) and preferred name will be summarized for each age group by treatment group and for all subjects for each study period as described in the next paragraph. A subject may take the same medication more than once or

multiple medications for a subject may be classified under the same ATC level or preferred name. A subject is counted only once for each level of medication classification within a summary.

Medications will be assigned to one or both of two study periods (pretreatment period vs. postbaseline period) based on the medication start and stop dates relative to the first dose of study drug. For example, medications that were started and stopped prior to the date of the first dose of study drug will be assigned to the pretreatment period only, while medications started prior to the first dose of study drug and either stopped during the postbaseline period or indicated as "ongoing" will be assigned to both the pretreatment period and the postbaseline period.

6.17. Additional Data Presentations

6.17.1. Inclusion and Exclusion Criteria Deviations

Inclusion and exclusion criteria deviations will be presented in a data listing by age group and subject.

6.17.2. Serology

Serology data (ie, hepatitis B surface antigen [HBsAg], and hepatitis C virus antibody [HCV-Ab]) will be presented in a data listing by age group and subject.

6.17.3. Pregnancy Tests

Pregnancy test results will be presented in a data listing by age group and subject.

6.17.4. Urine Drug Screen and Alcohol Breathalyzer Test

Urine drug screen and alcohol breathalyzer test results will be presented in a data listing by age group and subject.

7. DEVIATIONS FROM PROTOCOL PLANNED ANALYSES

The analyses described in this SAP are consistent with the planned analyses described in the study protocol except for the following:

- Study drug dosing compliance will be "by visit" only and not cumulative (Section 6.13.1)
- RTRS scores will not be summarized (Section 6.15.2)

8. PERFORMANCE QUALIFICATION OF SAS® PROGRAMS

The data from this study will be summarized using SAS® 9.3 (or a later release if available). All SAS® programs used in the production of tables, figures, and listings described in this SAP will undergo performance qualification (verification that the program produces the intended output) in accordance with department standard operating procedures. The performance qualification may include independent programming and/or peer review of the SAS® log files. In addition, tables, figures, and listings will be independently reviewed for completeness and accuracy.

9. REFERENCES

None.