Sponsor	Cadent Therapeutics, Inc.
Protocol Title:	A Phase 2a Open-Label Study to Evaluate the Safety, Tolerability and Efficacy of CAD-1883 Oral Treatment in Adults with Essential Tremor (CADENCE-1)
Protocol Number:	CAD 1883-20 l Protocol Amendment 3 / NCT03688685
Document Version:	Final 1.0
Document Date:	04-Mar-2020

Approvals

Role	Signatures	Date (DDMMMYYYY)
	Personal Protected Data	

Document History

Document version	Date of availability	Note
1.0	04-Mar-2020	Final Version

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1. Overview

This statistical analysis plan (SAP) describes the planned analysis and reporting for Cadent Therapeutics, Inc. protocol number CAD1883-201 (A Phase 2a Open-Label Study to Evaluate the Safety, Tolerability and Efficacy of CAD-1883 Oral Treatment in Adults with Essential Tremor [CADENCE-1]), dated 09-Jul-2019 Amendment 3. Reference materials for this SAP include the protocol and the accompanying sample data collection documents. Operational aspects related to data collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

The structure and content of this SAP provides 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[1]. All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association[2] and the Royal Statistical Society[3], for statistical practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts.

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2. Study Objectives and Endpoints

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective is to evaluate the safety and tolerability of twice-daily oral dosing of CAD-1883 over 14 days of treatment in adult subjects with Essential Tremor (ET).

2.1.2. Secondary Objectives

The secondary objectives are to evaluate the efficacy of twice-daily oral dosing of CAD-1883 over 14 days of treatment as measured by:

- The Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS) total score change from Baseline to Day 14
- TETRAS-PS upper limb subscale score change from Baseline to Day 14

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- Change from Baseline to Day 14 in upper limb tremor severity, mean amplitude, and mean frequency, measured in the clinic using a wearable sensor

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2.2. Study Endpoints

2.2.1. Safety Endpoints

The primary safety endpoint of the study is the occurrence and severity of treatment emergent AEs (TEAEs).

2.2.2. Efficacy Endpoints

2.2.2.1. Primary Efficacy Endpoint

Not applicable. The primary endpoint of this study is safety and tolerability.

2.2.2.2. Secondary Efficacy Endpoints

The secondary efficacy endpoints of this study are:

- TETRAS-PS total score change from Baseline to Day 14
- TETRAS-PS upper limb subscale score change from Baseline to Day 14

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- Change from Baseline to Day 14 in upper limb tremor severity, mean amplitude, and mean frequency, measured in the clinic using a wearable sensor
- Change from Baseline in mean frequency of tremor in arm on table posture, measured in the clinic using a wearable sensor

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3. Overall Study Design and Plan

3.1. Overall Design

This is an open-label study designed to evaluate the safety, tolerability, and efficacy of CAD-1883 administered twice daily orally to adult subjects with ET. The diagnosis of ET must be established by the Principal Investigator at Screening based on the Movement Disorder Society (MDS) criteria with a documented severity of tremor based on the clinician-administered TETRAS-PS. Commercially Confidential Information

Subjects will undergo a screening period of a minimum of 14 days up to a maximum of 35 days in which the subject will washout from prior Commercially Confidential Information medications, to allow the effects of previous medication(s) CCI to be eliminated. Subjects will return to the site for further assessments on Day 7 (-1 day) and Day 14 (±1 day) and a Follow-up visit (Day 21 [±1 day]). The wearable sensor measurements of upper limb tremor assessments will be completed in the clinic once at any time during the Screening visit and at two different times during the Baseline/Pre-dose site visit. Commercially Confidential Information subjects will have the option to complete at-home assessments of tremor using the wearable sensor Commercially Confidential Information

3.2. Sample Size and Power

Up to 30 subjects will be enrolled. No formal statistical power analysis was conducted.

3.3. Study Population

This study includes subjects between 18 and 75 years old, inclusive, with a history of tremor for at least 3 years.

3.4. Treatments Administered

The study will be open-label consisting of 1 treatment group receiving 300 mg twice-daily oral dosing of CAD-1883 for a treatment period of 14 days. Dose intervals on Days 1, 7 and 14 are changed from the protocol amendment 1 through 3. Subjects enrolled under the protocol amendment 1 take the first dose of CAD-1883 300 mg (3 capsules of 100 mg each) at the site, 2nd dose are taken 8 hours (±2 hours) after the first dose. On Days 7 and 14, the subjects are instructed to ingest the first daily dose of CAD-1883 of 300 mg at home. The second daily dose are taken in the clinic 8 hours (±2 hours) after the first daily dose. For subjects enrolled under the protocol amendment 2 and 3 the first dose on Day 1 is taken in clinic and the second dose is taken 4 to 5 hours later. On Days 7 and 14, the first daily dose is taken at home and the second daily dose is taken in the clinic 4 to 5 hours later.

3.5. Method of Assigning Subjects to Treatment Groups

There is 1 treatment group. Eligible subjects are enrolled sequentially. There was no randomization, blinding, or stratification employed in this study.

3.6. Blinding and Unblinding

This is an open-label study with no blinding.

3.7. Schedule of Events

A detailed schedule of events for the study is provided in Table 1.

Table 1: Schedule of Events

ASSESSMENTS	SCREENING	BASELINE	TREATMENT								FOLLOW-UP
	14-35 days prior to Day 1	Pre-dose[1,2] (≤ 3 days prior to Day 1) (In-clinic)	Day 1[2] (In-clinic: Pre-Dose 1)	Day 1[2] (In-clinic: Dosing & Post-Dose 1)	Day 1[2] (In-clinic: Dosing & Post Dose 2)	Days 2-6 (At-home)	Day 7[2] (-1 day) (In-clinic)	Days 8-13 (At-home)	Day 14[2] (±1 day) / Early Termination[24] (In-clinic)	Days 15-20 (At-home)	Day 21[2] (±1 day) (In-clinic)
Eligibility Check	X	X									
Informed Consent	X										
Inclusion/Exclusion Criteria	X	X									
Demographics	X										
Medical History	X										
Neurological Exam	X[3]	X					X		X		X
Physical Exam	X	X[4]	X				X		X		X[4]
Height	X										
Weight CCI	X[5]								X		X
12-lead ECG[6]	X	X	X[8]	X[8] (30 min, 60 min, 2 hours post 1st dose)	X[8] (30 min, 60 min, 2 & 4 hours post 2nd dose		X[8] (30 min, 60 min, 2 & 4 hours post 2nd dose		X[8] (30 min, 60 min, 2 & 4 hours post 2nd dose		X
Vital Signs[7]	X	X	X[8]	X[8] (30 min, 60 min, 2 hours post 1st dose)	X[8] (30 min, 60 min, 2 & 4 hours post 2nd dose)		X[8] (30 min, 60 min, 2 & 4 hours post 2nd dose)		X[8] (30 min, 60 min, 2 & 4 hours post 2nd dose)		X

ASSESSMENTS	SCREENING	BASELINE	TREATMENT								FOLLOW-UP
	14-35 days prior to Day 1	**Pre-dose[1,2] (≤ 3 days prior to Day 1) (In-clinic)**	**Day 1[2] (In-clinic: Pre-Dose 1)**	**Day 1[2] (In-clinic: Dosing & Post-Dose 1)**	**Day 1[2] (In-clinic: Dosing & Post Dose 2)**	**Days 2-6 (At-home)**	**Day 7[2] (-1 day) (In-clinic)**	**Days 8-13 (At-home)**	**Day 14[2] (±1 day) / Early Termination[24] (In-clinic)**	**Days 15-20 (At-home)**	**Day 21[2] (±1 day) (In-clinic)**
Orthostatic VS[9]	X (3 times, 15-20 min apart)	X		X (2-4 hours post 1st dose)	X (2-4 hours post 2nd dose)		X (2-4 hours post dose)		X (2-4 hours post dose)		X
Clinical Chemistry	X	X			X[27]		X[27]		X[27]		X
Hematology	X	X			X[27]		X[27]		X[27]		X
Urinalysis[10]	X	X			X[27]		X[27]		X[27]		X
Biomarker panel for renal tubular injury		X			X[27]		X[27]		X[27]		X
Pregnancy Test	X[11]	X[12]					X[12]		X[12]		X[12]
HIV, CCI HBsAg, HCVAb	X										
TSH – FSH (optional for females only; if needed)	X										

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ASSESSMENTS	SCREENING	BASELINE	TREATMENT								FOLLOW-UP
	14-35 days prior to Day 1	**Pre-dose[1,2] (≤ 3 days prior to Day 1) (In-clinic)**	**Day 1[2] (In-clinic: Pre-Dose 1)**	**Day 1[2] (In-clinic: Dosing & Post-Dose 1)**	**Day 1[2] (In-clinic: Dosing & Post Dose 2)**	**Days 2-6 (At-home)**	**Day 7[2] (-1 day) (In-clinic)**	**Days 8-13 (At-home)**	**Day 14[2] (±1 day) / Early Termination[24] (In-clinic)**	**Days 15-20 (At-home)**	**Day 21[2] (±1 day) (In-clinic)**
Administer CAD-1883 Study Drug				X[26] (in clinic)	X[26] (in clinic 4-5 hours post 1st dose)	X	X[14] (in clinic 4-5 hours post 1st dose)	X	X[14] (in clinic 4-5 hours post 1st dose)		
Dispense Study Drug					X		X				
Medication Diary						X		X			
CAD-1883 PK Sample					X[15] CCI		X[16] CCI		X[16] CCI		X[17] (Anytime during visit)
TETRAS Performance Subscale[18]	X[19]	X			X[20]		X[21]		X[21]		X
Commercially Confidential Information											
In-clinic Wearable Sensor on Upper Limb	X[22]	X[23]			X[24]		X[24]		X[24]		X[22]

ASSESSMENTS	SCREENING	BASELINE	TREATMENT								FOLLOW-UP
	14-35 days prior to Day 1	**Pre-dose[1,2] (≤ 3 days prior to Day 1) (In-clinic)**	**Day 1[2] (In-clinic: Pre-Dose 1)**	**Day 1[2] (In-clinic: Dosing & Post-Dose 1)**	**Day 1[2] (In-clinic: Dosing & Post Dose 2)**	**Days 2-6 (At-home)**	**Day 7[2] (-1 day) (In-clinic)**	**Days 8-13 (At-home)**	**Day 14[2] (±1 day) / Early Termination[24] (In-clinic)**	**Days 15-20 (At-home)**	**Day 21[2] (±1 day) (In-clinic)**
Commercially Confidential Information											
Commercially Confidential Information											
C-SSRS[25]		X							X		X
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AEs	X	Continuous reporting of adverse events									

*** Refer to list of abbreviations**

Schedule of Assessment Footnotes:

1 The Baseline/Pre-dose visit is the last day of the Screening period. The Baseline/Pre-dose visit must be conducted in the afternoon.

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3 In addition to the complete neurological exam, a focused neurological exam is conducted during the Screening visit to include full assessment of tremor per Movement Disorder Society classification criteria (Bhatia, 2018).

4 Complete PE at Screening, Days 1, 7, and 14 (includes: General; HEENT; Cardiovascular; Respiratory; Abdomen; Skin; Extremities; Lymphatic system and Musculoskeletal); symptom-based PE at Baseline/Pre-dose and Day 21 Follow-up visit (includes: General, HEENT, Cardiovascular, Respiratory, Abdomen, Skin, Extremities).

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6 Triplicate ECG recordings, after a minimum of 5 minutes of rest in supine position: 3 consecutive recordings will be made in succession, no more than 2 minutes apart. The full set of triplicates should be completed in less than 4 minutes. These ECGs will be read by the Investigator to rule out any clinically significant findings. ECGs are to be performed prior to vital signs and blood sampling.

7 Blood pressure (systolic and diastolic), heart rate, respiratory rate and oral temperature.

[8] Obtained prior to dosing and post dosing at 30min, 60min, 2 hours and 4 hours following the dose of study drug in the clinic. For Day 1, this is to be done Baseline/Pre-dose and 30min, 60min, and 2 hours after the first dose in the clinic, and again 30 min, 60 min, 2 hours, and 4 hours after the second dose in the clinic. There is a +/- 5-minute allowable time window for these assessments. ECG to be done before the corresponding vital sign measurements.

[9] For details re: orthostatic vital signs measurements, refer to Section 7.10.

[10] Urinalysis includes: Bilirubin, Blood, Creatinine, Glucose, Ketones, Leukocyte esterase, Microscopy, Nitrite, pH, Protein, Specific gravity, Microalbumin and Urobilinogen

[11] A serum pregnancy test is done at Screening only.

[12] A urine pregnancy test is done at Baseline/Pre-dose, Days 7, 14, and 21.

[13] Commercially Confidential Information

[14] The subject should be instructed to self-administer their first daily dose of CAD-1883 4 to 5 hours prior to the scheduled and/or anticipated dosing of the second daily dose of CAD-1883. The second daily dose of CAD-1883 should be taken in the clinic 4 to 5 hours after the first daily dose.

[15] Commercially Confidential Information

[16]

[17]

[18] TETRAS Performance Subscale assessments at Screening, Baseline/Pre-dose, Days 1, 7, 14, and 21 will be recorded via videography for central rating.

[19] Screening: Commercially Confidential Information

[20] Performed between 2-4 hours following the second dose in the clinic.

[21] Performed between 2-4 hours following the second daily dose in the clinic.

[22] Wearable sensor measurement of upper-limb tremor will be captured once at the site, at any time during Screening and Day 21.

[23] Wearable sensor measurements of upper limb tremor will be captured at two different times during the Baseline/Pre-dose visit.

[24] Wearable sensor measurements of upper limb tremor will be captured once, 2 to 4 hours following the in-clinic dose. For Day 1, this is to be done 2-4 hours after the 2nd in-clinic dose.

[25] At the Baseline/Pre-dose visit, the "baseline" version of the C-SSRS will be administered. This version assesses Suicidal Ideation and Suicidal Behavior during the subject's lifetime and during a predefined period. At the Day 21 visit (and the Early Termination visit for subjects withdrawing early), the "since last visit" version will be administered. The C-SSRS does not need to be completed at the Day 14 visit if it is not an Early Termination visit. During Early Termination visit, the subject will not receive study drug, will undergo all required procedures as well as the C-SSRS.

[26] (Protocol Amendment 3) Both doses of study drug are to be administered in the clinic with the second dose being administered 4-5 hours after the first.

[27] All laboratory collections on Days 1, 7, 14 should be performed after the TETRAS-PS assessment.

4. Statistical Analysis and Reporting

4.1. Introduction

Data processing, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will be performed primarily using SAS (release 9.4 or higher). Commercially Confidential Information If the use of other software is warranted, the final 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, standard deviation (SD), median, minimum, and maximum.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category for each possible value. In general, the denominator for the percentage calculation will be based upon the total number of subjects in the study population, unless otherwise specified. The denominator for by-visit displays will be the number of subjects in the relevant study population with non-missing data at each visit. If there is any missing value for a categorical analysis, a "Missing" category will be displayed as the last category in the table for the variable.

For weight, height, CCI one decimal place will be used for all summary statistics. For all other summaries, 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) and confidence interval boundaries will be reported to 1 degree of precision more than the observed data, up to 3 decimal places. Measures of spread (SD) will be reported to 2 degrees of precision more than the observed data, up to 3 decimal places.

Percentages will be presented to 1 decimal place, unless otherwise specified. Percentages equaling 0 or 100 will be displayed with no decimal places or percentage symbols.

Fractional numeric values will be presented with a zero to the left of the decimal point (for example, 0.12 – 0.30).

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, where applicable.

4.2. Interim Analysis and Data Monitoring

There will be no interim analyses in this study. Commercially Confidential Information

5. Analysis Populations

The following analysis populations are planned for this study:

- **Safety Population:** The Safety population includes all subjects who took at least 1 dose of study drug, regardless of the Protocol Amendment under which subjects were enrolled. This population will be used to summarize all safety data.

- **Full Analysis Set (FAS):** The FAS consists of subjects in the Safety Population at least one TETRAS-PS assessment Total Score at Day 7, Day 14 or early termination visit. The FAS will be used to summarize all efficacy data.

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- **Per-Protocol Population:** The Per-Protocol Population includes all subjects in the FAS who did not have any major protocol deviation and follow the study protocol for TRETRAS-PS assessment at Day 14 or ET visit.

6. General Considerations for Statistical Analysis

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

The last non-missing observed value recorded on or before the date of the first dose of treatment at the Pre-dose visit will be used as the baseline observation for all calculations of change from baseline.

Wearable sensor measurements of upper limb tremor will be captured at 2 different times during the Pre-dose visit (Visit 2); the average of the 2 assessments will be used as the baseline observation for all calculations of change from baseline in wearable sensor assessments.

During the Pre-dose visit, baseline orthostatic vital signs will include 3 separate measurements, and the average of the 3 (or fewer if missing data occur) baseline orthostatic vital signs measurements will be used as baseline for comparison to all post-treatment measurements.

6.1.2. Categorization of Subjects

All subjects will be categorized into the following 2 groups based on under which protocol amendment they were enrolled:

- Cohort-1: Subjects enrolled under Protocol Amendment 1.0
- Cohort-2: Subjects enrolled under Protocol Amendment 2.0 or 3.0

All analyses will be presented overall and by cohort.

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6.1.4. Multiple Comparisons

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6.1.5. Handling of Dropouts or Missing Data

There was no replacement for subjects who had withdrawn from the study or were lost to follow up. Individual items of TETRAS-PS, CCI , and Kinesia scores will not be imputed as described in Section 6.1.8.

6.1.6. Analysis Visit Windows

Visits will be analyzed as scheduled. Unscheduled and/or repeated measurements will only be included if a scheduled measurement is not available and the unscheduled/repeated measurement falls within the analysis visit windows as described in Table 2. The windows follow the Schedule of Events in Table 1. Unscheduled/repeated measurements will be listed. Study day is defined in Section 6.1.8.

Table 2: Analysis Visit Windows

Visit Name	Visit Number	Target Start Day	Lower Limit	Upper Limit
Screening	1		-35	-14
Baseline Pre-dose	2		-14	-3
Day 1	3	1	1	1
Day 7	4	7	6	8
Day 14	5	14	13	15
Day 21	6	21	20	22

6.1.7. Pooling of Sites

Not applicable.

6.1.8. Derived Variables

- **TETRAS-PS Total score** = sum of the 16 individual item scores (only the maximum of the item 5 lower limb tremor scores will be counted), with a maximum total score of 64. There will be no missing value imputation performed.

- **TETRAS-PS Upper Limb Subscale score** = sum of the item 4, item 6, item 7 and item 8 scores (forward outstretched postural tremor, lateral "wing beating" postural tremor, kinetic tremor, Archimedes spirals, and dot approximation task from both sides of the body, as well as handwriting), with a maximum total score of 44. There will be no missing value imputation performed.

- **TETRAS-PS Upper Limb Tremor (Item 4) Total score =** sum of the 6 individual scores under item 4 scores (forward outstretched postural tremor, lateral "wing beating"

postural tremor, and kinetic tremor scores for left and right hand, respectively) from both sides of the body, with a maximum total score of 24. There will be no missing value imputation performed.

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- **Kinesia Upper Limb Tremor score** = sum of the scores from the extended arms posture, wing-beating posture, and kinetic "finger-to-chin" wearable sensor maneuvers from both sides of the body, with a maximum total score of 24. There will be no missing value imputation performed.

- **Change from baseline** = value at current time point – value at baseline.

    - For calculation of change from baseline to Day 14 for discontinued subjects their assessment value at the early termination (ET) visit should be used

- **Percent change from baseline** = (change from baseline / baseline) * 100. If both baseline and change from baseline are 0 then percent change from baseline will be set to 0.

- **Study day** = number of days relative to the first dose date of study drug and will be calculated using the following formulas:
  For pre-dose: study day= Start Date/ Stop Date – first dose date;
  For post-dose: study day= Start Date/ Stop Date – first dose date + 1.

- **TEAE (treatment-emergent AE)** = any AE with an onset date/time after the first dose of treatment. If an AE was present at baseline and worsened on or after the first dose of treatment it will be considered a TEAE.

- **Orthostatic hypotension** is defined as a reduction in SBP of 20 mmHg or more, and/or a reduction in DBP of 10 mmHg or more, for the standing measurement compared to the supine or semi-supine measurement.

- **Time since first ET symptom** = Day 1 (Visit 3) date - Date of first ET symptom as recorded on the Disease History case report form (CRF) + 1

- **Time since ET diagnosis** = Day 1 (Visit 3) date - Date of ET diagnosis as recorded on the Disease History case report form (CRF) + 1

- **Study drug compliance** (capsule count) = total number of capsules taken / total number of expected doses from the first dose date to the last dose date, inclusive * 100%.

- **Number of expected doses** for subjects who completed study treatment = number of capsules taken at the clinic + number of capsules dispensed for self-administration at home = [Day 14 (Visit 5) date – Day 1 (Visit 3) date + 1] x 6 capsules/day

  Expected doses are summed up to the point of discontinuation (eg, if a subject discontinued, only planned doses up to that discontinuation day are counted in the denominator).

- **Number of capsules taken** = number of expected doses - number of capsules lost - number of unused capsules returned at next clinic visit, as collected in the case report form (CRF).

  For subjects who discontinued and did not return remaining capsules, the number of capsules taken will include all doses up to the last dose the subject reported, or the discontinuation date (the second dose on that day will be excluded in this calculation).

  For treatment completers with additional treatment (for example the subject received study treatments for 15 days) their number of expected doses remains 84. Thus, the resulting compliance rate will likely be over 100%.

6.1.9. 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 in the data listings.

All *P* values will be displayed in three decimals and rounded using standard scientific notation (eg, 0.XXX). If a *P* value less than 0.001 occurs, it will be shown in tables as <0.001.

Adverse events and medical histories will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 21.1 thesaurus or higher. Concomitant medications will be coded using WHO Global B3 September 1, 2018.

A treatment-related AE is any AE with a relationship to the study drug of possibly, probably, or definitely related.

If partial AE or medication dates occur, the convention for replacing missing dates for the purpose of statistical analysis is as follows:

For partial AE and medication start dates:

- If the year is unknown, then do not impute the date but assign a missing value.
- If the year is known, but the month or month and day is unknown, then:
  - If the year matches the year of first dose date and the end date (if present) is after first dose date, then impute as the month and day of the first dose date.
  - Otherwise, assign 01 January.

- If the year and month are known, but the day is unknown, then:
    - If the month and year match the month and year of the first dose date, then impute as the day of the first dose date.
    - Otherwise, assign 01.

For partial AE and medication end dates:

- If the year is unknown, then do not impute the date but assign as missing value.
- If the year is known, but the month or month and day is unknown, then:
    - If the year matches the year of the last date of the study (date of last contact if subject lost to follow-up; date of completion or early termination otherwise), then impute as the month and day of the last date of the study.
    - Otherwise, assign 31 December.
- If the year and month are known, but the day is unknown, then:
    - If the month and year match the month and year of the last date of the study, then impute as the day of the last date of the study.
    - Otherwise, assign the last day of the month.

If partial times occur, the convention is as follows:

- if the missing time occurs on the day of the first dose and both the hour and minute are missing then the time assigned is the time of the first dose, otherwise if both the hour and minute are missing and the date is not the date of first dose the time assigned is 12:00;
- if the date is the same as the date of the first dose and
    - only hour is missing the hour assigned is 12 or the hour of first dose, whichever is later;
    - only the minute is missing the minute assigned is 30 or the minute of first dose, whichever is later;
- Otherwise if the date is not the same as the date of first dose, the hour assigned is 12 if the hour is missing and the minute assigned is 30 if the minute is missing.

Partial dates of first ET symptom and partial dates of ET diagnosis will be imputed similar to the rules outlined for AE start dates mentioned above.

7. Study Subjects and Demographics

7.1. Disposition of Subjects and Withdrawals

Disposition will include tabulations of the number of subjects who received treatment, reasons for discontinuation from the study, and number of subjects in each analysis population. This summary will be based on all subjects enrolled.

All disposition information will be included in a listing.

7.2. Protocol Violations and Deviations

Protocol deviations will be listed.

7.3. Demographics and Other Baseline Characteristics

Summary statistics for age, gender, race, ethnicity, height, weight, Commercially Confidential Information will be presented.

Medical history will be listed, and the number and percentage of subjects reporting various medical histories grouped by MedDRA System Organ Class (SOC) and Preferred Term (PT) will be tabulated.

Time since first ET symptom, time since ET diagnosis, treatment type, trigger type, and frequency of triggers will be summarized descriptively. The number of subjects who report that alcohol reduces tremor severity and the number of subjects with a first or second-degree blood relative with ET will also be summarized.

Disease history, including prior treatments for ET, ET triggers, and family history of ET, will also be listed.

These analyses will be conducted for the Safety population.

7.4. Exposure and Compliance

All subjects were expected to receive treatment twice daily for 14 consecutive days for a total of 28 doses. Total number of doses taken, number of missed doses, and compliance (%) will be summarized and listed for the Safety Population. Compliance via capsule count is defined in Section 6.1.8 as the rate of actual number of doses taken compared to the intended number of doses taken during the 2-week treatment period. Treatment compliance (rounded to the whole number) will also be categorized as <70%, ≥70 to 79%, ≥80 to 89%, ≥90% to 100%, and >100%.

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8. Efficacy Analysis

All efficacy data (including change from baseline) will be summarized and presented in tabular format and in data listings.

Efficacy variables include TETRAS-PS score, TETRAS-PS upper limb subscale score, TETRAS-PS upper limb tremor item 4 total score, Kinesia Upper Limb Tremor score,

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Analyses of these data will be conducted on both the FAS and Per-Protocol Population within the same output for tables; figures will only be presented on the FAS.

8.1. Primary Efficacy Analysis

Not applicable. The primary analysis for this study is safety.

8.2. Secondary Efficacy Analysis

Normality assumptions of efficacy endpoints will be tested using the Anderson-Darling method. If the *P* value for the normality test is >0.05 the data will be considered normally distributed and will be analyzed as specified in subsequent sections. Otherwise, if the *P* value is ≤0.05 the data will be considered non-normal and the Wilcoxon signed rank test will be used to assess the within-subject changes. The estimates, CIs and P values will be displayed.

8.2.1. TETRAS Performance Subscale Scores

The TETRAS-PS Subscale (Version 3.1) score includes the following 9 items: head tremor, face (including jaw) tremor, voice tremor, upper limb tremor (left/right), lower limb tremor, Archimedes spirals, handwriting, dot approximation task, and standing tremor. Scores for each item range from 0 to 4 in increments of 0.5. Derivation for the TETRAS-PS Total score is described in Section 6.1.8. For lower limb tremor, only the maximum of the item 5 scores will be used. The TETRAS-PS assessments will be administered by a certified rater (referred to as a local rater hereafter) at Screening, Pre-dose, Day 1, Day 7, Day 14, and Day 21. The TETRAS-PS assessments will also be recorded using videography for centralized evaluation and rating by independent blinded central raters (neurologists) with expertise in the assessment of ET. All scores (item scores and total scores) by both local and central raters will be analyzed in the same way as described below for central rater data.

Observed values and change from baseline in each item score and in TETRAS-PS total score by central rater will be summarized overall, by cohort (see Section 6.1.2), and by study visit using descriptive statistics.

Additionally, tests of hypotheses comparing mean and median TETRAS-PS total scores between baseline and subsequent study visits will be conducted using a 2-sided paired t-test or Wilcoxon signed rank test. The null hypothesis is that the change from baseline in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not 0 (significant changes in tremor).

As a supportive analysis, change from Screening to Baseline and change from Day 14 to Day 21 in each item score and in TETRAS-PS total score will be summarized overall and by cohort (see Section 6.1.2) using descriptive statistics.

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8.2.2. TETRAS Upper Limb Subscale Score

Upper limb tremor is assessed during the following maneuvers: forward outstretched posture, lateral "wing beating" posture, kinetic (finger-chin-finger) testing, Archimedes spirals, handwriting, and dot approximation task. Each side of the body (right and left) is assessed and scored individually for all maneuvers except handwriting. The individual item question scores for each side of the body range from 0 to 4, with higher scores indicating more tremors. Derivation for the upper limb subscale score is described in Section 6.1.8.

Assessments will be administered at Screening, Pre-dose, Day 1, Day 7, Day 14, and Day 21. Assessment results (scores) by local and central rater will be analyzed in the same way as described below for central rater score data. Observed values and change from baseline to all subsequent study visits in the upper limb subscale score will be summarized overall, by cohort (see Section 6.1.2), and by study visit using descriptive statistics.

Additionally, tests of hypotheses comparing mean and median TETRAS-PS upper limb subscale scores between baseline and subsequent study visits will be conducted using a 2-sided paired t-test and a Wilcoxon signed rank test, respectively. The null hypothesis is that the change from baseline in TETRAS-PS upper limb subscale score to subsequent visit is 0 with a 2-sided alternative considering a difference in either direction (i.e., change from baseline not equal to 0, representing significant change in tremor).

As a supportive analysis, change from Screening to Baseline and change from Day 14 to Day 21 in each item score and in TETRAS-PS upper limb subscale score will be summarized overall and by cohort (see Section 6.1.2) using descriptive statistics.

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8.2.3. TETRAS-PS Upper Limb Tremor (Item 4) Total Score

Item 4 of the TETRAS-PS represents upper limb tremor. Upper limb tremor is assessed during three maneuvers: forward outstretched posture, lateral "wing beating" posture, and kinetic (finger-chin-finger) testing. Each side of the body (right and left) is assessed and scored individually. The upper limb individual item score for each side of the body ranges from 0 to 4, with higher scores indicating more tremors. Derivation for the TETRAS-PS Upper Limb Tremor (Item 4) Total score is described in Section 6.1.8.

Assessments will be administered at Screening, Pre-dose, Day 1, Day 7, Day 14, and Day 21. Assessment results (scores) by local and central rater will be analyzed in the same way as described below for central rater score data. Observed values and change from baseline to all subsequent study visits in the upper limb subscale score will be summarized overall, by cohort (see Section 6.1.2), and by study visit using descriptive statistics.

Additionally, tests of hypotheses comparing mean and median TETRAS-PS Upper Limb Tremor (Item 4) Total scores between baseline and subsequent study visits will be conducted using a 2-sided paired t-test and a Wilcoxon signed rank test, respectively. The null hypothesis is that the change from baseline in TETRAS-PS Upper Limb Tremor (Item 4) Total score to subsequent visit is 0 with a 2-sided alternative considering a difference in either direction (i.e., change from baseline not equal to 0, representing significant change in tremor).

As a supportive analysis, change from Screening to Baseline and change from Day 14 to Day 21 in each item score and in TETRAS-PS Upper Limb Tremor (Item 4) Total score will be summarized overall and by cohort (see Section 6.1.2) using descriptive statistics.

A waterfall plot presenting mean change from baseline and 95% CI in TETRAS-PS Upper Limb Tremor (Item 4) Total Score by study visit will also be displayed. Additionally, a line graph of mean change from baseline and percent change from baseline will be displayed by study visit.

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8.2.9. Wearable Sensor (Kinesia)

In addition to the assessment of efficacy via rating scales, treatment effect will be evaluated by measuring tremor with a sensor worn on the upper limb (right and left index fingers). These assessments will be conducted during the clinic visits and optionally at-home. The motion sensor uses three orthogonal accelerometers and three orthogonal gyroscopes to monitor three-dimensional motion. Data are then transmitted from the sensor to a computer using Bluetooth technology. These measures of three-dimensional motion for each maneuver are then converted to Kinesia scores. Each Kinesia score ranges from 0.0 to 4.0; higher scores indicate more severe tremor.

The wearable sensor measurements of upper limb tremor assessments will be completed in the clinic once at any time during the Screening visit and at two different times during the Pre-dose clinic visit. During the clinic visit on Days 1, 7 and 14, the wearable sensor measurements of upper limb tremor will be captured once, 2 to 4 hours following the in-clinic dose. During the Follow-up visit (Day 21), the wearable sensor measurements of upper limb tremor will be

completed at any time during the visit. In-clinic assessments will be obtained during the performance of 4 maneuvers:

1. extended arms posture,
2. wing-beating posture,
3. kinetic “finger-to-chin” movement, and
4. arm on table posture.

Two measurements at Pre-dose will be averaged and the means of 2 sets of measurements (mean of Kinesia score, mean amplitude, and mean frequency) will be used to represent Pre-dose values.

These assessments will be performed twice, once with the sensor on the left index finger and once with the sensor on the right index finger.

Observed values and change from baseline in the in-clinic wearable sensor measures of upper limb tremor severity, mean amplitude, and mean frequency will be summarized overall, by cohort (see Section 6.1.2), Commercially Confidential Information and study visit using descriptive statistics.

As a supportive analysis, change from Screening to Baseline and change from Day 14 to Day 21 in the in-clinic wearable sensor measures of upper limb tremor severity, mean amplitude, and mean frequency for the above maneuvers will also be summarized.

A waterfall plot presenting mean change from baseline and 95% CI in Wearable Sensor (Kinesia, in-clinic) measures by study visit will also be displayed.

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9. Safety and Tolerability Analysis

The primary endpoint of the study is the occurrence and severity of TEAEs.

Safety will be evaluated from reported AEs, serious AEs (SAEs), changes in clinical laboratory values, changes in vital signs, changes in orthostatic vital signs, 12-lead electrocardiograms (ECG), Columbia-Suicide Severity Rating Scale (C-SSRS), and physical and neurological examination results.

All safety analyses will be performed on the Safety population.

9.1. Adverse Events

Any AE occurring after the date/time of informed consent signature but prior to the first dose of study medication (ie, occurring during the Screening and Baseline periods) will be listed. All AEs that occur after the first dose of study drug will be considered TEAEs. This includes any AEs that started or worsened (if present at baseline, increased in frequency or severity) after taking the first dose of the study drug. For AEs occurring on the date of first dose, if the time of onset is missing, the AE will be assumed to be treatment emergent.

All AEs will be coded using the MedDRA Version 21.1 or higher coding dictionary.

The causal relationship of the AE to the study drug is determined by the investigator as Not Related, Unlikely Related, Possibly Related, Probably Related, and Definitely Related. These will be mapped to Unrelated (*Not Related or Unlikely Related*) and Related *(Possibly Related, Probably Related,* and *Definitely Related*).

Adverse events severity grades are reported as mild, moderate, or severe.

Summaries of incidence rates (frequencies and percentages) of individual TEAEs will be presented by SOC, PT, and cohort. Such summaries will be displayed for all TEAEs, TEAEs by maximum severity, and TEAEs by relationship.

Each subject will be counted only once within each summation level (SOC and PT). If a subject experiences more than 1 TEAE within each summation level only the TEAE with the strongest relationship or the maximum severity, as appropriate, will be included in the summaries by subject for relationship and severity, respectively. 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 = definitely related).

Incidences will be presented by descending frequency of SOC and PT within SOC, and then alphabetically within PT where the incidence is the same.

Missing and partially missing AE start and/or stop dates will be imputed, for the purpose of statistical analysis, according to the specifications described in Section 6.1.9.

Numbers of AEs will also be presented in these AE summary tables.

In the AE data listings, all AEs will be displayed. AEs that are treatment emergent will be flagged.

9.1.1. Adverse Events Leading to Withdrawal

A summary of incidence rates (frequencies and percentages) of TEAEs leading to withdrawal of study drug or study discontinuation, by SOC, PT, and cohort will be prepared for the Safety population.

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

9.1.2. Deaths and Serious Adverse Events

Any deaths that occur during the study will be listed.

SAEs will be listed and also tabulated by SOC, PT, and cohort.

9.2. Clinical Laboratory Evaluations

Screening and safety laboratory tests will be performed at Screening, Pre-dose, Day 1, Day 7, Day 14, and at follow-up on Day 21. All laboratory test results will be summarized descriptively by study visit for the Safety Population overall and by cohort as both observed values and change from baseline values for each parameter. Categorical urinalysis results will be summarized using frequencies by study visit and cohort. Levels of composite biomarker panel for renal tubular injury will also be summarized by study visit and listed.

Shifts from baseline for clinical laboratory values below, within, or above the normal range will be provided for hematology and chemistry results by study visit. See Section 6.1.1 for the definition of baseline. Clinically significant abnormal findings will be reported as AEs. Abnormal laboratory results will be listed.

Pregnancy test results will be listed.

9.3. Vital Signs

Descriptive summaries of observed values and changes from baseline will be calculated for supine systolic blood pressure (SBP), standing SBP, supine diastolic blood pressure (DBP), standing DBP, supine heart rate (HR), standing HR, respiration rate, and oral temperature by study visit for the Safety Population overall and by cohort. Shifts from baseline for SBP, DBP, and HR values below, within, or above the normal range will be provided by study visit for the Safety Population overall and by cohort. Vital sign parameters outside the normal range will be flagged in the listings. The mean change from baseline in each parameter will also be plotted by study visit. Abnormal vital signs are as follows:

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- SBP >140 mmHg
- SBP <90 mmHg
- DBP >90 mmHg
- DBP <60 mmHg
- HR >100 bpm
- HR <60 bpm
- Respiration rate >20 breaths/min
- Respiration rate <12 breaths/min
- Oral temperature >99.1 ºF/37.2 ºC
- Oral temperature <97.8 ºF/36.5 ºC

Orthostatic vital signs (blood pressure and heart rate) will also be summarized by position and study visit and by cohort. During the Pre-dose visit, baseline orthostatic vital signs will include 3 separate measurements and the average of the 3 baseline orthostatic vital signs measurements will be used for comparison to all post-treatment measurements. The average HR, SBP, and DBP will be presented in the pre-dose baseline summaries and each of the individual measurements will be listed for that study visit.

Orthostatic hypotension will be defined as a reduction in systolic blood pressure of 20 mmHg or more and/or a reduction in diastolic blood pressure of 10 mmHg or more, for the standing measurement compared to the supine or semi-supine measurement. The frequency and percentage of subjects with orthostatic hypotension will also be presented by cohort. Any confirmed orthostatic hypotension or clinically significant measurements that are associated with clinical symptoms will be recorded as AEs. Orthostatic vital signs parameters outside the ranges specified above will be flagged in the listings.

9.4. Electrocardiograms

12-lead ECGs will be obtained at Screening, Pre-dose, Day 1, Day 7, Day 14, and Day 21.

Descriptive summaries will be presented for ECG measures of PR interval, RR interval, mean heart rate, QRS interval, QT interval, and QTcF interval. Corrected QTc intervals will be calculated using Fridericia's correction formula. These summaries will be presented by study visit for the Safety Population overall and by cohort. The mean change from baseline (pre-dose) for each parameter will be plotted by study visit. Values outside the normal range will be flagged in the listings.

The number and percentage of subjects with normal, abnormal but not clinically significant, and abnormal and clinically significant ECG results will be summarized for the Safety population by study visit.

Additionally, QTcF data will be summarized by the following categories by study visit:

- QTcF > 450 msec to ≤ 480 msec
- QTcF > 480 msec
- QTcF > 500 msec
- Change from baseline > 30 msec to ≤ 60 msec
- Change from baseline > 60 msec

9.5. Further Safety Evaluations

9.5.1. Physical Examination

A complete physical examination (PE) will include general observations; head, eyes, ears, nose, throat, and musculoskeletal. Physical examinations will be conducted at screening, Pre-dose, Day 1, Day 7, Day 14, and Day 21. All physical examination results will be listed.

9.5.2. Neurological Examination

Neurological examinations will include assessment of mental status, cranial nerves, motor, sensory, reflexes, coordination, and gait. Neurological examinations will be conducted at screening, Pre-dose, Day 7, Day 14, and Day 21. All results will be listed.

9.5.3. Columbia Suicide Severity Rating Scale

The C-SSRS is a questionnaire that prospectively assesses Suicidal Ideation and Suicidal Behavior. At the Pre-dose visit, the "baseline" version of the C-SSRS will be administered. This version assesses Suicidal Ideation and Suicidal Behavior during the subject's lifetime and during the past 12 months. At the Day 14 and Day 21 visits (and the Early Termination visit for subjects withdrawing early), the "since last visit" version will be administered.

Suicidality data collected on the C-SSRS will be listed for all subjects in the Safety Population. Tables will include results from the Suicidal Ideation and Suicidal Behavior sections of the C-SSRS. Frequencies and percentages of subjects with a response of "Yes" at any point on the

Suicidal Ideation and Suicidal Behavior items will be summarized for the Safety Population (overall and by cohort).

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9.7 Kidney safety Composite Measure Biomarker

The following 6 kidney safety composite measure biomarkers were tested using urine sample: uCreatine (uCr), uClusterin (uCLU) , uCystatin-C (uCysC), uKidney Injury Molecule-1 (uKIM-1), u N-Acetyl-beta-D-Glucosaminidase (uNAG), Neutrophil Gelatinase-Associated Lipocalin (uNGAL) and uOsteopontin (uOPN). Measured concentration is first normalized by dividing it by the concentration of uCR at the same timepoint. The fold change from baseline at a given timepoint is then calculated using the normalized concentration at a time point divided by the normalized concentration at baseline. For example, the normalized uCysC concentration at a given timepoint is calculated as the concentration of CysC at that timepoint divided by the concentration of uCr at the same timepoint. The uCysC fold change from baseline at a given timepoint is calculated as the normalized CysC concentration at a given timepoint divided by the normalized uCysC concentration at baseline. Similar calculations apply to other composite measures.

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10. Changes from the Protocol-Planned Analysis

TETRAS scores from both the central rater and local raters will be summarized. all rating scores will be listed.

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11. Other Planned Analysis

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12. References

1. US Federal Register. (1998) International Conference on Harmonization; Guidance on Statistical Principles for Clinical Trials. Department of Health and Human Services: Food and Drug Administration [Docket No. 97D-0174]. Federal Register Volume 63, Number 179, pages 49583-49598. September 16, 1998.
2. ASA. (2016) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2016. http://www.amstat.org/about/ethicalguidelines.cfm

3. RSS. (2014) The Royal Statistical Society: Code of Conduct, 2014. http://www.rss.org.uk/Images/PDF/join-us/RSS-Code-of-Conduct-2014.pdf.
4. FNIH and Critical Path Institute. (2019) User's Guide Kidney Safety Composite Measure Biomarker for Use in Clinical Development, Version 1. January 11, 2019.

13. Tables, Listings, and Figures

All listings, tables, and figures (TLFs) will have a header showing the sponsor company name and protocol on the left (Cadent Therapeutics, CAD1883-201) and Page x of y on the right, and a footer showing the version of SAS, the file name and path, and the source of the data (CRF page or listing number) on the left and production run date in DDMMMYYY HH:MM on the right.

Summary statistics will be presented to the following degree of precision unless otherwise specified:

Statistics	**Degree of Precision**
Mean, Median, Quartiles, Confidence limit boundaries	One more than the raw data, up to 3 decimal places.
Standard deviation, Standard error	One more than the mean, up to 3 decimal places.
Minimum, Maximum	The same as the raw data.
p-value	Rounded to 3 decimal places and therefore presented as 0.xxx; p-values smaller than 0.001 as "<0.001"; p-values greater than 0.999 as ">0.999".
Percentage	One decimal place. A percentage of 100% will be reported as 100%. Percentages of zero will be reported as 0.

For weight, height, CCI one decimal place will be used for all summary statistics. Fractional numeric values will be presented with a zero to the left of the decimal point (for example, 0.12 – 0.30).

For summary tables when there are no subjects in a given treatment group/time point, display 0 in the "n" row and leave the statistics blank.

For the AEs by SOC and PT, sort the SOC by alphabetical order and sort the PT under SOC by decreasing frequency in the cohort, unless specified otherwise.

If there is a missing value for any categorical analysis, add a "Missing" category as the last one for the variable.

13.1. Planned Table Descriptions

The following are planned summary tables for protocol number CAD1883-201. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

Table 4: Demographic Data Summary Tables and Figures

Number	Population	Title
Table 14.1.1	All Enrolled Subjects	Subject Disposition
Table 14.1.2.1	Safety	Demographics and Baseline Characteristics
Table 14.1.2.2	Safety	Disease History
Table 14.1.3	Safety	Summary of Medical History by SOC and PT
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Table 14.1.5.1	Safety	Summary of Treatment Exposure and Compliance via Capsule Counts
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13.2. Efficacy Data

Table 5: Efficacy Data

Number	Population	Title
Table 14.2.1.1.1	FAS/Exposed	Summary of Central Rater TETRAS-PS Scores by Study Visit
		Commercially Confidential Information
Table 14.2.1.1.3	FAS/Exposed	Summary of Central Rater Categorical TETRAS-PS Item Scores by Study Visit
		Commercially Confidential Information
Table 14.2.1.1.5	FAS/Exposed	Summary of Local Rater TETRAS-PS Scores by Study Visit
Table 14.2.1.2.1	FAS/Exposed	Summary of Central Rater TETRAS-PS Upper Limb Subscale Scores by Study Visit
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Number	Population	Title
		Commercially Confidential Information
Table 14.2.1.2.4	FAS/Exposed	Summary of Local Rater TETRAS-PS Upper Limb Subscale Scores by Study Visit
Table 14.2.1.3.1	FAS/Exposed	Summary of Central Rater TETRAS-PS Upper Limb Tremor (Item 4) Total Scores by Study Visit
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Table 14.2.1.3.3	FAS/Exposed	Summary of Local Rater TETRAS-PS Upper Limb Tremor (Item 4) Total Scores by Study Visit

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13.3. Safety Data

Table 6: Safety Data

Number	Population	Title
Table 14.3.1.1	Safety	Summary of Adverse Events
Table 14.3.1.2	Safety	Incidence of Treatment Emergent Adverse Events by SOC and PT
Table 14.3.1.3	Safety	Incidence of Treatment Emergent Adverse Events by SOC, and PT, and Maximum Severity

Number	Population	Title
Table 14.3.1.4	Safety	Incidence of Treatment Emergent Adverse Events by SOC, PT, and Relationship
Table 14.3.2.1	Safety	Incidence of TEAEs Leading to Withdrawal of Study Drug by SOC and PT
Table 14.3.2.2	Safety	Incidence of Serious Adverse Events by SOC and PT
Table 14.3.3.1	Safety	Listing of Adverse Events Leading to Study Drug Discontinuation
Table 14.3.3.2	Safety	Listing of Serious Adverse Events
Table 14.3.3.3	Safety	Listing of Deaths
Table 14.3.4.1	Safety	Abnormal Laboratory Results
Table 14.3.5.1.1	Safety	Summary of Hematology Laboratory Results by Study Visit
Table 14.3.5.1.2	Safety	Shift from Baseline in Hematology Laboratory Results by Study Visit
Table 14.3.5.2.1	Safety	Summary of Serum Chemistry Laboratory Results by Study Visit
Table 14.3.5.2.2	Safety	Shift from Baseline in Serum Chemistry Laboratory Results by Study Visit
Table 14.3.5.3.1	Safety	Summary of Quantitative Urinalysis Laboratory Results by Study Visit
Table 14.3.5.3.2	Safety	Shift from Baseline in Quantitative Urinalysis Laboratory Results by Study Visit
Table 14.3.5.3.3	Safety	Summary of Qualitative Urinalysis Laboratory Results by Study Visit
Table 14.3.5.4.1	Safety	Summary of Quantitative Biomarker Panel for Renal Injury Results by Study Visit
Table 14.3.5.4.2	Safety	Geometric Mean (GM) Composite Measure (CM) on Quantitative Biomarker Panel for Renal Tubular Injury Results by Study Visit
Table 14.3.6.1.1	Safety	Summary of Vital Signs by Study Visit
Table 14.3.6.1.2	Safety	Shift from Baseline in Vital Signs by Study Visit
Table 14.3.6.1.3	Safety	Summary of Orthostatic Vital Signs by Study Visit
Table 14.3.6.1.4	Safety	Shift from Baseline in Orthostatic Vital Signs by Study Visit

Number	Population	Title
Table 14.3.6.1.5	Safety	Summary of Orthostatic Vital Signs Shift from Baseline Categories by Study Visit
Table 14.3.6.1.6	Safety	Summary of Orthostatic Hypotension by Study Visit
Table 14.3.6.2.1	Safety	Summary of 12-Lead Electrocardiogram by Study Visit
Table 14.3.6.2.2	Safety	Summary of 12-Lead Electrocardiogram Interpretation by Study Visit
Table 14.3.6.2.3	Safety	Summary of QTcF Values by Study Visit
Table 14.3.6.4	Safety	Summary of Columbia-Suicide Severity Rating Scale (C-SSRS)
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13.5. Planned Listing Descriptions

The following are planned data and subject data listings for protocol number CAD1883-201.

In general, one listing will be produced per CRF domain. All listings will be sorted by treatment, site, and subject number unless otherwise specified. 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 (eg, repetition of subject number), then only the first occurrence will be displayed.

In data listings, the information for one subject will be kept on one page if at all possible, rather than splitting a subject's information across pages. If a subject's data are displayed on extended to another page, the subject number will be displayed again at the top of any subsequent pages

Table 6: Planned Listings

Number	Population	Title
Listing 16.2.1.1	All Subjects	Subject Disposition
Listing 16.2.1.2	All Subjects	Visit Status
Listing 16.2.2.1	All Subjects	Descriptions of Protocol Defined Inclusion and Exclusion Criteria
Listing 16.2.2.2	All Subjects	Inclusion and Exclusion Criteria Met/Not Met
Listing 16.2.2.3	All Subjects	Protocol Deviations
Listing 16.2.3	All Subjects	Analysis Populations
Listing 16.2.4.1	All Subjects	Demographics and Baseline Characteristics
Listing 16.2.4.2	All Subjects	Medical History
Listing 16.2.4.3	All Subjects	Disease History
Listing 16.2.5.1	All Subjects	Study Drug Administration
Listing 16.2.5.2	All Subjects	Drug Accountability
Listing 16.2.5.3	All Subjects	Missed Doses

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Listing 16.2.6.1.1	All Subjects	Local TETRAS Performance Subscale and Upper Limb Subscale Scores
Listing 16.2.6.1.2	All Subjects	Central TETRAS Performance Subscale and Upper Limb Subscale Scores

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Number	Population	Title
	Commercially Confidential	Information
Listing 16.2.6.6	All Subjects	Wearable Sensor (Kinesia) Scores
Listing 16.2.7	All Subjects	Adverse Events
Listing 16.2.8.1.1	All Subjects	Clinical Laboratory Data: Hematology
Listing 16.2.8.1.2	All Subjects	Clinical Laboratory Data: Serum Chemistry
Listing 16.2.8.1.3	All Subjects	Clinical Laboratory Data: Urinalysis
Listing 16.2.8.1.4	All Subjects	Clinical Laboratory Data: Biomarker Panel for Renal Tubular Injury
Listing 16.2.8.1.5	All Subjects	Clinical Laboratory Data: Urine Pregnancy Test
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Listing 16.2.8.1.7	Safety Population	Clinical Laboratory Data: Biomarker Panel for Renal Tubular Injury
Listing 16.2.8.2.1	All Subjects	Physical Examination
Listing 16.2.8.2.2	All Subjects	Neurological Examination
Listing 16.2.8.3.1	All Subjects	Vital Signs
Listing 16.2.8.3.2	All Subjects	Blood Pressure and Orthostatic Vital Signs
Listing 16.2.8.4.1	All Subjects	Qualitative 12-Lead Electrocardiogram (ECG) Investigator Results
Listing 16.2.8.4.2	All Subjects	12-Lead Electrocardiogram (ECG) Central Results
	Commercially Confidential	Information
Listing 16.2.8.6	All Subjects	Columbia-Suicide Severity Rating Scale (C-SSRS)

13.6. Planned Figure Descriptions

The following are planned summary figures for protocol number CAD1883-201. The figure numbers and page numbers are place holders only and will be determined when the figures are produced.

Table 7: Planned Figures

Number	Population	Title
		Commercially Confidential Information
Figure 14.2.1.1.4	FAS	Central and Local TETRAS-PS Total Scores by Study Visit
		Commercially Confidential Information
Figure 14.2.1.2.3	FAS	Central and Local TETRAS-PS Upper Limb Subscale Scores by Study Visit
		Commercially Confidential Information
Figure 14.2.1.3.2	FAS	Central and Local TETRAS-PS Upper Limb Tremor (Item 4) Scores by Study Visit
		Commercially Confidential Information
Figure 14.2.6.1	FAS	TETRAS-PS and Wearable Sensor (Kinesia) Upper Limb Tremor Scores by Study Visit
		Commercially Confidential Information
Figure 14.5	Safety	Geometric Mean (GM) Composite Measure (CM) of Kidney Injury Biomarkers by Study Visit

14. Tables, Listings, and Listing Shells

14.1. Standard Layout for all Tables, Listings, and Figures

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

Figure 1: Standardized Layout

Cadent Therapeutics, Inc.	Page xx of xx
Protocol: CAD1883-201	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>*	

Note:

- "Page x of x" should be aligned to the right. Page x of y is for individual TLF only, not for the entire table sets. For example there are 2 pages for T14.1.1, then it will be Page 1 of 2 and Page 2 of 2 respectively.
- Keep one space line only between TLF title and page headers
- Keep "program path and name" on the left while align "Run Date: ..." to the right
- Keep one more decimal place for SD than for mean
- Add "Missing" category where missing value is available
- keep under TLF abbreviations in alphabetical order
- keep different footnotes separately in different lines.
- For any conditions coded by SOC and PT, please sort the SOC by alphabetical order, and sort the PT under SOC by decreasing frequency in the overall column, unless specified otherwise.

14.2. Planned Table Shells

See Figure 2 below.

Figure 2: Planned Table Shells

Table 14.1.1
Subject Disposition
All Enrolled Subjects

Category	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Enrolled	XX	XX	XX
Analysis Populations:			
Safety Population [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
FAS Population [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Commercially Confidential Information	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Per-Protocol Population [4]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Completed Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Prematurely Discontinued from Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for Discontinuation:			
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%)
Newly Emerged Exclusion Criteria During Study	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%)
Pregnancy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Protocol Violation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Study Terminated by Sponsor	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Withdrawal by Subject	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: ADL = activities of daily living; FAS = full analysis set; ICF = informed consent form; CCI ; PS = performance subscale; TETRAS = Tremor Research Group Essential Tremor Rating Assessment Scale.
Note: Cohort-1 is composed of subjects enrolled under the Protocol Amendment 1. Protocol Amendment 1 was finalized on 03 Dec 2018 with dosing interval of 8±2 hours during entire treatment period (Day 1-14). Cohort-2 is composed of subjects enrolled under Amentment 2 or 3. Amendment 2 was finalized on 09 May 2019 and Amendment 3 on 09 July 2019. Dosing interval was changed to 4-5 hours on Days 1, 7 and 14 in both Amendments 2 and 3.
Percentages are n/Number of subjects in the enrolled*100.
[1] The Safety population includes all subjects who took at least 1 dose of study drug.
[2] The FAS consists of subjects in the Safety Population at least one TETRAS-PS assessment Total Score at Day 7, Day 14 or early termination visit. The FAS will be used to summarize all efficacy data.
[3] Commercially Confidential Information
[4] The Per-Protocol Population includes all subjects in the FAS who did not have any major protocol deviation and follow the study protocol for TRETRAS-PS assessment.
Personal Protected Data

Source: Listing 16.2.1.1

Table 14.1.2.1
Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Age (years)			
N	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Sex			
Male	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Female	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Child-Bearing Potential? [1]			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	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%)
Race			
American Indian or Alaska Native	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Asian	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Black or African-American	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Native Hawaiian or Other Pacific Islander	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
White	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Unknown	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
More than One Race	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety Population*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety Population.
SOURCE: Listing 16.2.4.1

Table 14.1.2.1 (cont.)
Demographics and Baseline Characteristics
Safety Population

Variable Statistic or Category	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Height (cm)			
N	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Weight (kg)			
N	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX

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Note: Percentages are n/Number of subjects in the Safety Population*100.
[1] Only captured for female subjects; percentages are based on the number of female subjects in the Safety Population.
SOURCE: Listing 16.2.4.1

Programming note: keep one decimal place for HT, WT CCI statistics except n.

Table 14.1.2.2
Disease History
Safety Population

Variable Statistic or Category	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Time Since First ET Symptom (days)			
N	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Time Since ET Diagnosis (days)			
N	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Treatment Type			
Medication	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Herbal Remedy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exercise	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Biofeedback	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Deep Brain Stimulator	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ultrasound Thalamotomy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Response Type			
Adequate Relief	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Some Relief (Partial Response)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No Relief	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviation: ET = Essential Tremor, Max=Maximum, Min=Minimum, SD=Standard Deviation.
Note: Percentages are n/Number of subjects in the Safety Population*100. Partial dates of first ET symptom or dates of ET diagnosis will be derived according to Section 6.1.9 of the statistical analysis plan.
SOURCE: Listing 16.2.4.3

Table 14.1.2.2 (cont.)
Disease History
Safety Population

Variable Statistic or Category	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Trigger Type			
Stress	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Food	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Diurnal Fluctuation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Season	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Travel	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Frequency of Trigger			
Rarely	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Occasionally	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Often	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Daily	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Did Alcohol Use Reduce Tremor Severity?			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Applicable	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
First or Second Degree Blood Relative Diagnosed with ET?			
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviation: ET = essential tremor.
Note: Percentages are n/Number of subjects in the Safety Population*100.
SOURCE: Listing 16.2.4.3

Table 14.1.3
Summary of Medical History by SOC and PT
Safety Population

System Organ Class Preferred Term	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Subjects with at least 1 Recorded Medical 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: PT = preferred term; SOC = system organ class.
Note: Percentages are n/Number of subjects in the Safety Population*100.
Medical histories were coded using MedDRA version 21.1.
Subjects were counted once for each SOC and once for each PT.
Medical history terms are displayed by alphabetical order of SOC, then by decreasing frequency of PT within SOC, and then alphabetically by PT.
SOURCE: Listing 16.2.4.2

Programming note: *ATC & PT text should be in title case in table, as shown in the shell. Ensure proper MedDRA version is printed in footnote.*

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Table 14.1.5.1
Summary of Treatment Exposure and Compliance via Capsule Count
Safety Population

Variable Statistic	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Number of Doses Taken			
n	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Number of Missed Doses			
n	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Compliance (%)			
n	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Compliance Category			
< 70%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
≥ 70% to 79%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
≥ 80% to 89%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
≥ 90% to 100%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 100%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety Population*100. Subjects were to receive treatment twice daily for 14 consecutive days for a total of 28 doses. Compliance is number of doses taken / number of expected doses * 100%. Number of doses taken is calculated as the number of expected doses (number of capsules dispensed) minus total number of pills not taken minus number of unused capsules returned, as collected in the case report form. Expected doses are summed up to the point of discontinuation (eg, if a subject discontinues early, only planned doses up to that discontinuation day are counted in the denominator).
SOURCE: Listings 16.2.5.1, 16.2.5.2, and 16.2.5.3

Table 14.1.5.2

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Table 14.2.1.1.1
Summary of Central Rater TETRAS-PS Scores by Study Visit
FAS and Per-Protocol Population

Parameter: TETRAS-PS Total Score

Study Visit Statistic	Full Analysis Set Cohort-1 (N=XX)	 Cohort-2 (N=XX)	 Overall (N=XX)	Per-Protocol Population Cohort-1 (N=XX)	 Cohort-2 (N=XX)	 Overall (N=XX)
Screening						
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
Baseline [1]						
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
Change from Screening						
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
Mean Change from Screening (SE) [2]	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for Mean Change from Screening)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
P value for Mean Change from Screening [3]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
P value for Median Change from Screening [4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

Abbreviations: CI = confidence interval; TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS); SE = standard error.
Note: TETRAS-PS Total score is derived as the sum of all of the individual item scores, with the exception of item 5, only the maximum of the lower limb tremor scores will be counted. Each individual item question score ranges from 0 to 4, where higher scores indicate worse performance. A negative change indicates improvement.
[1] The baseline value is the last observation recorded prior to the first dose of treatment.
[2] Estimates for mean change from screening/baseline and accompanying 95% CIs and P values are from a paired t-test
[3] P-value for testing mean change from screening/baseline is based on a paired t-test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
[4] P-value for testing median change from screening/baseline is based on a Wilcoxon signed-rank test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
SOURCE: Listing 16.2.6.1.1

Table 14.2.1.1.1 (cont.)

Summary of Central Rater TETRAS-PS Scores by Study Visit
FAS and Per-Protocol Population

Parameter: TETRAS-PS Total Score

	Full Analysis Set			Per-Protocol Population		
Study Visit Statistic	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
% Change from Screening						
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
Day 1, Post-dose						
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
Change from Baseline						
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; ET = essential tremor; TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS); SE = standard error.
Note: TETRAS-PS Total score is derived as the sum of all of the individual item scores, with the exception of item 5, only the maximum of the lower limb tremor scores will be counted. Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life. A negative change indicates improvement.
[1] The baseline value is the last observation recorded prior to the first dose of treatment.
[2] Estimates for mean change from screening/baseline and accompanying 95% CIs and P values are from a paired t-test
[3] P-value for testing mean change from screening/baseline is based on a paired t-test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
[4] P-value for testing median change from screening/baseline is based on a Wilcoxon signed-rank test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
SOURCE: Listing 16.2.6.1.1

Table 14.2.1.1.1 (cont.)
Summary of Central Rater TETRAS-PS Scores by Study Visit
FAS and Per-Protocol Population

Parameter: TETRAS-PS Total Score

	Full Analysis Set			Per-Protocol Population		
Study Visit Statistic	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Mean Change from Baseline (SE) [2]	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for Mean Change from Baseline)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
P value for Mean Change from Baseline [3]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
P value for Median Change from Baseline [4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
% Change from Baseline						
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

Continue for Days 7 and 14,.

Day 21						
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; ET = essential tremor; TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS); SE = standard error.
Note: TETRAS-PS Total score is derived as the sum of all of the individual item scores, with the exception of item 5, only the maximum of the lower limb tremor scores will be counted. Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life. A negative change indicates improvement.
[1] The baseline value is the last observation recorded prior to the first dose of treatment.
[2] Estimates for mean change from screening/baseline and accompanying 95% CIs and P values are from a paired t-test
[3] P-value for testing mean change from screening/baseline is based on a paired t-test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
[4] P-value for testing median change from screening/baseline is based on a Wilcoxon signed-rank test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
SOURCE: Listing 16.2.6.1.1

Table 14.2.1.1.1 (cont.)
Summary of Central Rater TETRAS-PS Scores by Study Visit
FAS and Per-Protocol Population

Parameter: TETRAS-PS Total Score

	Full Analysis Set			Per-Protocol Population		
Study Visit Statistic	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
Change from Baseline						
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
Mean Change from Baseline (SE) [2]	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for Mean Change from Baseline)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
P value for Mean Change from Baseline [3]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
P value for Median Change from Baseline [4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
% Change from Baseline						
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; ET = essential tremor; TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS); SE = standard error.
Note: TETRAS-PS Total score is derived as the sum of all of the individual item scores, with the exception of item 5, only the maximum of the lower limb tremor scores will be counted. Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life. A negative change indicates improvement.
[1] The baseline value is the last observation recorded prior to the first dose of treatment.
[2] Estimates for mean change from screening/baseline and accompanying 95% CIs and P values are from a paired t-test
[3] P-value for testing mean change from screening/baseline is based on a paired t-test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
[4] P-value for testing median change from screening/baseline is based on a Wilcoxon signed-rank test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
SOURCE: Listing 16.2.6.1.1

Table 14.2.1.1.1 (cont.)
Summary of Central Rater TETRAS-PS Scores by Study Visit
FAS and Per-Protocol Population

Parameter: TETRAS-PS Total Score

Study Visit Statistic	Full Analysis Set Cohort-1 (N=XX)	 Cohort-2 (N=XX)	 Overall (N=XX)	Per-Protocol Population Cohort-1 (N=XX)	 Cohort-2 (N=XX)	 Overall (N=XX)
Change from Day 14						
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
Mean Change from Day 14 (SE) [2]	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
(95% CI for Mean Change from Day 14)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
P value for Mean Change from Day 14 [3]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
P value for Median Change from Day 14 [4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
% Change from Day 14						
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; ET = essential tremor; TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS); SE = standard error.
Note: TETRAS-PS Total score is derived as the sum of all of the individual item scores, with the exception of item 5, only the maximum of the lower limb tremor scores will be counted. Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life. A negative change indicates improvement.
[1] The baseline value is the last observation recorded prior to the first dose of treatment.
[2] Estimates for mean change from screening/baseline and accompanying 95% CIs and P values are from a paired t-test
[3] P-value for testing mean change from screening/baseline is based on a paired t-test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
[4] P-value for testing median change from screening/baseline is based on a Wilcoxon signed-rank test with null hypothesis that the change in TETRAS-PS total score to subsequent visit is 0 with a 2-sided alternative considering a difference not equal to 0 (change in tremor).
SOURCE: Listing 16.2.6.1.1

Programming Note: *Continue for all parameters. Parameters include: Head Tremor, Face (including jaw) Tremor, Voice Tremor, Upper Limb Tremor: Forward Outstretched Postural Tremor-Right, Upper Limb Tremor: Forward Outstretched Postural Tremor-Left, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Right, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Left, Upper Limb Tremor: Kinetic Tremor-Right, Upper Limb Tremor: Kinetic Tremor-Left, Lower Limb Tremor: Extended-Right, Lower Limb Tremor: Extended-Left, Lower Limb Tremor: Heel-Shin-Right, Lower Limb Tremor: Heel-Shin-Left, Archimedes Spirals-Right, Archimedes Spirals-Left, Handwriting, Dot Approximation Task-Right, Dot Approximation Task-Left, and Standing Tremor. Change from Screening should only be presented after the baseline visit.*

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Table 14.2.1.1.3
Summary of Central Rater Categorical TETRAS-PS Item Scores by Study Visit
FAS and Per-Protocol Population

Protocol Amendment: 1.0

	Full Analysis Set				Per-Protocol Population			
Item Score	Baseline [1] (N=XX)	Day 7 (N=XX)	Day 14 (N=XX)	Day 21 (N=XX)	Baseline [1] (N=XX)	Day 7 (N=XX)	Day 14 (N=XX)	Day 21 (N=XX)
Head Tremor								
0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
0.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Face (including jaw) Tremor								
0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
0.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3.5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS).
Note: Percentages are n/Number of subjects in the respective population and cohort at each visit*100. TETRAS-PS Total score is derived as the sum of all of the individual item scores, with the exception of item 5, only the maximum of the lower limb tremor scores will be counted. Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life.
[1] The baseline value is the last observation recorded prior to the first dose of treatment.
SOURCE: Listing 16.2.6.1.1

Programming note: *Continue for Cohort-2 and Overall. Items include: Head Tremor, Face (including jaw) Tremor, Voice Tremor, Upper Limb Tremor: Forward Outstretched Postural Tremor-Right, Upper Limb Tremor: Forward Outstretched Postural Tremor-Left, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Right, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Left, Upper Limb Tremor: Kinetic Tremor-Right, Upper Limb Tremor: Kinetic Tremor-Left, Lower Limb Tremor: Extended-Right, Lower Limb Tremor: Extended-Left, Lower Limb Tremor: Heel-Shin-Right, Lower Limb Tremor: Heel-Shin-Left, Archimedes Spirals-Right, Archimedes Spirals-Left, Handwriting, Dot Approximation Task-Right, Dot Approximation Task-Left, and Standing Tremor.*

Table 14.2.1.1.4

Correlation between Central and Local TETRAS-PS Scores by Study Visit
FAS and Per-Protocol Population

Parameter: TETRAS-PS Total Score

	Full Analysis Set			Per-Protocol Population		
		Cohort-2			Cohort-2	
Study Visit Statistic	Cohort-1 (N=XX)	 (N=XX)	Overall (N=XX)	Cohort-1 (N=XX)	 (N=XX)	Overall (N=XX)
Screening						
Correlation [1]	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
P-Value [2]	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
Baseline [3]						
Correlation	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
P-Value	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
Day 1, Post-dose						
Correlation	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
P-Value	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX

Continue for Days 7, 14, and 21 and all parameters.

Abbreviations: TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS).
Note: TETRAS-PS Total score is derived as the sum of all of the individual item scores, with the exception of item 5, only the maximum of the lower limb tremor scores will be counted. Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life.
[1] Pearson correlation coefficient is presented for all study visits.
[2] P-value for testing the correlation is 0.
[3] The baseline value is the last observation recorded prior to the first dose of treatment.
SOURCE: Listings 16.2.6.1.1, 16.2.6.1.2

Programming Note: *Check Section 8.3.2 of SAP. If Spearman correlation coefficient is used, update footnote [1] accordingly.*

Table 14.2.1.1.5
Summary of Local Rater TETRAS-PS Scores by Study Visit
FAS and Per-Protocol Population

Same shell as Table 14.2.1.1.1

Programming Note: *Continue for all parameters. Parameters include: Head Tremor, Face (including jaw) Tremor, Voice Tremor, Upper Limb Tremor: Forward Outstretched Postural Tremor-Right, Upper Limb Tremor: Forward Outstretched Postural Tremor-Left, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Right, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Left, Upper Limb Tremor: Kinetic Tremor-Right, Upper Limb Tremor: Kinetic Tremor-Left, Lower Limb Tremor: Extended-Right, Lower Limb Tremor: Extended-Left, Lower Limb Tremor: Heel-Shin-Right, Lower Limb Tremor: Heel-Shin-Left, Archimedes Spirals-Right, Archimedes Spirals-Left, Handwriting, Dot Approximation Task-Right, Dot Approximation Task-Left, and Standing Tremor. Change from Screening should only be presented after the baseline visit.*

Table 14.2.1.2.1
Summary of Central Rater TETRAS-PS Upper Limb Subscale Scores by Study Visit
FAS and Per-Protocol Population

Same shell as Table 14.2.1.1.1

Programming Note: *Parameter will be TETRAS-PS Upper Limb Subscale Score, Upper Limb Tremor: Forward Outstretched Postural Tremor-Right, Upper Limb Tremor: Forward Outstretched Postural Tremor-Left, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Right, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Left, Upper Limb Tremor: Kinetic Tremor-Right, Upper Limb Tremor: Kinetic Tremor-Left, Archimedes Spirals-Right, Archimedes Spirals-Left, Handwriting, Dot Approximation Task-Right, and Dot Approximation Task-Left. Update footnote to read "The TETRAS Upper limb subscale score is the sum of the item 4, item 6, item 7 and item 8 scores (forward outstretched postural tremor, lateral "wing beating" postural tremor, kinetic tremor, Archimedes spirals, and dot approximation task from both sides of the body, as well as handwriting. The upper limb individual item question scores for each side of the body range from 0 to 4, with higher scores indicating more tremors. A negative change indicates improvement."*

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Table 14.2.1.2.3
Correlation between Central and Local TETRAS-PS Upper Limb Subscale Scores by Study Visit
FAS and Per-Protocol Population

Same shell as Table 14.2.1.1.4

Programming Note: *Update footnote to read "The TETRAS Upper limb subscale score is the sum of the item 4, item 6, item 7 and item 8 scores (forward outstretched postural tremor, lateral "wing beating" postural tremor, kinetic tremor, Archimedes spirals, and dot approximation task from both sides of the body, as well as handwriting. The upper limb individual item question scores for each side of the body range from 0 to 4, with higher scores indicating more tremors."*

Table 14.2.1.2.4
Summary of Local Rater TETRAS-PS Upper Limb Subscale Scores by Study Visit
FAS and Per-Protocol Population

Same shell as Table 14.2.1.1.1

Programming Note: *Parameter will be TETRAS-PS Upper Limb Subscale Score, Upper Limb Tremor: Forward Outstretched Postural Tremor-Right, Upper Limb Tremor: Forward Outstretched Postural Tremor-Left, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Right, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Left, Upper Limb Tremor: Kinetic Tremor-Right, Upper Limb Tremor: Kinetic Tremor-Left, Archimedes Spirals-Right, Archimedes Spirals-Left, Handwriting, Dot Approximation Task-Right, and Dot*

Approximation Task-Left. Update footnote to read "The TETRAS Upper limb subscale score is the sum of the item 4, item 6, item 7 and item 8 scores (forward outstretched postural tremor, lateral "wing beating" postural tremor, kinetic tremor, Archimedes spirals, and dot approximation task from both sides of the body, as well as handwriting. The upper limb individual item question scores for each side of the body range from 0 to 4, with higher scores indicating more tremors. A negative change indicates improvement."

Table 14.2.1.3.1
Summary of Central Rater TETRAS-PS Upper Limb Tremor (Item 4) Scores by Study Visit
FAS and Per-Protocol Population

Same shell as Table 14.2.1.1.1

Programming Note: *Parameters will be TETRAS-PS Upper Limb Tremor (Item 4) Score, Upper Limb Tremor: Forward Outstretched Postural Tremor-Right, Upper Limb Tremor: Forward Outstretched Postural Tremor-Left, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Right, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Left, Upper Limb Tremor: Kinetic Tremor-Right, Upper Limb Tremor: Kinetic Tremor-Left. Update footnote to read "The TETRAS-PS Upper Limb Tremor (Item 4) Total score is the sum of the 6 item 4 scores (forward outstretched postural tremor, lateral "wing beating" postural tremor, and kinetic tremor scores) from both sides of the body, as well as handwriting. The upper limb individual item question scores for each side of the body range from 0 to 4, with higher scores indicating more tremors. A negative change indicates improvement."*

Table 14.2.1.3.2
Correlation between Central and Local TETRAS-PS Upper Limb Tremor (Item 4) Scores by Study Visit
FAS and Per-Protocol Population

Same shell as Table 14.2.1.1.4

Programming Note: *Update footnote to read "The TETRAS-PS Upper Limb Tremor (Item 4) Total score is the sum of the 6 item 4 scores (forward outstretched postural tremor, lateral "wing beating" postural tremor, and kinetic tremor scores) from both sides of the body, The upper limb individual item question scores for each side of the body range from 0 to 4, with higher scores indicating more tremors."*

Table 14.2.1.3.3
Summary of Local Rater TETRAS-PS Upper Limb Tremor (Item 4) Scores by Study Visit
FAS and Per-Protocol Population

Same shell as Table 14.2.1.1.1

Programming Note: *Parameters will be TETRAS-PS Upper Limb Tremor (Item 4) Score, Upper Limb Tremor: Forward Outstretched Postural Tremor-Right, Upper Limb Tremor: Forward Outstretched Postural Tremor-Left, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Right, Upper Limb Tremor: Lateral Wing Beating Postural Tremor-Left, Upper Limb Tremor: Kinetic Tremor-Right, Upper Limb Tremor: Kinetic Tremor-Left. Update footnote to read "The TETRAS-PS Upper Limb Tremor (Item 4) Total score is the sum of the 6 item 4 scores (forward outstretched postural tremor, lateral "wing beating" postural tremor, and kinetic tremor scores) from both sides of the body, as well as handwriting. The upper limb individual item question scores for each side of the body range from 0 to 4, with higher scores indicating more tremors. A negative change indicates improvement."*

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Table 14.2.5.1
Summary of In-Clinic Wearable Sensor (Kinesia) by Study Visit
FAS and Per-Protocol Population

Same Shell as Table 14.2.1.1.1

Parameter: Kinesia Score, Side: Right, Task: Extended Arms Posture

	Full Analysis Set			Per-Protocol Population		
Study Visit Statistic	Protocol Amendment 1.0 (N=XX)	Protocol Amendment 2.0 or 3.0 (N=XX)	Overall (N=XX)	Cohort-1 (N=XX)	Protocol Amendment 2.0 or 3.0 (N=XX)	Overall (N=XX)

Programming Note: *Remove footnote describing TETRAS-PS. Update SOURCE: to Listing 16.2.6.6.1. Continue for all study days and the following:*
Parameter: Kinesia Score, Side: Right, Task: Wing-beating posture,
Parameter: Kinesia Score, Side: Right, Task: Kinetic "finger-to-chin" Movement,
Parameter: Kinesia Score, Side: Right, Task: Arm on Table Posture

Parameter: Kinesia Score, Side: Left, Task: Extended Arms Posture,
Parameter: Kinesia Score, Side: Left, Task: Wing-beating Posture,
Parameter: Kinesia Score, Side: Left, Task: Kinetic "finger-to-chin" Movement,
Parameter: Kinesia Score, Side: Left, Task: Arm on Table Posture

Parameter: Tremor Amplitude, Side: Right, Task: Extended Arms Posture,
Parameter: Tremor Amplitude, Side: Right, Task: Wing-beating Posture,
Parameter: Tremor Amplitude, Side: Right, Task: Kinetic "finger-to-chin" Movement,
Parameter: Tremor Amplitude, Side: Right, Task: Arm on Table Posture
Parameter: Tremor Amplitude, Side: Left, Task: Extended Arms Posture,
Parameter: Tremor Amplitude, Side: Left, Task: Wing-beating Posture,
Parameter: Tremor Amplitude, Side: Left, Task: Kinetic "finger-to-chin" Movement,
Parameter: Tremor Amplitude, Side: Left, Task: Arm on Table Posture

Parameter: Tremor Frequency, Side: Right, Task: Extended Arms Posture,
Parameter: Tremor Frequency, Side: Right, Task: Wing-beating Posture,
Parameter: Tremor Frequency, Side: Right, Task: Kinetic "finger-to-chin" Movement,
Parameter: Tremor Frequency, Side: Right, Task: Arm on Table Posture

Parameter: Tremor Frequency, Side: Left, Task: Extended Arms Posture,
Parameter: Tremor Frequency, Side: Left, Task: Wing-beating Posture,
Parameter: Tremor Frequency, Side: Left, Task: Kinetic "finger-to-chin" Movement,
Parameter: Tremor Frequency, Side: Left, Task: Arm on Table Posture

Parameter: Finger-Chin-Finger Quality, Side: Right, Task: Extended Arms Posture,
Parameter: Finger-Chin-Finger Quality, Side: Right, Task: Wing-beating Posture,
Parameter: Finger-Chin-Finger Quality, Side: Right, Task: Kinetic "finger-to-chin" Movement,
Parameter: Finger-Chin-Finger Quality, Side: Right, Task: Arm on Table Posture
Parameter: Finger-Chin-Finger Quality, Side: Left, Task: Extended Arms Posture,
Parameter: Finger-Chin-Finger Quality, Side: Left, Task: Wing-beating Posture,
Parameter: Finger-Chin-Finger Quality, Side: Left, Task: Kinetic "finger-to-chin" Movement,
Parameter: Finger-Chin-Finger Quality, Side: Left, Task: Arm on Table Posture

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Table 14.3.1.1
Summary of Adverse Events
Safety Population

Category	Cohort-1 (N=XX) Subjects n (%)	Cohort-1 (N=XX) Events	Cohort-2 (N=XX) Subjects n (%)	Cohort-2 (N=XX) Events	Overall (N=XX) Subjects n (%)	Overall (N=XX) Events
Subjects with at least 1 TEAE	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Maximum Severity of TEAE						
Mild	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Moderate	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Severe	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Subjects with a Related TEAE [1]	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Subjects with a TEAE Leading to Discontinuation of Study Drug	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Subjects with an AE leading to Death	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Subjects with at least 1 SAE	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Maximum Severity of SAE						
Mild	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Moderate	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Severe	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Subjects with a Related SAE [1]	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Subjects with a SAE Leading to Discontinuation of Study Drug	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Subjects with an SAE leading to Death	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX

Abbreviations: TEAE = treatment emergent adverse event; SAE = serious adverse event.
Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment*100. AEs were coded using MedDRA version 21.1. A TEAE is any AE that occurs after the time of treatment with the study agent. Events meeting this definition will be those events that are a change from the subject's baseline conditions, including an increase in frequency or severity.
[1] Related TEAEs are those marked as Possibly Related, Probably Related, or Definitely Related on the case report form.
SOURCE: Listing 16.2.7

Table 14.3.1.2
Incidence of Treatment Emergent Adverse Events by SOC and PT
Safety Population

System Organ Class Preferred Term	Cohort-1 (N=XX) Subjects n (%)	Events	Cohort-2 (N=XX) Subjects n (%)	Events	Overall (N=XX) Subjects n (%)	Events
Subjects with at least 1 TEAE	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
System Organ Class 1	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 1	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 2	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 3	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
System Organ Class 1	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 1	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 2	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 3	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX

Abbreviations: PT = preferred term; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment * 100.
AEs were coded using MedDRA version 21.1.
A TEAE is any AE that occurs after the time of treatment with the study agent. Events meeting this definition will be those events that are a change from the subject's baseline conditions, including an increase in frequency or severity.
Subjects are 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.
SOURCE: Listing 16.2.7

Programming note: *SOC & PT text should be in title case in table, as shown in the shell. Ensure correct MedDRA version is printed in footnote.*

Table 14.3.1.3
Incidence of Treatment Emergent Adverse Events by SOC, PT, and Maximum Severity
Safety Population

System Organ Class Preferred Term Maximum Severity	Cohort-1 (N=XX) Subjects n (%)	Events	Cohort-2 (N=XX) Subjects n (%)	Events	Overall (N=XX) Subjects n (%)	Events
Subjects with at least 1 TEAE	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Any Event (Total)						
Mild	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Moderate	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Severe	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
System Organ Class 1						
Any Event (Total)						
Mild	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Moderate	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Severe	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 1						
Mild	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Moderate	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Severe	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX

Abbreviations: PT = preferred term; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment *100.
AEs were coded using MedDRA version 21.1.
A TEAE is any AE that occurs after the time of treatment with the study agent. Events meeting this definition will be those events that are a change from the subject's baseline conditions, including an increase in frequency or severity.
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.
SOURCE: Listing 16.2.7

Programming note: *SOC & PT text should be in title case in table, as shown in the shell. Ensure correct MedDRA version is printed in footnote.*

Table 14.3.1.4
Incidence of Treatment Emergent Adverse Events by SOC, PT, and Relationship
Safety Population

System Organ Class Preferred Term Relationship	Cohort-1 (N=XX) Subjects n (%)	Events	Cohort-2 (N=XX) Subjects n (%)	Events	Overall (N=XX) Subjects n (%)	Events
Subjects with at least 1 TEAE	XX (XX.X%)		XX (XX.X%)		XX (XX.X%)	
Any Event (Total)						
Related	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Not Related	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
System Organ Class 1						
Any Event (Total)						
Related	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Not Related	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Preferred Term 1						
Related	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX
Not Related	XX (XX.X%)	XX	XX (XX.X%)	XX	XX (XX.X%)	XX

Abbreviations: CRF = case report form; PT = preferred term; SOC = system organ class; TEAE = treatment emergent adverse event.
Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment *100.
AEs were coded using MedDRA version 21.1.
A TEAE is any AE that occurs after the time of treatment with the study agent. Events meeting this definition will be those events that are a change from the subject's baseline conditions, including an increase in frequency or severity.
Subjects are counted once for each SOC and once for each PT.
Subjects are classified according to the strongest relationship if the subject reported one or more events. Related TEAEs are those marked as Possibly Related, Probably Related, or Definitely Related on the CRF. AEs with a missing relationship will be considered related for this summary.
AEs are displayed by descending frequency of SOC, then PT within SOC, and then alphabetically by PT.
SOURCE: Listing 16.2.7

Programming note: *SOC & PT text should be in proper case in table, as shown in the shell. Ensure correct MedDRA version is printed in footnote.*

Table 14.3.2.1
Incidence of TEAEs Leading to Withdrawal of Study Drug by SOC and PT
Safety Population

Same shell as Table 14.3.1.2

Table 14.3.2.2
Incidence of Serious Adverse Events by SOC and PT
Safety Population

Same shell as Table 14.3.1.2

Programming note: *Add SAE to abbreviations.*

Table 14.3.3.1
Listing of Adverse Events Leading to Study Drug Discontinuation
All Subjects

Subject ID	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day) Start Time/ End Date (Study Day) End Time	Severity/ Relationship	Outcome/ Study Drug Action Taken/ Other Action Taken	TEAE?/ Serious?/ Criteria Met
XXXXXX	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY/HH:MM (XX)/ DDMMMYYYY/HH:MM (XX)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXXXX/ XXXXXXXXXXXXX/ XXXXXXXXXXXXXXX	XX/ XXX/ XXXXXXXXX
	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	DDMMMYYYY/HH:MM (XX)/ DDMMMYYYY/HH:MM (XX)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXXXXX	XX/ XX
	XXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX	DDMMMYYYY/HH:MM (XX)/ DDMMMYYYY/HH:MM (XX)	XXXXXXX/ XXXXXXX	XXXXXXXXXXXXXX	XX/ XX

Abbreviation: TEAE = treatment emergent adverse event.
Note: Study day is calculated relative to the date of first dose. For pre-dose: study day= Start Date/ Stop Date – first dose date; For post-dose: study day= Start Date/ Stop Date – first dose date + 1.
AEs were coded using MedDRA version 21.1.
A TEAE is any AE that occurs after the time of treatment with the study agent. Events meeting this definition will be those events that are a change from the subject's baseline conditions, including an increase in frequency or severity.

Programming note: *"Other Action Taken" will be either None, Medication Required, Relevant Procedure, or Other; if specify text is needed, concatenate "Relevant Procedure:" or "Other:" with the text. If Serious? Is Yes, concatenate all serious criteria marked as Yes with a semicolon. If no events meet the criteria for display, present "No events are reported." SOC & PT text should be in proper case in table, as shown in the shell. Ensure correct MedDRA version is printed in footnote.*

Table 14.3.3.2
Listing of Serious Adverse Events
Safety Population

Same shell as Table 14.3.3.1

Table 14.3.3.3
Listing of Deaths
Safety Population

Same shell as Table 14.3.3.1

Table 14.3.4.1
Abnormal Laboratory Results
Safety Population

Subject ID	Treatment Received	Parameter (unit)	Study Visit	Date/Time of Assessment (Study Day)	Standard Results	Change from Baseline [1]	Reference Range [2]	Reference Range Flag	Lab Panel	Comments/Reason Not Done
XXXXXX	CAD-1883	Hemoglobin (unit)	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY		XXXXXXX	
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY		XXXXXXX	
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY	XXX	XXXXXXX	
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY		XXXXXXX	
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY		XXXXXXX	
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY		XXXXXXX	
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY		XXXXXXX	
			XXXXXX		ND					XXXXXXX
			XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX	XX – YY		XXXXXXX	

Abbreviations: AL = abnormal-low; AH = abnormal-high; CS = clinically significant; NCS = not clinically significant; ND = not done.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Start Date/ Stop Date – first dose date; For post-dose: study day= Start Date/ Stop Date – first dose date + 1.
If any parameter has an abnormal value, results for all study visits are presented.
[1] Baseline is the last observation recorded prior to the first dose of treatment.
[2] Reference range is used to identify potentially clinically significant laboratory values.

Programming note: *update abbreviations to reflect actual data. If test was not done, set results to ND; make sure last column is populated accordingly. Do not display serum HCG results in this listing. For reference range flag, concatenate AL or AH with clinical significance like "XX-YY" (eg, AL-CS).*

Table 14.3.5.1.1
Summary of Hematology Laboratory Results by Study Visit
Safety Population

Parameter: XXXXXXXXXXXX

Study Visit Statistic	Cohort-1 (N=XX)	Cohort-2 (N=XX)	Overall (N=XX)
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 [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
Day 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
Change from Baseline			
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

[1] The baseline value for each variable is the last observation recorded prior to the first dose of treatment.
SOURCE: Listing 16.2.8.1.1

Programming Note: *Continue all parameters for Day 7, Day 14, and Day 21. Sort alphabetically by parameter.*

Table 14.3.5.1.2
Shift from Baseline in Hematology Laboratory Results by Study Visit and Treatment
Safety Population

Parameter: XXXXXXX

	Baseline [1]				
	Cohort-1 (N=XX)				
Study Visit Category	Low n (%)	Normal n (%)	High n (%)	Abnormal n (%)	Missing n (%)
Day 7					
Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 14					
Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 21					
Low	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
High	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment*100.
[1] The baseline value for each variable is the last observation recorded prior to the first dose of treatment.
SOURCE: Listing 16.2.8.1.1

Programming Note: *Continue all parameters, for Protocol Version: 2.0 or 3.0 and Overall as well as for Day 7, Day 14, and Day 21. Sort alphabetically by parameter.*

Table 14.3.5.2.1
Summary of Serum Chemistry Laboratory Results by Study Visit
Safety Population

Same shell as Table 14.3.5.1.1
Programming note: *Update footnote to SOURCE: Listing 16.2.8.1.2*

Table 14.3.5.2.2
Shift from Baseline in Serum Chemistry Laboratory Results by Study Visit
Safety Population

Same shell as Table 14.5.1.2
Programming note: *Update footnote to SOURCE: Listing 16.2.8.1.2*

Table 14.3.5.3.1
Summary of Quantitative Urinalysis Laboratory Results by Study Visit
Safety Population

Same shell as Table 14.3.5.1.1
Programming note: *Update footnote to SOURCE: Listing 16.2.8.1.3*

Table 14.3.5.3.2
Shift from Baseline in Quantitative Urinalysis Laboratory Results by Study Visit
Safety Population

Same shell as Table 14.3.5.1.2
Programming note: *Update footnote to SOURCE: Listing 16.2.8.1.3*

Table 14.3.5.3.3
Summary of Qualitative Urinalysis Laboratory Results by Study Visit
Safety Population

Parameter: XXXXXXXX

Study Visit Category	Cohort-1 (N=XX) n (%)	Cohort-2 (N=XX) n (%)	Overall (N=XX) n (%)
Screening			
Category 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Baseline [1]			
Category 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 1			
Category 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 7			
Category 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 14			
Category 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 21			
Category 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Category 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment*100.
[1] The baseline value for each variable is the last observation recorded prior to the first dose of treatment.
SOURCE: Listing 16.2.8.1.3

Programming Note: *Continue all parameters. Sort alphabetically by parameter.*

Table 14.3.5.4.1
Summary of Quantitative Biomarker Panel for Renal Tubular Injury Results by Study Visit
Safety Population

Parameter: uCreatine (uCr); CAD-1883 Treatment 300mg BID

	Cohort-1 (N=XX)		Cohort-2 (N=XX)		Overall (N=XX)	
Study Visit Statistic	Results (Measured) ng/mL	Results (Measured) ng/mL	Results (Normalized) ng/mg Cr	Results (Normalized) ng/mg Cr	Results (Normalized) ng/mg Cr	Results (Normalized) ng/mg Cr
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Min, Max	x, xxx	x, xxx	x, xxx	x, xxx	x, xxx	x, xxx
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
Median	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Min, Max	x, xxx	x, xxx	x, xxx	x, xxx	x, xxx	x, xxx
Fold Change from Baseline to Day 1						
n	-	-	xx	xx	xx	xx
Mean (SD)	-	-	xx.xxx (xx.xxxx)	xx.xxx (xx.xxxx)	xx.xxx (xx.xxxx)	xx.xxx (xx.xxxx)
Median	-	-	x.xxx	x.xxx	x.xxx	x.xxx
Min, Max	-	-	x.xx, xx.xx	x.xx, xx.xx	x.xx, xx.xx	x.xx, xx.xx

BID=Twice a day, SD=Standard Deviation, Min=Minimum, Max=Maximum.

Note: The normalized concentration at a given time point is calculated as the concentration at that time point divided by the concentration of uCreatinine (mg/dL) at the same time point. Fold Change from Baseline at a given time point is calculated as the normalized concentration at the time point divided by the normalized concentration at baseline.

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[1] The baseline value for each measure is the last observation recorded prior to the first dose of treatment.

SOURCE: Listing 16.2.8.1.4.

Programming note:
Parameters are uCreatine (uCr)), uClusterin (uCLU) , uCystatin-C (uCysC), uKidney Injury Molecule-1 (uKIM-1), u N-Acetyl-beta-D-Glucosaminidase (uNAG), Neutrophil Gelatinase-Associated Lipocalin (uNGAL) and uOsteopontin (uOPN).
Keep the decimal places as exactly the same as what is shown in this table shells
Exten the table for visits Day 7, 14 and 21.

Table 14.3.5.4.2

Geometric Mean (GM) Composite Measure (CM) on Quantitative Biomarker Panel for Renal Tubular Injury Results by Study Visit
Safety Population

Visit	Number of Subjects (N=xx)	GM CM
Baseline	xx	x.xx
Day 1	xx	x.xx
Day 7	xx	x.xx
Day 14	xx	x.xx
Day 21	xx	x.xx

GM CM = Geometric Mean (GM) Composite Measure (CM)

Programming note: *Update footnote to SOURCE: Listing 16.2.8.1.4*

Table 14.3.6.1.1
Summary of Vital Signs by Study Visit
Safety Population

Same shell as Table 14.3.5.1.1

Programming note: *Visits include Screening, Baseline, Day 1, Day 7 Pre-Dose, Day 7 Post-Dose, Day 14 Pre-Dose, Day 14 Post-Dose, and Day 21; parameters include Temperature (C), Respiration Rate (breaths per min), Systolic Blood Pressure (mmHg), Heart Rate (bpm), Diastolic Blood Pressure (mmHg), and Weight (kg); SOURCE: Listing 16.2.8.3.1, Listing 16.2.8.3.2.*

Table 14.3.6.1.2
Shift from Baseline in Vital Signs by Study Visit
Safety Population

Same shell as Table 14.3.5.1.2

Programming note: *Visits include Screening, Baseline, Day 1, Day 7 Pre-Dose, Day 7 Post-Dose, Day 14 Pre-Dose, Day 14 Post-Dose, and Day 21; parameters include Temperature (C), Respiration Rate (breaths per min), Systolic Blood Pressure (mmHg), Heart Rate (bpm), Diastolic Blood Pressure (mmHg), and Weight (kg); Add the following footnote: "Abnormal vital signs are as follows.* CCI *SBP >140 mmHg, SBP <90 mmHg, DBP >90 mmHg, DBP <60 mmHg, HR >100 bpm, HR <60 bpm, Respiration rate >20 breaths/min, Respiration rate <12 breaths/min, Oral temperature >99.1 ºF/37.2 ºC, Oral temperature <97.8 ºF/36.5 ºC" Update footnote to SOURCE: Listing 16.2.8.3.1, Listing 16.2.8.3.2*

Table 14.3.6.1.3
Summary of Orthostatic Vital Signs by Study Visit
Safety Population

Same shell as Table 14.3.5.1.1

Programming note: *Visits include Screening, Baseline, Day 1, Day 7 Post-Dose, Day 14 Post-Dose, and Day 21; parameters include Standing Systolic Blood Pressure (mmHg), Supine Systolic Blood Pressure (mmHg), Supine Heart Rate (bpm), Standing Heart Rate (bpm), Standing Diastolic Blood Pressure (mmHg), and Supine Diastolic Blood Pressure (mmHg); SOURCE: Listing 16.2.8.3.1, Listing 16.2.8.3.2.*

Table 14.3.6.1.4
Shift from Baseline in Orthostatic Vital Signs by Study Visit
Safety Population

Same shell as Table 14.3.5.1.2

Programming note: *Visits include Screening, Baseline, Day 1, Day 7 Post-Dose, Day 14 Post-Dose, and Day 21; parameters include Standing Systolic Blood Pressure (mmHg), Supine Systolic Blood Pressure (mmHg), Supine Heart Rate (bpm), Standing Heart Rate (bpm), Standing Diastolic Blood Pressure (mmHg), and Supine Diastolic Blood Pressure (mmHg); Update footnote to SOURCE: Listing 16.2.8.3.1, Listing 16.2.8.3.2*

Table 14.3.6.1.5
Summary of Orthostatic Vital Signs Shift from Baseline Categories by Study Visit
Safety Population

	Cohort-1			Cohort-2		
Study Visit Shift Category	SBP [1] (N=XX) n (%)	DBP [1] (N=XX) n (%)	HR [1] (N=XX) n (%)	SBP [1] (N=XX) n (%)	DBP [1] (N=XX) n (%)	HR [1] (N=XX)
Day 7						
Shifted	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Unshifted	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 14						
Shifted	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Unshifted	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 21						
Shifted	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Unshifted	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: DBP= diastolic blood pressure (mmHg); HR = heart rate (bpm); SBP = systolic blood pressure (mmHg).
Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment * 100. Shift status is defined as a reduction in SBP of 20 mmHg or more, and/or a reduction in DBP of 10 mmHg or more, and/or an increase in heart rate >20 beats/min for the standing measurement compared to the supine or semi-supine measurement.
[1] The baseline value for each variable is the last observation recorded prior to the first dose of treatment.
SOURCE: Listing 16.2.8.3.2

Programming note: *Repeat table for Overall.*

Table 14.3.6.1.6
Summary of Orthostatic Hypotension by Study Visit
Safety Population

Study Visit Category	Cohort-1 (N=XX) n (%)	Cohort-2 (N=XX) n (%)	Overall (N=XX) n (%)
Baseline [1]			
Reduction of SBP of 20 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reduction of DBP of 10 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 7 Post-Dose			
Reduction of SBP of 20 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reduction of DBP of 10 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 14 Post-Dose			
Reduction of SBP of 20 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reduction of DBP of 10 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 21			
Reduction of SBP of 20 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reduction of DBP of 10 mmHg or more	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Abbreviations: DBP = diastolic blood pressure; SBP= systolic blood pressure.
Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment*100. Orthostatic hypotension is defined as a reduction in SBP of 20 mmHg or more, and/or a reduction in DBP of 10 mmHg or more, for the standing measurement compared to the supine or semi-supine measurement.
[1] The average of the 3 baseline orthostatic vital signs measurements will be used for comparison to all post-treatment measurements.
SOURCE: Listing 16.2.8.3.2

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

Same shell as Table 14.3.5.1.1

Programming Note: *Visits include Screening, Baseline, Day 1, Day 7 Pre-Dose, Day 7 Post-Dose, Day 14 Pre-Dose, Day 14 Post-Dose, and Day 21; parameters include PR interval (msec), RR interval (msec), mean heart rate (beats/min) QRS interval (msec), QT interval (msec), and QTcF interval (msec); SOURCE: Listing 16.2.8.4.2*

Table 14.3.6.2.2
Summary of 12-Lead Electrocardiogram Interpretation by Study Visit
Safety Population

Study Visit Category	Cohort-1 (N=XX) n (%)	Cohort-2 (N=XX) n (%)	Overall (N=XX) n (%)
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 [1]			
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%)
Day 1			
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 and respective Protocol Amendment*100.
[1] The baseline value for each variable is the last observation recorded prior to the first dose of treatment.
SOURCE: Listing 16.2.8.4.1

Programming note: *Continue for Day 7 Pre-Dose, Day 7 Post-Dose, Day 14 Pre-Dose, Day 14 Post-Dose, and Day 21.*

Table 14.3.6.2.3
Summary of QTcF Values by Study Visit
Safety Population

Study Visit Category	Cohort-1 (N=XX) n (%)	Cohort-2 (N=XX) n (%)	Overall (N=XX) n (%)
Screening			
QTcF Value			
> 450 msec to ≤ 480 msec [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 480 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 500 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Baseline [3]			
QTcF Value			
> 450 msec to ≤ 480 msec [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 480 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 500 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Day 1			
QTcF Value			
> 450 msec to ≤ 480 msec [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 480 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 500 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
QTcF Increase from Baseline [3]			
> 30 msec to ≤60 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
> 60 msec	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment*100.
[1] Percentages are based on the number of male subjects in the Safety Population.
[2] Percentages are based on the number of female subjects in the Safety Population.
[3] The baseline value for each variable is the last observation recorded prior to the first dose of treatment
SOURCE: Listing 16.2.8.4.2

Programming note: *Continue for Day 7 Pre-Dose, Day 7 Post-Dose, Day 14 Pre-Dose, Day 14 Post-Dose, and Day 21.*

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

C-SSRS Section C-SSRS Item	Cohort-1 (N=XX) Pre-treatment (N=XX)	Cohort-1 (N=XX) Post-treatment (N=XX)	Cohort-2 (N=XX) Pre-treatment (N=XX)	Cohort-2 (N=XX) Post-treatment (N=XX)	Overall (N=XX) Pre-treatment (N=XX)	Overall (N=XX) Post-treatment (N=XX)
Suicidal Ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Wish to be Dead	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Non-Specific Active Suicidal Thoughts	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Any Methods	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Some Intent	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active Suicidal Ideation with Specific Plan	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Actual Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subject Engaged in Non-Suicidal Self-Injurious Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Interrupted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Aborted Attempt	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	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 Behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Percentages are n/Number of subjects in the Safety Population and respective Protocol Amendment*100. The C-SSRS scale consists of a Baseline evaluation that assesses the lifetime and more recent experience (past 12 months) of the subject with suicidal ideation and behavior, a baseline evaluation that focuses on suicidality since Screening that occurs before first dose of study drug (all of which is summarized under “pre-treatment”), and a post-baseline evaluation (“post-treatment”) administered at either Day 21 visit or early termination visit for discontinued subjects, which focuses on suicidality since the last study visit. Subjects are counted once for each C-SSRS section and once for each C-SSRS item answered “Yes” in pre-treatment and post-treatment.
SOURCE: Listing 16.2.8.6

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14.3. Planned Listing Shells

Listing 16.2.1.1
Subject Disposition
All Subjects

Subject ID	Protocol Amendment	Subject Status	Date of Last Dose (Study Day)	Date of Discontinuation/Completion (Study Day)	Reason for Discontinuation
XXXXXX	1.0	XXXXXXXX	DDMMMYYYY (X)	DDMMMYYYY (X)	
XXXXXX	2.0	XXXXXXXX	DDMMMYYYY (X)	DDMMMYYYY (X)	
XXXXXX	2.0	XXXXXXXX	DDMMMYYYY (X)	DDMMMYYYY (X)	
XXXXXX	3.0	XXXXXXXX	DDMMMYYYY (X)	DDMMMYYYY (X)	XXXXXXXXXX: XXXXXXXXX
XXXXXX	3.0	XXXXXXXX	DDMMMYYYY (X)	DDMMMYYYY (X)	XXXXXXXXXXXXXXXXXXXXX

Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Event Date – Date of the first dose of date; For post-dose: study day= Start Date/ Stop Date – first dose date + 1.

Programming note: *Concatenate specify text with a colon. If reason for early termination is Other, concatenate the specify text as follows: "Other: XXXXXXXXX". If the reason for Discontinuation is Death, then concatenate cause of death and date of death as shown above. If lost to follow-up, concatenate with date of last contact and specify text as follows: "Lost to follow-up: XXXXXXX; date of last contact: DDMMMYYYY".*

Listing 16.2.1.2
Visit Status
All Subjects

		Day 7 Visit Status				Day 14 Visit Status				
Subject ID	Protocol Amendment	Complete Day 7 as Scheduled?	If No, Early Terminate from the Study?	Complete the Early Termination Visit?	Day 7 Visit Date (Study Day)	Complete Day 14 as Scheduled?	If No, Early Terminate from the Study?	Complete the Early Termination Visit?	Day 7 Visit Date (Study Day)	Date of Early Termination (Study Day)
XXXXXX	X.X	XXX	XXX	XXX	DDMMMYYYY (X)	XXX	XXX	XXX	DDMMMYYYY (X)	DDMMMYYYY (X)
XXXXXX	X.X	XXX	XXX	XXX	DDMMMYYYY (X)	XXX	XXX	XXX	DDMMMYYYY (X)	DDMMMYYYY (X)
XXXXXX	X.X	XXX	XXX	XXX	DDMMMYYYY (X)	XXX	XXX	XXX	DDMMMYYYY (X)	DDMMMYYYY (X)
XXXXXX	X.X	XXX	XXX	XXX	DDMMMYYYY (X)	XXX	XXX	XXX	DDMMMYYYY (X)	DDMMMYYYY (X)

Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Assessment Date – Date of the first dose of date; For post-dose: study day= Assessment Date – first dose date + 1.

Listing 16.2.2.1
Descriptions of Protocol Defined Inclusion and Exclusion Criteria
All Subjects

Protocol Amendment	Inclusion/Exclusion	Criterion Number	Criteria Description
X.X	Inclusion	1	Adult subjects between 18 and 75 years of age, inclusive, with history of tremor that fulfills the diagnostic criteria of ET according to Movement Disorder Society (MDS) Consensus Statement on the classification of tremors from the task force on tremor of the International Parkinson and Movement Disorder Society
X.X	Inclusion	2	XXXXXXXXXXXX
…	…	…	…
X.X	Exclusion	1	XXXXXXXXXXXX
X.X	Exclusion	2	XXXXXXXXXXXX

Programming note: *This listing will be programmed similarly to how SDTM.TI would be created.*

Listing 16.2.2.2
Inclusion and Exclusion Criteria Met/Not Met
All Subjects

Subject ID	Protocol Amendment	Date (Study Day) of: Informed Consent	All Inclusion Criteria Met?	Any Exclusion Criteria Met?
XXXXXX	X.X	DDMMMYYYY (X)	Yes	No
XXXXXX	X.X	DDMMMYYYY (X)	No: 05, 10	No
XXXXXX	X.X	DDMMMYYYY (X)	No: 05	No
XXXXXX	X.X	DDMMMYYYY (X)	Yes	Yes: 04
XXXXXX	X.X	DDMMMYYYY (X)	Yes	No
XXXXXX	X.X	DDMMMYYYY (X)	Yes	No

Note: Study day is calculated relative to the date of first dose of study drug (= ICF Date – Date of the first dose of date)
Refer to Listing 16.2.2.1 for inclusion and exclusion criteria text.

Programming note: *If more than 1 inclusion or exclusion criterion number exists, concatenate with a comma as shown above.*

Listing 16.2.2.3
Protocol Deviations
All Subjects

Subject ID	Protocol Amendment	Date (DDMMMYYYY) (Study Day)	Event Type	Violation Level	Description
XXXXXX	X.X		XXXXXXXXXX	MAJOR	XXXXXXX
			XXXXXXXXXXXXX	MINOR	XXXXXXXXXXXXXX
XXXXXX	X.X		XXXXXXXXXXX	MINOR	XXXXXXXXXXXXXXXXXX
			XXXXXXXXXXXXXXX	MINOR	XXXXXXXXXX
XXXXXX	X.X		XXXXXXXXXXX	MAJOR	XXXXXXXXXXXXXXXXXXX

Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Event Date – Date of the first dose of date;
For post-dose: study day= Event Date – first dose date + 1.

Programming note: *the structure of this listing may change depending on the information in the protocol deviations file.*

Listing 16.2.3
Analysis Populations
All Subjects

Subject ID	Protocol Amendment	Analysis Population			CCI	Primary Reason for Exclusion
		Safety [1]	FAS [2]	Exposed [3]		
XXXXXX	X.X	Yes	Yes	Yes		XXXXXXXXXXXXX
XXXXXX	X.X	Yes	No	Yes		XXXXXXXXXXXXX
XXXXXX	X.X	Yes	Yes	Yes		XXXXXXXXXXXXX
XXXXXX	X.X	Yes	Yes	Yes		XXXXXXXXXXXXX
XXXXXX	X.X	Yes	Yes	No		XXXXXXXXXXXXXXXXXX

Abbreviations: FAS = full analysis set; CCI ; TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)- CCI ; TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS).
Note: All subjects received CAD-1883 300 mg BID. [1] The Safety population includes all subjects who take at least 1 dose of study drug.
[2] The FAS consists of subjects in the Safety population who had at least 1 post-baseline assessment of both TETRAS-PS CCI .
[3] Commercially Confidential Information

[4] Commercially Confidential Information

Programming note: *Concatenate all reasons for exclusion with a semi-colon.*

Listing 16.2.4.1
Demographics and Baseline Characteristics
All Subjects

Subject ID	Protocol Amendment	Site	Sex	Child-Bearing Potential?	Date of Birth	Age (years)	Ethnicity	Race
XXXXXX	X.X	XXXXXX	XXXX	No	DDMMMYYY	XX	XXXXXXX	XXXXXXX
XXXXXX	X.X	XXXXXX	XXXXXX	No	DDMMMYYY	XX	XXXXXXX	XXXXXX
XXXXXX	X.X	XXXXXX	XXXXXX		DDMMMYYY	XX	XXXXXXX	XXXXXX
XXXXXX	X.X	XXXXXX	XXXX		DDMMMYYY	XX	XXXXXXX	XXXXX

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Programming Note: *If subject has multiple races, concatenate them.*

Listing 16.2.4.2
Medical History
All Subjects

Subject ID	Protocol Amendment		System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)/Ongoing
XXXXXX	X.X		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)
		Commercially Confidential Information	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	MMMYYYY (X)/ Ongoing
			XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ Ongoing
XXXXXX	X.X		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)

Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Start Date/ Stop Date – Date of the first dose of date;
For post-dose: study day= Start Date/ Stop Date – first dose date + 1.
Medical history was coded using MedDRA version 20.1. Only subjects with medical history recorded are listed.
[1] Commercially Confidential Information

Programming note: *SOC & PT text should be in title case in table, as shown in the shell.*

Listing 16.2.4.3
Disease History
All Subjects

Subject ID	Protocol Amendment	Date of First ET Symptom (Study Day)	Date of ET Diagnosis (Study Day)		ET Triggers		Did Alcohol Use Reduce Tremor Severity?	First or Second-Degree Blood Relative with Prior ET Diagnosis?
					Trigger Type	Frequency		
XXXXXX	X.X	DDMMMYYY (XX)	DDMMMYYY (XX)	Commercially Confidential Information	XXX	XXX	XXX	XXX
XXXXXX	X.X	DDMMMYYY (XX)	DDMMMYYY (XX)		XXX	XXX	XXX	XXX
XXXXXX	X.X	DDMMMYYY (XX)	DDMMMYYY (XX)		XX	XX	XX	XX
XXXXXX	X.X	DDMMMYYY (XX)	DDMMMYYY (XX)		XX	XX	XX	XX

Abbreviation: ET = Essential Tremor.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Start Date/ Stop Date – Date of the first dose of date; For post-dose: study day= Start Date/ Stop Date – first dose date + 1.

Programming note: *Concatenate specify text for Treatment Type, Trigger Type, Frequency Type as shown above if the answer is "OTHER"*

Listing 16.2.5.1
Study Drug Administration
All Subjects

Subject ID	Protocol Amendment	Study Visit	Administered Proper Dosage of Study Drug?	Reason Dose Not Administered	Date/Time of In-Clinic Administration (Study Day)	Date/Time of Last Dose Prior to Clinic Visit (Study Day)
XXXXXX	X.X	XXXXXXX	Yes		DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM
	X.X	XXXXXXX	Yes		DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM
	X.X	XXXXXXX	Yes		DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM
	X.X	XXXXXXX	Yes		DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM
		XXXXXXX	No	XXXXXXXXXXXXXX		
XXXXXX	X.X	XXXXXXX	Yes		DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM
	X.X	XXXXXXX	Yes		DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM
	X.X	XXXXXXX	Yes		DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM

Note: Study day is calculated relative to the date of first dose of study drug.
Time for last dose prior to clinic visit is approximate.

Listing 16.2.5.2
Drug Accountability
All Subjects

Subject ID	Protocol Amendment	Total Daily Dose	Bottle	Date Dispensed (Study Day)	Number of Capsules Dispensed	Was Bottle Returned to the Clinic?	Date Returned (Study Day)	Number of Unused Capsules Returned
XXXXXX	X.X	300 mg BID	Bottle A	DDMMMYYYY (X)	XX	Yes	DDMMMYYYY (X)	XX
XXXXXX	X.X	300 mg BID	Bottle A	DDMMMYYYY (X)	XX	Yes	DDMMMYYYY (X)	XX

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

Programming note: Concatenate specify text with a colon if the Capsules Dispensed is OTHER.

Listing 16.2.5.3
Missed Doses
All Subjects

Subject ID	Protocol Amendment	Were any Doses Missed?	Date of Missed Dose (Study Day)	AM/PM Dose	Number of Pills not Taken	Reason for Missed Dose
XXXXXX	X.X	No				
XXXXXX	X.X	Yes	DDMMMYYYY (X)	AM	XX	XXXXXXXXXX
XXXXXX	X.X	Yes	DDMMMYYYY (X)	PM	XX	XXXXXXXXXX

Note: Study day is calculated relative to the date of first dose of study drug (= Date of Missed Dose – first dose date + 1).

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Listing 16.2.6.1.1
Local TETRAS Performance Subscale and Upper Limb Subscale Scores
All Subjects

Subject ID	Protocol Amendment	Study Visit	CAD-1883 Administered In-Clinic?	Was Assessment Completed?	Date/Time of Assessment (Study Day)	Number of Minutes Assessment Started after Dosing	Was the Videography Uploaded to Portal?	Item	Result
XXXXXX	X.X	XXXXXX	XXX	Yes	DDMMMYYYY/HH:MM (X)	XX	Yes	Head Tremor	XX
								Face (including jaw) Tremor	XX
								Voice tremor	XX
								Upper limb tremor: Forward outstretched postural tremor – Right	XX
								…	
								TETRAS-PS Upper Limb Subscale Score	XX
								TETRAS-PS Upper Limb Tremor (Item 4) Score	XX
								TETRAS-PS Total Score	XX

Abbreviation: TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale Performance Subscale.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Assessment Date – Date of the first dose of date; For post-dose: study day= Assessment Date – first dose date + 1.
Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life.
TETRAS-PS Total score is derived as the sum of the 16 individual item scores (only the maximum of the item 5, lower limb tremor scores will be counted), with a maximum total score of 64.
TETRAS-PS Upper Limb Subscale score is derived as the sum of the item 4, item 6, item 7 and item 8 scores (forward outstretched postural tremor, lateral “wing beating” postural tremor, kinetic tremor, Archimedes spirals, and dot approximation task from both sides of the body, as well as handwriting, with a maximum total score of 44.
TETRAS-PS Upper Limb Tremor (Item 4) Total score is derived as the sum of the 6 item 4 scores (forward outstretched postural tremor, lateral “wing beating” postural tremor, and kinetic tremor scores) from both sides of the body, with a maximum total score of 24.

Programming Note: *If Assessment was not completed or videography was not uploaded to the portal, concatenate reason. CAD-1883 Administered In-Clinic will come from EX CRF, if date of in-clinic administration at the corresponding visit is not null. If not administered in clinic, concatenate reason not administered with a semicolon.*

Listing 16.2.6.1.2
Central TETRAS Performance Subscale and Upper Limb Subscale Scores
All Subjects

Same Shell as Listing 16.2.6.1.1

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Listing 16.2.6.6
Wearable Sensor (Kinesia) Scores
All Subjects

Subject ID	Protocol Amendment	Study Visit	Date/Time of Assessment (Study Day)	Side	Task	Kinesia Score	Tremor Amplitude	Tremor Frequency	Finger-Chin-Finger Quality
XXXXXX	X.X	XXXXXX	DDMMMYYYY/HH:MM (X)	Left	Extended arms posture	X	XX	XX	XXXX
					Wing-beating posture	X	XX	XX	XXXX
					Kinetic “finger-to-chin” movement	X	XX	XX	XXXX
					Arm on table posture	X	XX	XX	XXXX
				Right	Extended arms posture	X	XX	XX	XXXX
					Wing-beating posture				
					Kinetic “finger-to-chin” movement	X	XX	XX	XXXX
					Arm on table posture	X	XX	XX	XXXX
				Both	Kinesia Upper Limb Tremor Score	X	XX	XX	XXXX

Note: Study day is calculated relative to the date of first dose of study drug.
Kinesia score ranges from 0 to 4; higher scores indicate more severe tremor. Finger-Chin-Finger quality values of 1 represent good quality and values of 0 represent poor quality. Kinesia Upper Limb Tremor score is derived as the sum of the scores from the extended arms posture, wing-beating posture, and kinetic “finger-to-chin” wearable sensor maneuvers from both sides of the body, with a maximum total score of 24.

Programming Note: *If assessment was done at home, place ‘NA’ in study visit column and add to abbreviations.*

Listing 16.2.7
Adverse Events
All Subjects

Subject ID	Protocol Amendment	TEAE/Disc	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship	Action Taken/ Outcome	Serious (SAE)?/ Criteria Met
XXXXX	X.X	Yes/No	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX	Yes/xxxxxx
XXXXX	X.X	No/No	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX	No
		Yes/Yes	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXX	DDMMMYYYY/HH:MM (X))/ DDMMMYYYY/HH:MM (X)	XXXXXXXXX/ XXXXXXXXXX	XXXXXXXXX/ XXXXXXXXXX	

DISC = Discontinued, SAE = Serious Adverse Event, TEAE = Treatment Emergent Adverse Event
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Start/End Date – Date of the first dose of date; For post-dose: study day= Start/End Date – first dose date + 1.

Programming note: *If time missing, display "- -:- -". If Serious? is Yes, concatenate all serious criteria marked as Yes with a semicolon. If no events meet the criteria for display, present "No events are reported." SOC & PT text should be in proper case in table, as shown in the shell. "Other Action Taken" will be either None, Medication Required, Relevant Procedure, or Other; if specify text is needed, concatenate "Relevant Procedure:" or "Other:" with the text.*

Listing 16.2.8.1.1
Clinical Laboratory Data: Hematology
All Subjects

Subject ID: XXXXXX, Protocol Amendment: X.X, Sex: M/F, Age: XX, Date of First/Last Dose (Study Day): DDMMMYYYY (X)/ DDMMMYYYY (X)

Parameter (unit)	Study Visit	Date/Time of Assessment (Study Day)	Standard Results	Change from Baseline (%) [1]	Reference Range [2]	Reference Range Flag	Lab Panel	Comments/Reason Not Done
Hemoglobin (unit)	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX	XX (XX.X)	XX – YY		XXXXXXX	
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY	XXX	XXXXXXX	
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	
	XXXXXX		ND					XXXXXXX
	XXXXXX	DDMMMYYYY/HH:MM (X)	XX		XX – YY		XXXXXXX	

Abbreviations: AL = abnormal-low; AH = abnormal-high; CS = clinically significant; NCS = not clinically significant; ND = not done.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Assessment Date – Date of the first dose of date; For post-dose: study day= Assessment Date – first dose date + 1.
[1] Baseline is the last observation recorded prior to the first dose of treatment.
[2] Reference range is used to identify potentially clinically significant laboratory values.

Programming note: *Update abbreviations to reflect actual data. If test was not done, set results to ND; make sure last column is populated accordingly. Do not display serum HCG results in this listing. For reference range flag, concatenate AL or AH with clinical significance like "XX-YY" (eg, AL-CS). Sort by Subject ID, Treatment, Sex, Age, First Dose Date, Parameter, Study visit, Date of Assessment.*

Listing 16.2.8.1.2
Clinical Laboratory Data: Serum Chemistry
All Subjects

Same shell as Listing 16.2.8.1.1

Listing 16.2.8.1.3
Clinical Laboratory Data: Urinalysis
All Subjects

Same shell as Listing 16.2.8.1.1

Listing 16.2.8.1.4
Clinical Laboratory Data: Biomarker Panel for Renal Tubular Injury
All Subjects

Same shell as Listing 16.2.8.1.1

Listing 16.2.8.1.5
Clinical Laboratory Data: Urine Pregnancy Test
All Subjects

Subject ID	Protocol Amendment	Age (years)	Sex	Was Pregnancy Test Performed?	Date Performed (Study Day)	Reason not Performed	Result
XXXXX	X.X	XX	XXXXXX	Yes	DDMMMYYYY (XX)		XXXXXXXX
XXXXX	X.X	XX	XXXXXX	Yes	DDMMMYYYY (XX)		XXXXXXXXX
XXXXX	X.X	XX	XXXXXX	No		XXXXXXXXXXXX	XXXXXXXXX

Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Assessment Date – Date of the first dose of date; For post-dose: study day= Assessment Date – first dose date + 1.

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Listing 16.2.8.1.7
Clinical Laboratory Data: Biomarker Panel for Renal Tubular Injury
Safety Population

Subject ID: 840002-005, Age=xx years, Sex=F, CAD-1883 Treatment: 300 mg BID, First/Last Dosing Date=25APR2019 (Day 1)/09MAY2019 (Day 15), Subject Status=Completed

Parameter	Study Visit	Date/Time of Assessment (Study Day)	Results				Fold Change from Baseline [1]
			Measured	Unit	Normalized	Unit	
uCreatinine (uCr)	SCREENING	01APR2019/14:03 (-24)	127.1	mg/dL			
	PRE-DOSE	22APR2019/12:44 (-3)	116	mg/dL			
	DAY 1	25APR2019/15:45 (1)	78.1	mg/dL			
	DAY 7	02MAY2019/12:50 (8)	78.8	mg/dL			
	DAY 14	09MAY2019/12:17 (15)	93.4	mg/dL			
	DAY 21/FOLLOW UP	14MAY2019/12:58 (20)	124.4	mg/dL			
uClusterin (uCLU)	PRE-DOSE	22APR2019/12:44 (-3)	131	ng/mL	113	ng/mg Cr	1.00
	DAY 1	25APR2019/15:45 (1)	12	ng/mL	15	ng/mg Cr	0.13
	DAY 7	02MAY2019/12:50 (8)	235	ng/mL	298	ng/mg Cr	2.64
	DAY 14	09MAY2019/12:17 (15)	117	ng/mL	125	ng/mg Cr	1.11
	DAY 21/FOLLOW UP	14MAY2019/12:58 (20)	85	ng/mL	68	ng/mg Cr	0.60

Note: The normalized concentration at a given time point is calculated as the concentration at that time point divided by the concentration of uCreatinine (mg/dL) at the same time point.
[1] Fold Change from Baseline at a given time point is calculated as the normalized concentration at the time point divided by the normalized concentration at baseline.

PROGRAM: L_16.2.8.1.4_Biomarker.sas
Run Date: 28AUG2019 18:09

Programming note: Parameters include uCreatine (uCr), uClusterin (uCLU) , uCystatin-C (uCysC), uKidney Injury Molecule-1 (uKIM-1), uN-Acetyl-beta-D-Glucosaminidase (uNAG), Neutrophil Gelatinase-Associated Lipocalin (uNGAL) and uOsteopontin (uOPN).
Units are different for different parameters.

Listing 16.2.8.2.1
Physical Examination
All Subjects

Subject ID: XXXXXX, Protocol Amendment: X.X, Sex: M/F, Age: XX, Date of First/Last Dose (Study Day): DDMMMYYYY (X)/ DDMMMYYYY (X)

Study Visit	Physical Exam Performed?	Any CS Changes since Last Visit?	Exam Date (Study Day)	Body System	Result	Abnormal Findings	Clinically Significant?
XXXXXX	Yes	NA	DDMMMYYYY (XX)	XXXXXXX	NORMAL		
			DDMMMYYYY (XX)	XXXXXXX	NORMAL		
XXXXXX	Yes	XX	DDMMMYYYY (XX)	XXXXXXX	ABNORMAL	XXXXXXXXXXXXX	No
XXXXXX	No; XXXXXX		DDMMMYYYY (XX)	XXXXXXX	NORMAL		

Abbreviations: CS = clinically significant; NA = not applicable.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Exam Date – Date of the first dose of date; For post-dose: study day= Exam Date – first dose date + 1.

***Programming Note**: If exam was not performed, concatenate reason. Any Clinically Significant Changes since Last Visit? will be NA at the Screening visit.*

Listing 16.2.8.2.2
Neurological Examination
All Subjects

Subject ID: XXXXXX, Protocol Amendment: X.X, Sex: M/F, Age: XX, Date of First/Last Dose (Study Day): DDMMMYYYY (X)/ DDMMMYYYY (X)

Study Visit	Neurological Examination Performed?	Any Clinically Significant Changes since Last Visit?	Exam Date (Study Day)	Body System	Result	Abnormal Findings	Clinically Significant?
XXXXXX	Yes	XX	DDMMMYYYY (XX)	XXXXXXX	NORMAL		
XXXXXX	Yes	XX	DDMMMYYYY (XX)	XXXXXXX	ABNORMAL	XXXXXXXXXXXXXX	No
XXXXXX	No	XX	DDMMMYYYY (XX)	XXXXXXX	NORMAL		

Abbreviations: CS = clinically significant; NA = not applicable.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Exam Date – Date of the first dose of date; For post-dose: study day= Exam Date – first dose date + 1.

***Programming Note**: If exam was not performed, concatenate reason. Any Clinically Significant Changes since Last Visit? will be NA at the Screening visit.*

Listing 16.2.8.3.1
Vital Signs
All Subjects

Subject ID	Protocol Amendment	Study Visit	Were Vital Signs Collected?	Date/Time Collected (Study Day)	Body Temperature (F)	Respiration Rate (breaths/min)	Height (cm)	Weight (kg)		Abnormal?
XXXXXX	X.X	XXXXXX	XXX	DDMMMYYYY/ HH:MM (X)	XX.X	XX	XX.X	XX.X		XXX
				DDMMMYYYY/ HH:MM (X)	XX.X	XX		XXX	Commercially Confidential Information	
XXXXXX	X.X	XXXXXX	XXX; XXXXXX	DDMMMYYYY/ HH:MM (X)	XX.X	XX		XXX		
				DDMMMYYYY/ HH:MM (X)	ND	ND		ND		

Abbreviation: CCI ND = not done.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Assessment Date – Date of the first dose of date; For post-dose: study day= Assessment Date – first dose date + 1.
Abnormal vital signs are as follows: CCI Systolic blood pressure >140 mmHg; Systolic blood pressure <90 mmHg; Diastolic blood pressure >90 mmHg; Diastolic blood pressure <60 mmHg; Heart rate >100 bpm; Heart rate <50 bpm; Respiration rate >20 breaths/min; Respiration rate <12 breaths/min; Oral temperature >99.5 ºF; Oral temperature <97 ºF.
[1] Treatment is based on treatment received.

***Programming Note**: If vital signs were not collected, concatenate reason, as shown above. If a measurement is outside the normal range, place an asterisk (*) next to the value in the cell.*

Listing 16.2.8.3.2
Blood Pressure and Orthostatic Vital Signs
All Subjects

Subject ID	Protocol Amendment	Study Visit/ Date/Time Collected (Study Day)	Measurement No. / /Total No. Measurements	Position	Parameter (unit)	Result	Change from Baseline	Orthostatic Hypotension? [1]
XXXXXX	1	XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Standing	SBP (mmHg)	XXX	XXX	NA
	2 or 3	XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Standing	DBP (mmHg)	XXX	XXX	XX
		XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Standing	HR (bpm)	XXX	XXX	XX
		XXXXXX/ DDMMMYYYY/ HH:MM (X)	NA	Supine	SBP (mmHg)	ND	NA	NA
		XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Supine	DBP (mmHg)	XXX	XXX	XX
		XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Supine	HR (bpm)	XXX	XXX	XX
		XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Standing-Average	SBP (mmHg)	XXX	XXX	NA
		XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Average	DBP (mmHg)	XXX	XXX	XX
		XXXXXX/ DDMMMYYYY/ HH:MM (X)	X / X	Average	HR (bpm)	XXX	XXX	XX

Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Assessment Date – Date of the first dose of date; For post-dose: study day= Assessment Date – first dose date + 1.
[1] Orthostatic hypotension is defined as a reduction in SBP of 20 mmHg or more, and/or a reduction in DBP of 10 mmHg or more, for the standing measurement compared to the supine or semi-supine measurement.

Programming Note: *If measurements are not orthostatic, put 'NA' in the "Measurement Number/Was Measurement Performed?" and "Average" Columns. If a measurement is outside the normal range, place an asterisk (*) next to the value in the cell.*
Please use "Standing-Average", "Supine-Average" respectively for averaged values. "Standing-Supine" for difference.

Listing 16.2.8.4.1
Qualitative 12-Lead Electrocardiogram (ECG) Investigator Results
All Subjects

Subject ID	Protocol Amendment	3 ECGs Performed Per Protocol?	Time Point	Study Visit/ Date of Assessment (Study Day)	Time			Reason not Performed	Investigator Interpretation	Comments
					1st Reading	2nd Reading	3rd Reading			
XXXXXX	X.X	Yes	XX	XXXXX / DDMMMYYYY (XX)	HH:MM	HH:MM	HH:MM		Normal	
			XX	XXXXX / DDMMMYYYY (XX)	HH:MM	HH:MM	HH:MM		Normal	
			XX	XXXXX / DDMMMYYYY (XX)	HH:MM	HH:MM	HH:MM		Abnormal-NCS	XXXXXXXXXXXXXX
			XX	XXXXX / DDMMMYYYY (XX)	HH:MM	HH:MM	HH:MM			
			XX	XXXXX / DDMMMYYYY (XX)	HH:MM	HH:MM	HH:MM		Normal	
XXXXXX	X.X	No	XX					XXXXXXXXXXX		

Abbreviations: CS = clinically significant; NCS = not clinically significant.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= Assessment Date – Date of the first dose of date; For post-dose: study day= Assessment Date – first dose date + 1.

Programming Note: *time point will be pre-dose or post-dose.*

Listing 16.2.8.4.2
12-Lead Electrocardiogram (ECG) Central Results
All Subjects

Subject ID	Protocol Amendment	Study Visit	Date/Time of ECG (Study Day)	Overall Interpretation	PR Interval (msec)	QRS Interval (msec)	QT Interval (msec)	QTcF Interval (msec)
XXXXXX	1	XXXXX	DDMMMYYYY/ HH:MM (XX)	XXXXXXX	XXX	XXX	XXX	XXX
		XXXXX	DDMMMYYYY/ HH:MM (XX)	XXXXXXXXXXX	XXX	XXX	XXX	XXX
		XXXXX	DDMMMYYYY/ HH:MM (XX) ND	XXXXXXXXX	XXX	XXX	XXX	XXX
XXXXXX	2 or 3	XXXXX	DDMMMYYYY/ HH:MM (XX)	XXXXXXX;XXXXX	XXX	XXX	XXX	XXX
		XXXXX	DDMMMYYYY/ HH:MM (XX)	XXXXXXXXXXX	XXXX	XXXX	XXXX	XXXX

ECG = electrocardiogram; ND = not done.
Note: Study day is calculated relative to the date of first dose of study drug. For pre-dose: study day= ECG Date – Date of the first dose of date; For post-dose: study day= ECG Date – first dose date + 1.

Programming Note: *If a measurement is outside the normal range, place an asterisk (*) next to the value in the cell.*

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Listing 16.2.8.6
Columbia-Suicide Severity Rating Scale (C-SSRS)
All Subjects

Subject ID	Protocol Version	Study Visit	Date of Assessment (Study Day)	Reference Period	Reason not Completed	Category	Assessment	Result
XXXXXX	X.X	XXXXXX	DDMMMYYYY (XX)	Baseline/ Screening		Suicidal Ideation	1. Wish to be dead	XX
							If yes, describe:	
							2. Non-Specific Active Suicidal Thoughts	XX
							If yes, describe:	
							3. Active Suicidal Ideation with Any Methods (not Plan) without Intent to Act	XX
							If yes, describe:	
							4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan	XX
							If yes, describe:	
							5. Active Suicidal Ideation with Specific Plan and Intent	XX
							If yes, describe:	
						Intensity of Ideation	Most Severe Ideation Type # (1-5)	X
							Description of Ideation	XXXXXXXXXXXXXXXX
							Frequency	1 = 1-4 hours/a lot of time
							Duration	1 = Fleeting – few seconds or minutes
							Controllability	1 = Easily able to control thoughts
						…	…	…

Note: All subjects received CAD-1883 300 mg BID. At the Pre-dose visit, the “baseline” version of the C-SSRS was administered. This version assesses Suicidal Ideation and Suicidal Behavior during the subject’s lifetime and during a predefined period. At the Day 21 visit (and the Early Termination visit for subjects withdrawing early), the “since last visit” version was administered.
Study day is calculated relative to the date of the first dose of study drug.

14.4. Planned Figure Shells

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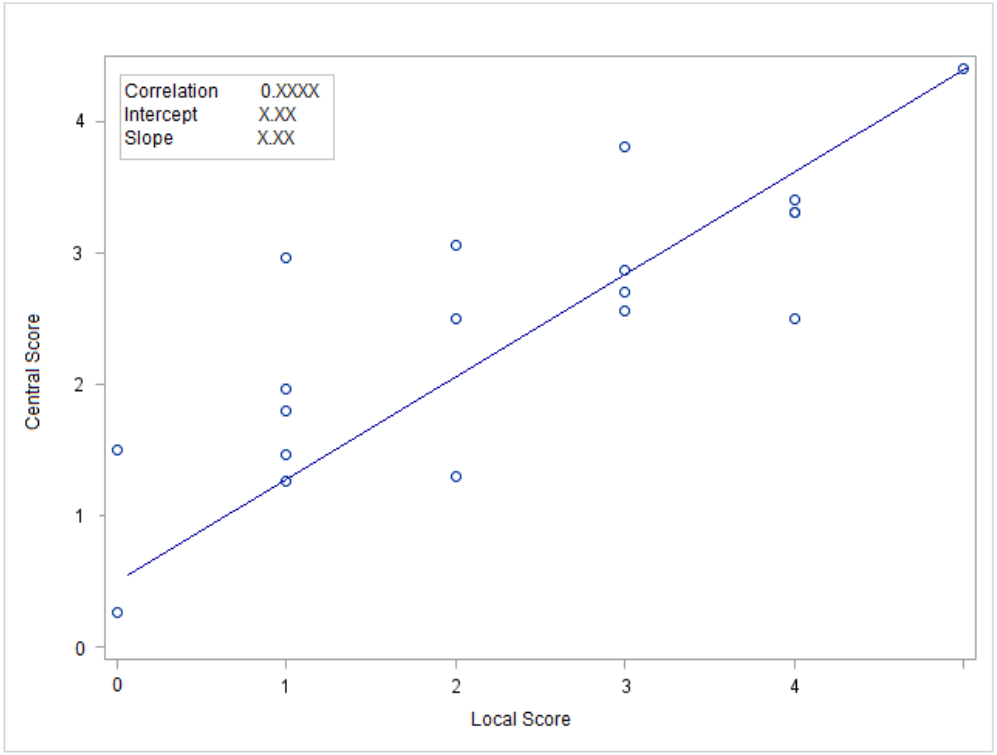
Figure 14.2.1.1.4
Central and Local TETRAS-PS Total Scores by Study Visit
Full Analysis Set

Study Visit=Screening



Abbreviation: TETRAS-PS = Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)-performance subscale (PS).
Note: TETRAS-PS Total score is derived as the sum of all of the individual item scores. Each individual item question score ranges from 0 to 4, where higher scores indicate worse quality of life. Pearson correlation coefficient and regression lines are presented for all study visits.
Reference Table: 14.2.1.1.4
SOURCE: Listings 16.2.6.1.1, 16.2.6.1.2

Programming Note: *Check Section 8.3.2 of SAP. If Spearman correlation coefficient is used, update footnote [1] accordingly. A separate graph will be produced for each study visit.*

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Figure 14.2.1.2.3
Central and Local TETRAS-PS Upper Limb Subscale Scores by Study Visit
Full Analysis Set

Same shell as Figure 14.2.1.1.4

Y-axis: Central Score
X-axis: Local Score
Programming notes: A separate graph will be produced for each study visit. Update footnote to read: TETRAS-PS Upper Limb Subscale score is derived as the sum of the item 4, item 6, item 7 and item 8 scores (forward outstretched postural tremor, lateral “wing beating” postural tremor, kinetic tremor, Archimedes spirals, and dot approximation task from both sides of the body, as well as handwriting, with a maximum total score of 44.
Reference Table: 14.2.1.2.3
SOURCE: Listings 16.2.6.1.1, 16.2.6.1.2

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Figure 14.2.1.3.2
Central and Local TETRAS-PS Upper Limb Tremor (Item 4) Scores by Study Visit
Full Analysis Set

Same shell as Figure 14.2.1.1.4

Y-axis: Central Score
X-axis: Local Score
Programming notes: A separate graph will be produced for each study visit. Update footnote to read: TETRAS-PS Upper Limb Tremor (Item 4) Total score is derived as the sum of the 6 item 4 scores (forward outstretched postural tremor, lateral “wing beating” postural tremor, and kinetic tremor scores) from both sides of the body, with a maximum total score of 24.
Reference Table: 14.2.1.3.2
SOURCE: Listings 16.2.6.1.1 and,16.2.6.1.2

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Figure 14.2.4
TETRAS-PS and Wearable Sensor (Kinesia) Upper Limb Tremor Scores by Study Visit
Full Analysis Set

Same shell as Figure 14.2.1.1.4

Y-axis: Central Score
X-axis: Local Score
Programming notes: A separate graph will be produced for each study visit. Update the footnote to read: TETRAS-PS Upper Limb Tremor (Item 4) Total score is derived as the sum of the 6 item 4 scores (forward outstretched postural tremor, lateral “wing beating” postural tremor, and kinetic tremor scores) from both sides of the body, with a maximum total score of 24. Kinesia Upper Limb Tremor score is derived as the sum of the scores from the extended arms posture, wing-beating posture, and kinetic “finger-to-chin” wearable sensor maneuvers from both sides of the body, with a maximum total score of 24.
Reference Table: 14.2.6.1
SOURCE: Listings 16.2.6.1.1 and 16.2.6.6.1

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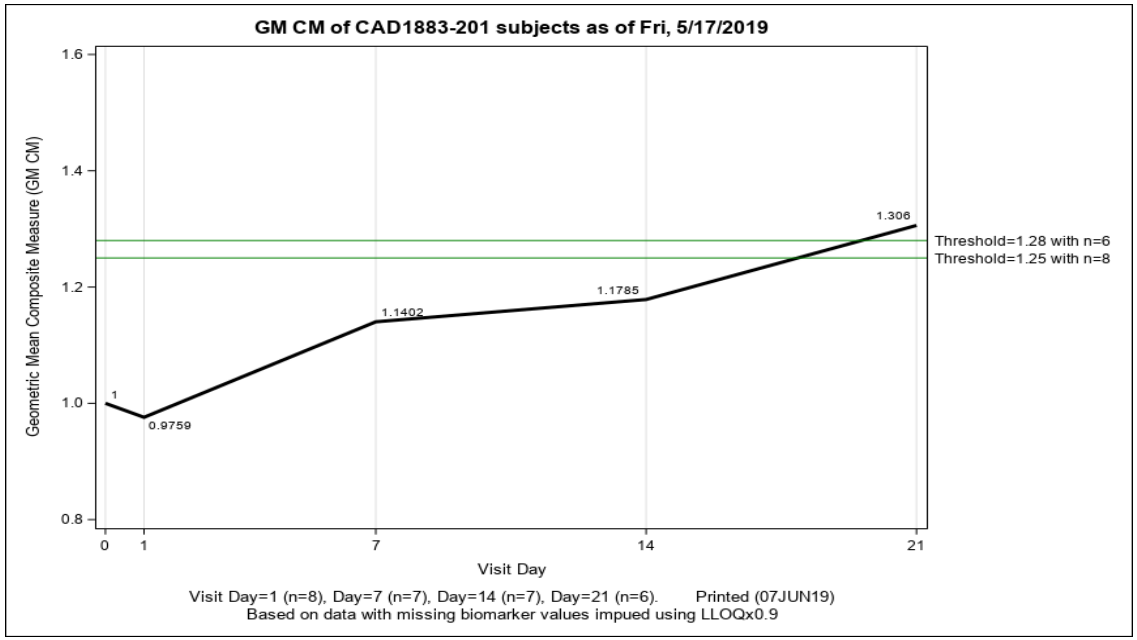
Figure 14.5
Geometric Mean (GM) Composite Measure (CM) of Kidney Injury Biomarkers by Study Visit
Safety Population



Programming note: Remove “GM CM of CAD1883-201 subjects as of Fri, 5/17/2019” from the graph. The threshold values need to be updated per the user guide (Threshold=1.18 with n=20).

Appendix 1: List of Abbreviations

Abbreviation	Definition
	Commercially Confidential Information
AE	adverse event
ATC	anatomical therapeutic chemical
BLQ	beneath limit of quantification
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CI	confidence intervals
CM	Composite Measure
CRF	case report form
CRO	contract research organization
CS	clinically significant
CSR	clinical study report
DBP	diastolic blood pressure
DEA	drug enforcement administration
DIA	drug information association
DOB	date of birth
DSMB	data safety monitoring board
ECG	electrocardiogram
eCRF	electronic case report form

Abbreviation	Definition
GM	Geometric Mean
EMA	European Medicines Agency
ET	Essential Tremor
FDA	Food and Drug Administration
GCP	good clinical practice
HEENT	Head, Ears, Eyes, Nose, Throat
HR	heart rate
IB	investigator's brochure
IC or ICF	informed consent or informed consent form
ICH	International Council for Harmonization
ID	identification
IEC	independent ethics committee
IND	investigational new drug
IP	investigational product
ITT	intent-to-treat
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MDS	Movement Disorder Society
MedDRA	medical dictionary for regulatory activities
N	number
NA	not applicable
NCS	non-clinically significant

Abbreviation	Definition
	Commercially Confidential Information
PD	protocol deviation
PE	physical examination
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PS	Performance subscale
QOL	quality of life
RR	respiratory rate or relative rate
SAE	serious adverse event
SAP	statistical analysis plan
SAS®	a software system used for data analysis
SBP	systolic blood pressure
SD	standard deviation
SOC	system organ class
SOP	standard operating procedure
TEAE	treatment-emergent adverse event
TETRAS	Tremor Research Group Essential Tremor Rating Assessment Scale
UTC	universal coordinated time
WHO	World Health Organization
WHO-DD	World Health Organization drug dictionary