1.0 TITLE PAGE

1936-201-008

A Phase 2 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Safety and Efficacy of BOTOX® (Botulinum Toxin Type A) Purified Neurotoxin Complex for the Treatment of Platysma Prominence

STATISTICAL ANALYSIS PLAN

Version 1.0: 10 JULY 2019
Amendment 1: 22 MAY 2020

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3.0 LIST OF ABBREVIATIONS

AE	adverse event
[redacted]	[redacted]
ANCOVA	analysis of covariance
C-APPS	Clinician Allergan Platysma Prominence Scale
CMH	Cochran-Mantel-Haenszel
EDC	electronic data capture
IDR	Independent Drug Reconstitutor
MCP	Multiple Comparisons Procedure
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat
P-APPS	Participant Allergan Platysma Prominence Scale
PDSOT	possible distant spread of toxin
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
PRO	patient-reported outcome
PT	preferred term
SAE	serious adverse event
SAP	statistical analysis plan
SOC	system organ class
TEAE	treatment-emergent adverse event
WOCBP	woman of childbearing potential

4.0 INTRODUCTION

This statistical analysis plan (SAP) provides a more technical and detailed elaboration of the statistical analyses of the efficacy and safety data as outlined and/or specified in the protocol of Study 1936-201-008 (Amendment 1 dated 12 August 2019). Specifications of tables, figures, and data listings will be provided in a separate document.

Analyses for patient-reported outcomes (PROs) will be specified in a separate document, and the results will be summarized in a separate report. However, analyses for the Participant Allergan Platysma Prominence Scale (P-APPS) will be described in this document.

Study 1936-201-008 is a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study. [redacted] Platysma prominence will be assessed at maximum contraction by the investigator using the C-APPS and by the participant using the P-APPS.

The length of this study will be approximately 4 months for each participant. Signed informed consent from the participant will be obtained at Screening (Day -14 to Day -7) before any study-related procedures. After verification that the participant meets all inclusion and exclusion criteria, and completion of all baseline study procedures, the participant will be randomized in a 1:1:1 ratio to receive BOTOX® high dose, BOTOX low dose or placebo at Visit 2/Day 1. [redacted] After randomization on Day 1, participants will return to the research facility at Days 7, 14, 30, 60, and 90 (Visits 3 to 7, respectively) for protocol-defined efficacy and safety assessments. Study exit protocol-defined assessments will occur at Day 120 (Visit 8) or at early termination.

The schedule of activities is presented in Table 4-1 (footnotes refer to sections within the protocol).

Table 4-1 Schedule of Activities

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visits 7	Visit 8
Study Procedures	**Screening Day -14 to Day -7**	**Baseline/ Randomization/ Treatment Day 1[a]**	**Day 7**	**Day 14**	**Day 30**	**Day 60**	**Day 90**	**Study Exit[b] Day 120**
Visit Windows	**-**	**-**	**± 3 Days**	**± 3 Days**	**± 3 Days**	**± 7 Days**	**± 7 Days**	**± 7 Days**
Informed Consent, Privacy Authorization	X							
Inclusion/Exclusion Criteria	X	X						
Demographics	X							
Medical/Surgical History	X							
[redacted]	[redacted]							
Weight	X	X	X	X	X	X	X	X
Fitzpatrick Skin Phototype[d]	X							
Abbreviated Physical Examination[e]	X							
Vital Signs[f]	X	X	X	X	X	X	X	X
Urine Pregnancy Test (WOCBP only)[g]	X	X						X
[redacted]	[redacted]	[redacted]						
Standardized Photography	X	X	X	X	X	X	X	X
[redacted]	[redacted]	[redacted]		[redacted]				
Self Assessment by Participants:								
Participant Allergan Platysma Prominence Scale (P-APPS)[i]		X	X	X	X	X	X	X
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]						
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visits 7	Visit 8
Study Procedures	**Screening Day -14 to Day -7**	**Baseline/ Randomization/ Treatment Day 1[a]**	**Day 7**	**Day 14**	**Day 30**	**Day 60**	**Day 90**	**Study Exit[b] Day 120**
Visit Windows	-	-	**± 3 Days**	**± 3 Days**	**± 3 Days**	**± 7 Days**	**± 7 Days**	**± 7 Days**
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Clinician Assessment:								
Clinician Allergan Platysma Prominence Scale (C-APPS)	X	X	X	X	X	X	X	X
Randomization		X						
Study Intervention Administration[j]		X						
Concomitant Medications/Procedures	X	X	X	X	X	X	X	X
Adverse Events[k]	X	X	X	X	X	X	X	X

a All baseline (Day 1) study procedures, including patient-reported outcome questionnaires, must be completed before randomization and study intervention.

b Or early discontinuation from the study. All exit assessments should be completed as soon as possible after a decision to discontinue a participant from the study.

c [redacted]

d Fitzpatrick Skin Phototype is provided in Section 10.11 of the study protocol.

e An abbreviated physical examination will be completed at the screening visit and will include the investigator assessment of general appearance, head, ears, eyes, nose, throat, and neck.

f Vital Signs (blood pressure, respiratory rate, pulse rate) will be taken while the participant is sitting for at least 5 minutes.

g Woman of childbearing potential (WOCBP) must have a negative urine test result before receiving study intervention. A urine pregnancy test may also be performed at any other visit, at the investigator's discretion.

h [redacted]

i [redacted]

j Prepared by an Independent Drug Reconstitutor (IDR) and injected by the investigator. **NOTE**: **The IDR must not perform any other study-related procedures.**

k On Day 1, AEs will be collected prior to and after treatment. Participants will be observed at least 30 minutes after study intervention administration for AEs. In the case of an AESI, see Section 8.3.6 of the study protocol.

5.0 OBJECTIVE

The objective of this study is to evaluate the safety and efficacy of a high and low dose of BOTOX versus placebo in the treatment of participants with moderate to severe platysma prominence. See Section 3 of the protocol for additional details.

6.0 PARTICIPANT POPULATIONS

6.1 MODIFIED INTENT-TO-TREAT POPULATION

The modified intent-to-treat (mITT) population will consist of all randomized participants who had at least 1 post-baseline assessment of the primary efficacy parameter, the C-APPS, as described in the protocol.

6.2 SAFETY POPULATION

The safety population will consist of all participants who were administered study intervention.

7.0 PARTICIPANT DISPOSITION

The number of participants in the 2 study populations (safety and mITT) will be summarized by study intervention and overall.

The number of participants screened will be summarized overall. The number and percentage of participants who were randomized, who were treated, who completed the study or who prematurely discontinued will be presented for each study intervention group and pooled across study intervention groups for all screened participants. The reasons for discontinuation will also be summarized (number and percentage).

8.0 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

Demographic parameters (age; [redacted] race; ethnicity; sex)~~,~~ and baseline characteristics (weight; height; [redacted] C-APPS grade; P-APPS grade; Fitzpatrick Skin Phototype) will be summarized descriptively by study intervention group for the mITT population. Continuous variables will be summarized by number of participants, mean, standard deviation (SD), median, minimum, and maximum values. Categorical variables will be summarized by number and percentage of participants.

Participants' medical and surgical histories will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 23.0 or newer. The number and percentage of participants with medical and surgical histories ongoing at screening will be

summarized by system organ class (SOC) and preferred term (PT) in each study intervention group and overall for the mITT population. In addition, any concomitant procedures, defined as any procedure performed on or after the date of the first dose of study intervention, will be summarized by SOC and PT in each study intervention group for the mITT population.

Prior medication is defined as any medication taken before the date of the first dose of study intervention. Concomitant medication is defined as any medication taken on or after the date of the first dose of study intervention. The use of prior and concomitant medications will be summarized by drug class and drug name in each study intervention group for the mITT population.

9.0 EXTENT OF EXPOSURE AND TREATMENT COMPLIANCE

Participants will receive study intervention only on Day 1. The number of participants treated will be presented by the study intervention group:

- BOTOX high dose
- BOTOX low dose
- Placebo

If a subject does not receive the full dose, this will be indicated; significant deviations to dosing will be reported.

10.0 PROTOCOL DEVIATIONS

The number and type of significant protocol deviations will be summarized in total and by study intervention group for all randomized participants.

A listing of significant protocol deviations will be provided.

11.0 EFFICACY ANALYSES

The efficacy analyses will be based on the mITT population. Observed data will be used for all analyses. Baseline for efficacy is defined as the last non-missing efficacy assessment before study intervention.

The following set of hypotheses will be used to compare the BOTOX groups with placebo for the primary endpoint analysis:

- Null hypothesis: BOTOX and placebo are equally effective in the probability of achieving ≥ 1-grade improvement in the C-APPS score [redacted] from baseline at Day 14.

- Alternative hypothesis: BOTOX and placebo are not equally effective in the probability of achieving ≥ 1-grade improvement in the C-APPS score [redacted] from baseline at Day 14.

The following set of hypotheses will be used to compare the BOTOX groups with placebo for the secondary endpoint analysis:

- Null hypothesis: BOTOX and placebo are equally effective in the probability of achieving ≥ 1-grade improvement in the P-APPS score [redacted] from baseline at Day 14.
- Alternative hypothesis: BOTOX and placebo are not equally effective in the probability of achieving ≥ 1-grade improvement in the P-APPS score [redacted] from baseline at Day 14.

For the primary endpoint analysis, the Cochran-Mantel Haenszel (CMH) test will be used to evaluate the equality of responder proportions of C-APPS between study intervention groups. [redacted] The BOTOX high dose group will be compared to the placebo group, and the BOTOX low dose group will be compared to the placebo group using a gate-keeping strategy (Dmitrienko 2005). If the comparison of the BOTOX high dose group versus the placebo group yields a p-value at the 0.05 significance level, the BOTOX low dose group will then be compared with the placebo group at the same 0.05 significance level. Otherwise, the BOTOX low dose group will not be considered statistically significantly superior to the placebo group, regardless of its p-value. (see Section 11.3.)

Similarly, for the secondary endpoint analysis, the statistical comparisons will be conducted for the P-APPS.

All statistical tests will be 2-sided hypothesis tests performed at the 0.05 level of significance for main effects. Wald confidence intervals for proportions of responders and difference in the proportion of responders will also be presented. All confidence intervals will be 2-sided 95% confidence intervals.

Continuous descriptive statistics include the following: the numbers of participants with non-missing values at both baseline and the specified post-baseline analysis visit, mean, SD, median, minimum, and maximum.

Categorical variables will be summarized by number and percentage of participants.

Efficacy analyses will be performed for all visits. The primary analysis timepoint is Day 14.

11.1 PRIMARY EFFICACY ENDPOINTS

The primary efficacy endpoint will be achievement of a ≥ 1-grade C-APPS improvement from baseline [redacted] on Day 14. [redacted]

The evaluation of the equality of the proportions of responders will be based on the CMH test [redacted]

11.2 SECONDARY EFFICACY ENDPOINTS

The secondary efficacy endpoint will be achievement of ≥ 1-grade P-APPS improvement from baseline [redacted] on Day 14, as rated at maximum contraction by the participant using the P-APPS.

11.3 MULTIPLE COMPARISONS PROCEDURE FOR PRIMARY AND SECONDARY ENDPOINTS

The overall familywise error rate (FWER) will be controlled at $\alpha = 0.05$ for the set of primary and secondary endpoint comparisons between each of the BOTOX groups versus placebo. The overall serial gatekeeping multiple comparisons procedure (MCP) is defined as follows:

Table 11-1 Multiple Comparisons Procedure

MCP Step[a]	Endpoint	MCP Criteria
1	C-APPS responder (BOTOX high dose vs placebo)	Nominal p-value ≤ α
2	P-APPS responder (BOTOX high dose vs placebo)	Nominal p-value ≤ α
3	C-APPS responder (BOTOX low dose vs placebo)	Nominal p-value ≤ α
4	P-APPS responder (BOTOX low dose vs placebo)	Nominal p-value ≤ α

[a] Serial gatekeeping MCP only proceeds to next step if all endpoints are statistically significant after application of MCP criteria in previous and current MCP steps for a BOTOX group.

11.4 ADDITIONAL EFFICACY ENDPOINTS

[redacted]

- [redacted]

Categorical and continuous descriptive statistics, including change from baseline, will be presented for all visits for C-APPS and P-APPS scores. Continuous descriptive statistics will be provided for all visits [redacted]

[redacted] Methods for analyzing additional PRO endpoints aside from the P-APPS will be described and summarized in a separate analysis plan and report.

12.0 SAFETY ANALYSES

The safety analyses will be performed using the safety population. The safety parameters will include adverse events (AEs) and vital signs. For vital signs, the last non-missing safety assessment before the first dose of study intervention will be used as the baseline.

Continuous variables will be summarized by number of participants, mean, SD, median, minimum, and maximum values. Categorical variables will be summarized by number and percentage of participants.

12.1 ADVERSE EVENTS

AEs will be coded by SOC and PT using MedDRA version 23.0 (or newer).

An AE will be considered a treatment-emergent adverse event (TEAE) if the AE began or worsened (increased in severity or became serious) on or after the date (and time, if known) of the first dose of study intervention. Per case report form instructions, a new AE record will be created with a new AE onset date for any AE that worsens. Therefore, TEAEs can simply be identified as those AEs with recorded onset date (and time, if known) on or after the date (and time) of intervention injection.

Procedure-related AEs due to injection are identified as, but not limited to, the following: localized pain, inflammation, paresthesia, hypoesthesia, tenderness, swelling/edema, erythema, localized infection, bleeding, and/or bruising. In addition, needle-related pain and/or anxiety have resulted in vasovagal responses, including transient symptomatic hypotension and syncope.

If more than 1 AE is coded to the same PT for the same participant, the participant will be counted only once for that PT using the greatest severity and strictest causality for the summarization by severity and causal relationship. An AE will be considered a serious TEAE if it is a TEAE that additionally meets any serious AE criteria.

The total number and percentage of participants reporting AEs, TEAEs, treatment-related TEAEs (ie, study drug-related TEAEs, study procedure-related TEAEs), serious TEAEs, treatment-related serious TEAEs, deaths, AESIs, PDSOTs, and discontinuations due to TEAEs will be summarized for each study intervention group.

The number and percentage of participants reporting TEAEs will be summarized in descending order by SOC and PT for each study intervention group. In addition, TEAEs will also be summarized in descending order by PT for each study intervention group.

The number and percentage of participants reporting treatment-related TEAEs will be summarized in descending order by PT for each study intervention group.

In addition, severity of TEAE will be summarized by PT for each study intervention group.

For the safety population, separate listings will be presented for all AEs, participants who died, serious AEs (SAEs), AEs leading to study discontinuation, and pretreatment AEs (ie, AEs that occur after signing of the informed consent and prior to first dose of study medication).

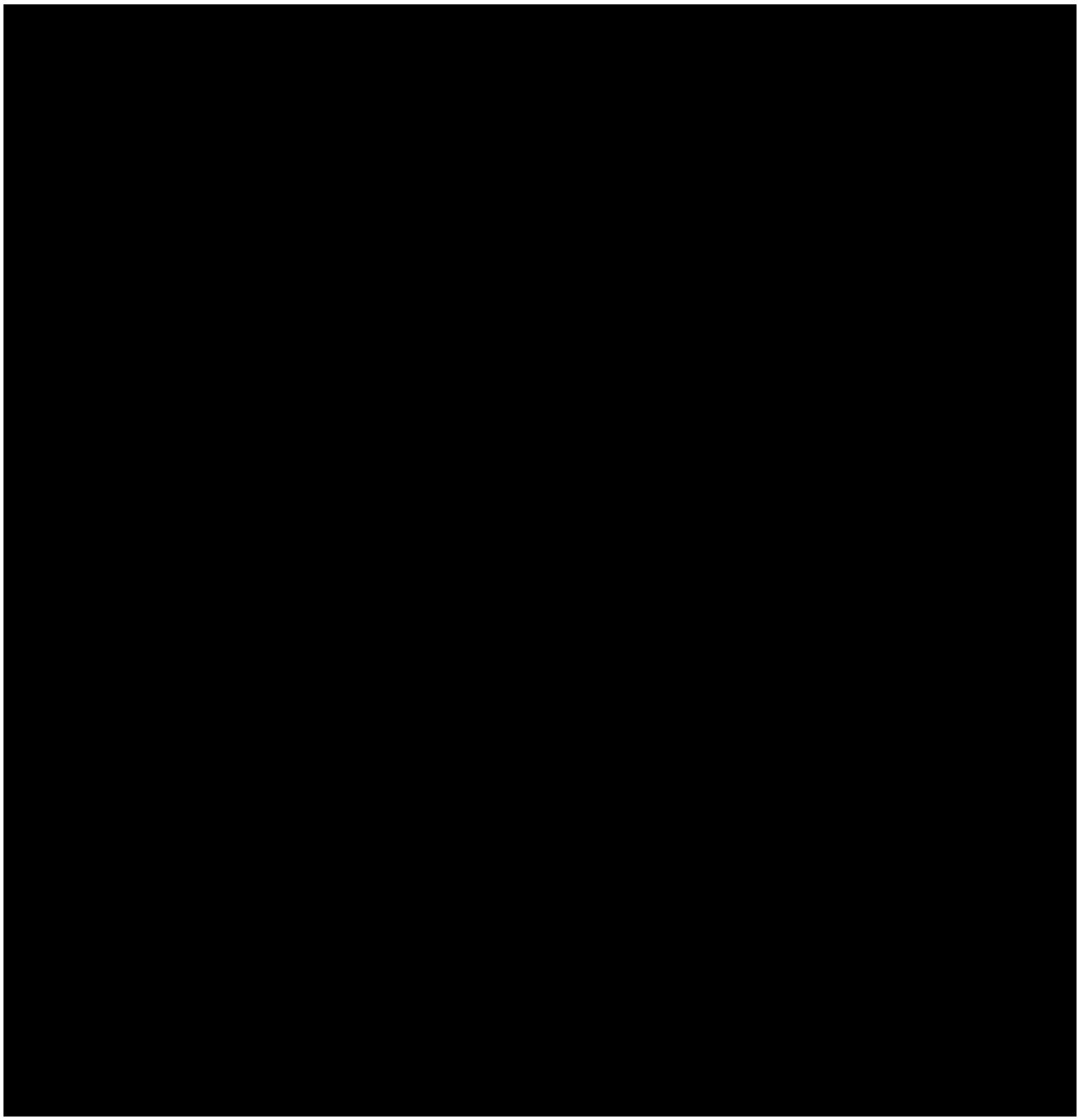
[redacted]

[redacted]

[redacted]

12.3 POSSIBLE DISTANT SPREAD OF TOXIN (PDSOT)

[redacted] All TEAEs associated with PDSOT will be tabulated by SOC, PT, and study intervention group; in addition, all PDSOT TEAEs will be listed by participant. [redacted]



12.4 CLINICAL LABORATORY PARAMETERS

A listing for positive pregnancy test results will be provided, including study intervention group, urine sample collection date, and date of study intervention administration.

12.5 VITAL SIGNS

Descriptive statistics for vital signs (systolic and diastolic blood pressures, respiratory rate, and pulse rate) and changes from baseline values at each study assessment visit will be presented by study intervention group.

13.0 INTERIM ANALYSIS

No interim analysis is planned for this study.

14.0 DETERMINATION OF SAMPLE SIZE

[redacted]

Approximately 165 participants will be enrolled in a 1:1:1 randomization allocation ratio, yielding approximately 55 participants in the BOTOX high dose group, 55 participants in the BOTOX low dose group, and 55 participants in the placebo group. With an anticipated attrition rate of approximately 10%, approximately 148 participants will be analyzable for the primary endpoint.

15.0 STATISTICAL SOFTWARE

Statistical analyses will be performed using SAS version 9.4 (or newer) on a Linux operating system.

16.0 DATA HANDLING CONVENTIONS

16.1 VISIT DAY WINDOWS

Table 16-1 presents the visits assigned for efficacy analyses and the corresponding range of study days (window) during which an actual visit may occur.

Table 16-1 Visit Day Windows

Derived Visit	***Scheduled Visit Day[a]***	***Analysis Window***
Baseline	Day 1	-
Day 7	Day 7	Days [2, 10]
Day 14	Day 14	Days [11, 21]
Day 30	Day 30	Days [22, 45]
Day 60	Day 60	Days [46, 75]
Day 90	Day 90	Days [76, 105]
Day 120	Day 120	Days 106 to study exit

a Relative to the date of the first dose of intervention. Day 1 is defined as the date of the first dose of study intervention. There is no Day 0 or Week 0.

If the assessment date (if unavailable, use visit date instead) is on or after the date of the first dose of study intervention, the study day is calculated by (assessment date – date of the first dose of study intervention + 1). If the assessment date is before the date of the first dose of study intervention, the study day is calculated by (assessment date – date of the first dose of study intervention). Therefore, a negative day indicates a day before the start of the study intervention.

If there are values from multiple visits in a given window, the value collected from the visit closest to the scheduled visit day will be used to represent the window. If two visits are equidistant from the scheduled visit day, the latter non-missing value will be used to represent the visit assessment.

[redacted]

If multiple unscheduled visits occur on the same day, but no collection times are available, the most conservative (ie, worst) values will be used for each parameter separately.

However, the P-APPS for the baseline analysis visit must be completed prior to or on Day 1; otherwise, the P-APPS for baseline/Day 1 visit will be considered missing.

16.2 REPEATED OR UNSCHEDULED ASSESSMENTS OF SAFETY PARAMETERS

If a participant has repeated assessments before the first dose of study intervention, the results from the final non-missing assessment made prior to the start of the study intervention administration will be used as baseline. If end-of-study assessments are repeated or if unscheduled visits occur, the last non-missing postbaseline assessment will be used as the end-of-study assessment for generating summary statistics. All assessments will be presented in the data listings.

16.3 MISSING SEVERITY ASSESSMENT FOR ADVERSE EVENTS

If severity is missing for an AE that started before the date of the first dose of study intervention, an intensity of mild will be assigned. If severity is missing for an AE that started on or after the date of the first dose of study intervention, an intensity of severe will be assigned. The imputed values for severity assessment will be used for the incidence summary; the values will be shown as missing in the data listings.

16.4 MISSING CAUSAL RELATIONSHIP TO STUDY TREATMENT FOR ADVERSE EVENTS

If the causal relationship to the study intervention is missing for an AE that started on or after the date of the first dose of study intervention, a causality of *yes* will be assigned. The imputed values for causal relationship to study intervention will be used for the incidence summary; however, the values will be shown as missing in the data listings.

16.5 MISSING DATE INFORMATION FOR ADVERSE EVENTS

Completely missing dates will not be imputed.

The following imputation rules only apply to cases in which the start date for AEs is incomplete (ie, partly missing).

Missing month and day

- If the year of the incomplete start date is the same as the year of the first dose of study intervention, the month and day of the first dose of study intervention will be assigned to the missing fields
- If the year of the incomplete start date is before the year of the first dose of study intervention, *December 31* will be assigned to the missing fields
- If the year of the incomplete start date is after the year of the first dose of study intervention, *January 1* will be assigned to the missing fields

Missing month only

- If only the month is missing, the day will be treated as missing and both the month and the day will be replaced according to the above procedure

Missing day only

- If the month and year of the incomplete start date are the same as the month and year of the first dose of study intervention, the day of the first dose of study intervention will be assigned to the missing day
- If either the year of the incomplete start date is before the year of the date of the first dose of study intervention or if both years are the same but the month of the incomplete start date is before the month of the date of the first dose of study intervention, the last day of the month will be assigned to the missing day
- If either the year of the incomplete start date is after the year of the date of the first dose of study intervention or if both years are the same but the month of the incomplete start date is after the month of the date of the first dose of study intervention, the first day of the month will be assigned to the missing day

If the start date of the AE is the same as the start date of the study intervention administration, then assign the start time of the AE to be 1 minute after the stop time of the last dose of study intervention administration.

If the stop date is complete and the imputed start date as above is after the stop date, the start date will be imputed by the stop date.

If the start date is completely missing and the stop date is complete, the following algorithm will be used to impute the start date:

- If the stop date is after the date of the first dose of study intervention, the date of the first dose of study intervention will be assigned to the missing start date
- If the stop date is before the date of the first dose of study intervention, the stop date will be assigned to the missing start date

Partially missing AE stop dates can follow the missing data methods in Section 16.6.2.

16.6 MISSING DATE INFORMATION FOR PRIOR OR CONCOMITANT MEDICATIONS OR PROCEDURES

For prior or concomitant medications or procedures, including rescue medications, incomplete (ie, partly missing) start dates and/or stop dates will be imputed. When the start date and the stop date are both incomplete for a participant, the start date will be imputed first.

16.6.1 Incomplete Start Date

The following rules will be applied to impute the missing numeric fields for an incomplete prior or concomitant medication or procedure start date. If the stop date is complete (or imputed) and the imputed start date is after the stop date, the start date will be imputed using the stop date.

Missing month and day

- If the year of the incomplete start date is the same as the year of the first dose of study intervention, the month and day of the first dose of study intervention will be assigned to the missing fields
- If the year of the incomplete start date is before the year of the first dose of study intervention, *December 31* will be assigned to the missing fields
- If the year of the incomplete start date is after the year of the first dose of study intervention, *January 1* will be assigned to the missing fields

Missing month only

- If only the month is missing, the day will be treated as missing and both the month and the day will be replaced according to the above procedure

Missing day only

- If the month and year of the incomplete start date are the same as the month and year of the first dose of study intervention, the day of the first dose of study intervention will be assigned to the missing day
- If either the year of the incomplete start date is before the year of the date of the first dose of study intervention or if both years are the same but the month of the incomplete start date is before the month of the date of the first dose of study intervention, the last day of the month will be assigned to the missing day.
- If either the year of the incomplete start date is after the year of the date of the first dose of study intervention or if both years are the same but the month of the incomplete start date is after the month of the date of the first dose of study intervention, the first day of the month will be assigned to the missing day

16.6.2 Incomplete Stop Date

The following rules will be applied to impute the missing numeric fields for an incomplete prior or concomitant medication or procedure stop date. If the imputed stop date is before the start date (imputed or nonimputed start date), the imputed stop date will be equal to the start date.

Missing month and day

- If the year of the incomplete stop date is the same as the year of the last dose of study intervention, the month and day of the last dose of study intervention will be assigned to the missing fields
- If the year of the incomplete stop date is before the year of the last dose of study intervention, *December 31* will be assigned to the missing fields
- If the year of the incomplete stop date is after the year of the last dose of study intervention, *January 1* will be assigned to the missing fields

Missing month only

- If only the month is missing, the day will be treated as missing and both the month and the day will be replaced according to the above procedure

Missing day only

- If the month and year of the incomplete stop date are the same as the month and year of the last dose of study intervention, the day of the last dose of study intervention will be assigned to the missing day
- If either the year of the incomplete stop date is before the year of the date of the last dose of study intervention or if both years are the same but the month of the incomplete stop date is before the month of the date of the last dose of study intervention, the last day of the month will be assigned to the missing day
- If either the year of the incomplete stop date is after the year of the date of the last dose of study intervention or if both years are the same but the month of the incomplete stop date is after the month of the date of the last dose of study intervention, the first day of the month will be assigned to the missing day

17.0 CHANGES TO ANALYSES SPECIFIED IN PROTOCOL

The hypothesis wording has been updated.

In addition, categorical descriptive statistics will be presented for all visits for C-APPS and P-APPS scores, [redacted]

All PROs except for P-APPS will be reported and summarized in a separate report.

18.0 REFERENCES

Dmitrienko A, Molenberghs G, Chuang-Stein C, Offen W. Analysis of Clinical Trials Using SAS: A Practical Guide. SAS Institute, Cary, North Carolina 2005;104-108.