Official Title: **A Study to Evaluate Maintenance of Hair Regrowth Following Dose Reduction of CTP-543 in Adult Patients With Moderate to Severe Alopecia Areata**

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STATISTICAL ANALYSIS PLAN

STUDY TITLE:

A STUDY TO EVALUATE MAINTENANCE OF HAIR REGROWTH FOLLOWING DOSE REDUCTION OF CTP-543 IN ADULT PATIENTS WITH MODERATE TO SEVERE ALOPECIA AREATA

PROTOCOL NUMBER:

CP543.2004

SPONSOR: Concert Pharmaceuticals, Inc.
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1. LIST OF ABBREVIATIONS

Table 1: List of Abbreviations

Abbreviation	Term
ATC	Anatomical-Therapeutic-Chemical
BID	Twice daily dosing
CGI-I	Clinician Global Impression of Improvement
CGI-S	Clinician Global Impression of Severity
CI	Confidence interval
CSR	Clinical study report
CTCAE	Common terminology criteria for adverse events
ECG	Electrocardiogram
eCRF	Electronic case report form
FDA	Food and Drug Administration
LS	Least squares
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed effect model of repeated measures
PCS	Potentially clinically significant
PGI-I	Patient Global Impression of Improvement
PGI-S	Patient Global Impression of Severity
PML	Progressive multifocal leukoencephalopathy
QPRO	Quality of Hair Patient Reported Outcome
SALT	Severity of Alopecia Tool
SAP	Statistical analysis plan
SPRO	Satisfaction of Hair Patient Reported Outcome
TEAE	Treatment-emergent adverse events
WHO	World Health Organization

2. PURPOSE OF THE ANALYSES

This statistical analysis plan (SAP) provides a detailed description of the strategy and statistical methodology to be used for analysis of data from the CP543.2004 protocol, amendment 3.0, dated 09SEP2022.

This study will be ongoing at the time of the New Drug Application (NDA) submission. A database freeze will be implemented, and an abbreviated report will be included in support of the NDA submission. Ongoing safety data will also be submitted with the 120-day safety update report.

The purpose of this SAP is to describe the pre-specified statistical approaches to the analysis of study data prior to database freeze for the NDA submission and prior to database lock for the final report. In addition to the analyses pre-specified for the final clinical study report (CSR) upon study completion, this SAP will also describe the subset of analyses to be provided in the abbreviated report for the NDA submission.

This analysis plan is meant to supplement the study protocol. If differences occur between analyses described in the SAP and the current protocol, those found in this SAP will assume primacy. Any deviations from this plan will be described in the applicable study report.

3. PROTOCOL SUMMARY

This is a two part, double-blind, randomized, multicenter study to evaluate the regrowth of hair with CTP-543 and subsequent durability of that regrowth following dose reduction or drug discontinuation in adult patients with moderate to severe alopecia areata. Patients will be between 18 and 65 years of age and experiencing an episode of hair loss associated with alopecia areata lasting at least 6 months and not exceeding 10 years. Patients not currently being treated for alopecia areata or with other treatments that might affect hair regrowth or immune response must have at least 50% hair loss as measured by the Severity of Alopecia Tool (SALT) at Screening and Baseline.

The study is divided into 2 Parts:

Part A: Period 1 (Treatment Phase) and Period 2 (Dose Modification Phase)

Part B: Re-Treatment Phase

Part A

Period 1

Patients will be screened up to 28 days prior to initiation of study drug. Patients will provide appropriately-obtained informed consent prior to initiating any screening procedures. Patients meeting initial screening criteria will be eligible to continue to the Day 1 (Baseline) visit for review of eligibility and baseline assessments, including SALT assessment, physical examination, clinical laboratory assessments, electrocardiograms (ECGs) and vital signs. Patients meeting all inclusion criteria and none of the exclusion criteria are eligible to enter Part A, Period 1 of the study.

Part A, Period 1 is a double-blind Treatment Period where patients will be randomized to receive either 8 mg BID or 12 mg BID CTP-543 for 24-weeks. Randomization will be stratified by scalp hair loss into one of the following two categories: 1) Partial scalp hair loss (SALT ≥ 50 and <95); 2) complete or near-complete scalp hair loss (SALT ≥95). Patients will take the first dose of study drug in the clinic on Day 1 and will be instructed to take study drug daily approximately every 12 hours for the duration of Period 1. Other baseline assessments for Part A, Period 1 will include Patient and Clinician Global Impression of disease Severity (CGI-S and PGI-S), and Patient Reported Outcome for Satisfaction (SPRO) and Hair Quality (QPRO). Blood samples for pharmacokinetic assessment will be taken periodically. At End of Treatment (EOT) for Part A, Period 1, treatment success (Responders) will be defined as patients from each dose group having an absolute SALT score of ≤20 at Week 24. These Responders will enter Part A, Period 2 of the study. Patients having an absolute SALT score > 20 will be defined as a Non-Responder and will have the opportunity to continue receiving treatment in the Open-Label Extension study (CP543.5001) or they will complete treatment at Week 24 and return in 4 weeks for the Post-Treatment Safety Follow-up.

Period 2

In Part A, Period 2, patients will be re-randomized to receive either a lower dose of CTP-543 (4 mg BID for patients previously receiving 8 mg BID or 8 mg BID for patients previously

receiving the 12 mg BID) or placebo. Patients in Part A, Period 2 will stay on their assigned dose for a maximum of 24 weeks or until they meet the criteria for loss of regrowth maintenance (LOM), defined as an absolute SALT score >20. Any patient meeting the LOM criteria at any assessment timepoint during Part A, Period 2 will enter Part B of the study and return to their original CTP-543 treatment from Part A, Period 1 (8 mg BID or 12 mg BID). Patients not meeting the LOM criteria (e.g., their absolute SALT score ≤ 20) at the end of 24 weeks will have the opportunity to continue receiving treatment in the Open-Label Extension study (CP543.5001) or they will complete treatment at Week 24 and return in 4 weeks for the Post-Treatment Safety Follow-up. The study design is depicted in the Study Flow Chart of the Appendix (Section 15.1).

An interim analysis to support regulatory activities related to an upcoming CTP-543 New Drug Application (NDA) submission will be conducted. The focus of the interim analyses will be on safety data and will occur following completion of Part A, Period 1. Additionally, after Part A, Period 1 completion, a PK population analysis will be completed. The PK analysis will be conducted by an outside vendor. This analysis will be described in a separate analysis plan and a separate report will be generated.

The primary efficacy assessment will be conducted when all patients have completed Part A, Period 2. An analysis of safety data will also be conducted. This analysis will be included in the NDA submission as an abbreviated report. Site personnel and patients will remain blinded to individual patient study treatments.

Part B

Any patient from Part A, Period 2 meeting the LOM criteria (SALT > 20) will enter into Part B of the study and return to their original 8 mg BID or 12 mg BID dose assigned in Part A, Period 1. Patients will stay on their assigned dose for 24 weeks regardless of whether they meet the criteria for Restoration of Regrowth (ROR) or not. ROR is defined as the patient's attainment of an absolute SALT score of ≤ 20. Assessment of treatment response using SALT for efficacy will occur monthly during the 24-week period. Patients will have the opportunity to continue receiving treatment in the Open-Label Extension study (CP543.5001) or they will complete treatment at Week 24 and return in 4 weeks for the Post- Treatment Safety Follow-up.

Patient safety will be monitored throughout the trial by the Investigator and supported by regular review by the Medical Monitor. Chemistry and hematology laboratory values will be assessed under fasted conditions bi-weekly for the first month of the treatment period (Part A, Period 1 and Part B), followed by every 4 weeks through the remainder of the study (all Parts). Lipid levels will be assessed every 4 weeks throughout the study. In light of the COVID-19 pandemic, challenges in the conduct of study visits may arise from quarantines, site closures, and/or travel limitations. To ensure the safety of trial participants and to minimize risk to trial integrity, alternative methods for drug dispensation and assessments, including telemedicine visits and clinical laboratory blood draws at a local laboratory or via a Home Health Care agency, may be offered for those trial participants who may no longer have access to the investigational site. Significant cytopenias or other hematologic abnormalities will be managed by severity through dose interruption or discontinuation, and signs and symptoms of infection will be closely monitored and treated promptly. Patients who experience intolerable symptoms during treatment may discontinue treatment at the judgement of the Investigator, but will be followed for safety

and efficacy assessments for the remainder of the study unless they withdraw consent. Patients may withdraw consent at any time.

4. GENERAL ANALYSIS AND REPORTING CONVENTIONS

The following is a list of general analysis and reporting conventions to be applied to this study, unless otherwise specified. Departures from these general policies will be described, if applicable, in the appropriate sections of this SAP. When this situation occurs, the rules set forth in the specific section take precedence over the general policies.

All data displays (tables, listings, and figures) will have a header showing the sponsor company name, protocol number, page number, and display status (i.e. "DRAFT" or "FINAL"), as well as a footer indicating file name and run date/time. Summary tables and data listings will be summarized by treatment group for efficacy and exposure, and by treatment group and overall otherwise. All data for analysis may be listed by-patient.

Specifically, for each Part and Period of the study, the summary table layout will be as follows:

For Part A, Period 1 tables:

Treatment Phase		
CTP-543 8 mg BID	CTP-543 12 mg BID	Total

For Part A, Period 2 tables:

Dose Reduction		Drug Discontinuation		
CTP-543 8 mg BID to 4 mg BID	CTP-543 12 mg BID to 8 mg BID	CTP-543 8 mg BID to Placebo	CTP-543 12 mg BID to Placebo	Total

For Part B tables:

Dose Reduction		Drug Discontinuation		
CTP-543 8 mg BID to 4mg BID to 8 mg BID	CTP-543 12 mg BID to 8 mg BID to 12 mg BID	CTP-543 8mg BID to Placebo to 8 mg BID	CTP-543 12 mg BID to Placebo to 12 mg BID	Total

Note that for all efficacy and exposure tables, the total column will not be displayed.

Categorical variables will be summarized using counts (n) and percentages (%) and will be presented in the form "n (xx.x)." If a count is 0, no percentage will be shown. If a percentage is 100%, 100 will be shown. To ensure completeness, summaries for categorical variables will include all categories, even if no patients had a response in a particular category. Unless otherwise specified, the denominator for each percentage will be based on the number of patients in the population being summarized (header n). Percentages will be rounded to one decimal place.

Continuous variables will be summarized using mean, standard deviation, minimum, maximum, median, and number of patients. The minimum and maximum will be the same precision as the

original collected data. The mean and median will be reported to an additional level of precision than the original observations, and the standard deviation will be reported to two additional levels of precision than the original observations. The precision for some original collected data and derived variables are longer than required for clinical interpretation (eg, >15 decimals). In these situations, the number of decimal places will be determined by the table of precision included as an attachment.

All efficacy summaries are descriptive with no statistical hypothesis testing. Confidence intervals and estimated treatment differences will be rounded to one additional decimal place from the original data, or a maximum of two decimal places. Standard error will be reported to an additional level of precision. Results which cannot be determined will be displayed as "NA", "NE", or similar.

Treatment start date for each part and period will be defined as the date of randomization or re-randomization for the respective part or period. If the treatment start date for Part A Period 2 is equal to the treatment end date for Part A Period 1 as collected on the eCRF, it will be assumed that the treatment day is associated with Part A Period 2. One day will be subtracted from the treatment end date for Part A Period 1. Similarly, if the treatment start date for Part B is equal to the treatment end date for Part A Period 2, it will be assumed that the treatment day is associated with Part B. One day will be subtracted from the treatment end date for Part A Period 2.

Date of last dose is collected on the *Treatment Discontinuation/Completion* eCRF page for each part/period. For patients with missing or partial date of last dose, or for patients who are ongoing at the time of the NDA submission, the date of last dose (ie, treatment end date) will be imputed. Date of last dose will be imputed as follows:

- For entirely missing dates for patients who are not ongoing or for partial dates where the month and day are missing, date of last dose will be imputed as the last visit date that is not a follow-up visit within a period or part.

- For partial dates where only the day is missing, the day will be imputed as the last day of the month. If this imputed date is after the treatment start date of the next part or period, or the study discontinuation date of that part or period, the day will be imputed to one day before the treatment start date of the next part or period.

- For patients who are ongoing, date of last dose will be imputed as the data cut date.

Summary tables and data listings:

- No preliminary rounding will be performed; rounding will only occur after analysis. Note that for the clinical purposes of moving patients through parts and periods, SALT scores were rounded to the nearest integer prior to determining the SALT ≤20 criterion.
- Data from patients excluded from an analysis population will be presented in the data listings but will not be included in the calculation of summary statistics, where applicable.

- Data from each patient will be separated by a blank line. Within a data listing, if a descriptive item appears line after line (e.g., repetition of a patient number, date, visit, etc.), only the first occurrence will be displayed (e.g., in Listing of Vital Signs, patient number, date and visit will only be displayed on first row when presenting all parameters collected at same visit). Repetition of actual results or outcomes (e.g., adverse events, lab results, vital sign values, etc.) will not be collapsed.
- Data listings will be sorted by treatment, patient, and date and/or time of assessment, as applicable. Data listings may be separated by study part.
- There will be 3 baselines in this study, defined as follows:
    - Part A Period 1 baseline is the last observation obtained on or before the day of dosing of study drug in Part A Period 1.
    - Part A Period 2 baseline is the last observation obtained on or before the day of dosing of study drug in Part A Period 2.
    - Part B baseline is the last observation obtained on or before the day of dosing of study drug in Part B.
- Unless otherwise noted, values reported as greater than or less than some quantifiable limit (e.g., "< 2.0") will be summarized as using the numeric equivalent in summary tables and figures (e.g. "<2.0" will be analyzed as 2.0). The reported value will be used in listings.

Mock tables and data listings will be provided as attachments to this analysis plan. Minor changes to the mocks after formal SAP approval will not necessitate re-approval unless changes to the text of the SAP are required.

All statistical deliverables will be produced, validated, and reviewed for accuracy/consistency in accordance with [redacted]. standard operating procedures and the processes described in the statistical validation plan.

SAS® (SAS Institute, Cary, North Carolina) statistical software, version 9.4 or later, will be used for all analyses. Adverse Events and Medical History will be coded in Medical Dictionary for Regulatory Activities (MedDRA) Version 23.1 or later. Concomitant medications will be coded in World Health Organization (WHO) Drug Version 2020-SEP or later, and Anatomical-Therapeutic-Chemical (ATC) classification and preferred term will be used for summaries.

5. ANALYSIS SAMPLES

The Efficacy Population will include all patients who are randomized in the study, dispensed study drug, and have at least 1 post-treatment SALT assessment.

The Safety Population will include all patients who receive study drug during the Treatment Period.

The Pharmacokinetic (PK) population will include all patients who received study drug in Part A, Period 1 and had at least 1 post-treatment blood draw.

All populations will be analyzed by the treatment received. In the event patients incorrectly receive treatment associated with a different treatment group per Part and/or Period of the study, they will be analyzed “as treated” if the patient received that treatment for more than 50% of doses for that Period/Part.

6. STUDY SUBJECTS

6.1. Disposition of Subjects

Disposition will be summarized by randomized treatment group and overall for all patients screened in the study for each of Part A Period 1, Part A Period 2, and Part B. The number and percentage of patients who are randomized, treated, prematurely discontinued, and completers will be summarized. Unless otherwise specified, percentages will be based on the number of patients randomized in the applicable study part.

The following disposition information will be summarized for Part A Period 1:

- The number of patients screened. Patients who rescreened will be counted only once.
- The number of patients randomized.
- The number and percentage of randomized patients within the Efficacy, Safety, and PK Populations.
- The number and percentage of randomized patients who:
    - completed treatment in Part A Period 1 per the *Treatment Discontinuation/Completion* eCRF page, where completed includes the following subcategories: complete-entering Part A Period 2, complete-entering Open Label, and complete-safety follow-up.
    - prematurely discontinued treatment in Part A Period 1.
        - The frequency and percentage of each discontinuation reason. The denominator for the percentage of each discontinuation reason will be the number of patients who discontinued treatment in Part A Period 1.
    - prematurely discontinued treatment in Part A Period 1 due to COVID-19
        - The frequency and percentage of reasons related to COVID-19. The denominator for the percentage of reasons related to COVID-19 will be the number of patients who discontinued treatment due to COVID-19.
    - completed the study in Part A Period 1 per the *Study Discontinuation/Completion* eCRF page, where completed includes the following subcategories: complete-entering Part A Period 2, complete-entering Open Label, and complete-safety follow-up.
    - prematurely discontinued the study in Part A Period 1.
        - The frequency and percentage of each study discontinuation reason. The denominator for the percentage of each discontinuation reason will be the number of patients who discontinued the study in Part A Period 1.
    - prematurely discontinued the study due to COVID-19
        - the frequency and percentage of reasons related to COVID-19. The denominator for the percentage of reasons related to COVID-19 will be the number of patients who discontinued treatment due to COVID-19.

The following disposition information will be summarized for Part A Period 2:

- The number of patients randomized.
- The number and percentage of randomized patients within the Efficacy and Safety Populations.
- The number and percentage of randomized patients who:
    - completed treatment in Part A Period 2 per the *Treatment Discontinuation/Completion* eCRF page, where completed includes the following subcategories: complete-LOM achieved-entering Part B, complete-entering Open Label, and complete-safety follow-up.
    - prematurely discontinued treatment in Part A Period 2.
        - The frequency and percentage of each discontinuation reason. The denominator for the percentage of each discontinuation reason will be the number of patients who discontinued treatment in Part A Period 2.
    - prematurely discontinued treatment in Part A Period 2 due to COVID-19
        - The frequency and percentage of reasons related to COVID-19. The denominator for the percentage of reasons related to COVID-19 will be the number of patients who discontinued treatment due to COVID-19.
    - completed the study in Part A Period 2 per the *Study Discontinuation/Completion* eCRF page, where completed includes the following subcategories: complete-LOM achieved-entering Part B, complete-entering Open Label, and complete-safety follow-up.
    - prematurely discontinued the study in Part A Period 2.
        - The frequency and percentage of each study discontinuation reason. The denominator for the percentage of each discontinuation reason will be the number of patients who discontinued the study in Part A Period 2.
    - prematurely discontinued the study due to COVID-19
        - the frequency and percentage of reasons related to COVID-19. The denominator for the percentage of reasons related to COVID-19 will be the number of patients who discontinued treatment due to COVID-19.

The following disposition information will be summarized for Part B:

- The number of patients re-randomized.
- The number and percentage of re-randomized patients within the Efficacy and Safety Populations.

- The number and percentage of re-randomized patients who:
    - completed treatment in Part B per the *Treatment Discontinuation/Completion* eCRF page, where completed includes the following subcategories: complete-entering Open Label and complete-safety follow-up.
    - prematurely discontinued treatment in Part B.
        - The frequency and percentage of each discontinuation reason. The denominator for the percentage of each discontinuation reason will be the number of patients who discontinued treatment in Part B.
    - prematurely discontinued treatment in Part B due to COVID-19
        - The frequency and percentage of reasons related to COVID-19. The denominator for the percentage of reasons related to COVID-19 will be the number of patients who discontinued treatment due to COVID-19.
    - completed the study in Part B per the *Study Discontinuation/Completion* eCRF page, where completed includes the following subcategories: complete-entering Open Label and complete-safety follow-up.
    - prematurely discontinued the study in Part B.
        - The frequency and percentage of each study discontinuation reason. The denominator for the percentage of each discontinuation reason will be the number of patients who discontinued the study in Part B.
    - prematurely discontinued the study due to COVID-19
        - the frequency and percentage of reasons related to COVID-19. The denominator for the percentage of reasons related to COVID-19 will be the number of patients who discontinued treatment due to COVID-19.

The number and percentage of patients randomized within each treatment group will also be summarized by investigative site for each Part and Period of the study.

Disposition and patient visits will also be presented for each patient in patient data listings. Patient data listings will list date of informed consent, date of first/last treatment, date of end of treatment/early treatment termination, date of end of study/early study termination, and reasons for treatment or study discontinuation. A Kaplan Meier curve of time to early treatment termination for any reason by study part will also be presented for the Safety Population. Patients who have completed treatment will be censored at date of last treatment or a maximum of 24 weeks. Consort diagrams may also be presented.

Screen failures will be provided in a separate listing. Rescreened patients who later enrolled will not be listed as screen failures.

6.2. Demographic and Other Baseline Characteristics

Demographic characteristics (i.e., sex, ethnic origin, race, age, and calculated body mass index) will be collected at the Screening Visit, between Day -28 and -1, and detailed on the eCRF. Demographic characteristics will be summarized using descriptive statistics for all randomized patients by treatment group and overall, for each of Part A Period 1, Part A Period 2, and Part B.

Baseline characteristics will be summarized using descriptive statistics for all randomized patients by treatment group and overall, for each study part, and will include the following:

- Baseline total SALT score
    - Note: Baseline total SALT score for Part A Period 2 will be the last SALT score obtained prior to dosing in Part A, Period 2 (ie, Week 24 SALT assessment from Part A, Period 1). Part B baseline total SALT score will be the last SALT score obtained in Part A, Period 2 prior to re-randomization into Part B.
- Alopecia areata classification (randomization strata): partial scalp hair loss (SALT ≥ 50 and < 95); complete or near-complete scalp hair loss (SALT ≥ 95)
- duration of current episode in years (calculated as: [date of randomization – date of current episode onset + 1] / 365.25)
- nasal hair involvement

For Part A Period 1, whether the patient has experienced any past and/or concomitant diseases, conditions, or exposures to serious infections (such as HIV), or past surgeries will also be summarized with baseline characteristics.

Other co-morbidities may be identified and included as baseline characteristics.

All demographics and baseline characteristics will also be listed within a by-patient data listing for all randomized patients.

6.3. Prior and Concomitant Medications

Concomitant medications will be recorded in the eCRF from Screening through the Follow-Up Visit at Week 28, for all Parts/Periods of the study. All medications will be coded using the WHO Drug Dictionary Version 2020-SEP.

Medications are classified as prior if the medication started prior to the first dose date of study drug or as concomitant if used on or after the first dose date of study drug for a given Part/Period.

Prior and concomitant medications will be summarized with counts and percentages separately for the Safety Population by treatment group, WHO Drug ATC classification level 2 and preferred term. For each summary, a patient will be counted only once for each medication.

Prior medications will be summarized for Part A Period 1 only. Concomitant medications will be summarized for each Part/Period.

Partial and completely missing dates will be imputed for the purposes of classifying concomitant medications as follows:

- Partial dates will be imputed following the same algorithm as in Section 9.3 for Treatment-emergent adverse events (TEAEs).
- For an entirely missing start date (i.e. day, month, and year are missing), the start date will be set to the date of administration of study drug for the given Part/Period unless the

stop date is prior to the date of administration of study drug, in which case the start date will be set to the stop date.

- For an entirely missing stop date (i.e. day, month, and year are missing), the medication will be treated as ongoing.

Partial dates will be compared to the start and end dates of each Part/Period to determine the study drug administration date that will be used to be imputed.

Prior and concomitant medications will also be listed by-patient.

6.4. Medical History

Medical history will be coded with the MedDRA terminology Version 23.1 and summarized as counts and percentages for the Safety Population by treatment group, system organ class, and preferred term for Part A Period 1. A patient will be counted only once for each condition. Conditions will be listed, including the verbatim investigator description of the relevant medical condition, the coded terms (system organ class, preferred term), start date, end date, and whether or not the condition is ongoing.

7. STUDY OPERATIONS

7.1. Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol or International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. Protocol deviations will be recorded on the source documents and with an explanation for the deviation. All protocol deviations will also be recorded as specified in the monitoring plan.

Protocol deviations will be identified by site staff, through medical reviews, and by clinical research associates during site monitoring. Protocol deviations are reviewed by the sponsor on an ongoing basis during the study to classify deviations as minor or major. Deviations that may alter or confound interpretation of the study results will be classified as major deviations. Protocol deviations will be summarized as counts and percentages by treatment group, deviation severity, and category for all randomized patients by study part. Reported deviation occurrence date will be compared to Part A Period 1 randomization date, Part A Period 2 randomization date, and Part B re-randomization date to determine the study part where the deviation will be summarized.

Deviations will also be presented by patient in a data listing for all randomized patients.

7.2. Randomization

Part A Period 1

Patients will be randomized such that approximately N = 130 for 12 mg BID and N = 170 for 8 mg BID) in an attempt to have approximately equal numbers of patients eligible for Part A, Period 2. Randomization will be stratified by scalp hair loss into one of the following two categories: 1) Partial scalp hair loss (SALT $\geq$ 50 and < 95); 2) Complete or near-complete scalp hair loss (SALT $\geq$ 95).

The randomization schedule will be generated prior to study start. Tablets and packaging of 8 mg and 12 mg CTP-543 will be identical in appearance.

Part A Period 2

For each dose group, patients identified as Responders in Period 1 will be randomized in a 1:1 ratio to a dose reduction arm or a placebo (drug discontinuation) arm. For the dose reduction arm, patients previously on 12 mg BID in Period 1 will be assigned to 8 mg BID and patients previously on 8 mg BID will be assigned to 4 mg BID. Given the previous experience with the primary endpoint for Period 1, it is expected that approximately 50 patients from each dose group in Period 1 will be Responders. Consequently, it is expected that approximately 25 patients from each dose group will be assigned to dose reduction and 25 patients will be assigned to drug discontinuation in Period 2.

The randomization schedule will be generated at the end of Period 1. Tablets and packaging for 4 mg CTP-543, 8 mg CTP-543 and placebo will be identical in appearance.

Part B
For each dose group, patients identified as having a LOM following either *dose reduction* or *drug discontinuation* in Part A, Period 2 will be assigned back to the original dose they received in Part A, Period 1. Study drug dosing regimen will be blinded by administering 2 x 8 mg tablets or 2 x 12 mg tablets twice-daily for 24 weeks. Tablets and packaging of 8 mg and 12 mg CTP-543 will be identical in appearance.

A by-patient listing of randomized treatment group and randomization number will be presented for each Part/Period.

All study patients, Investigators, and site study staff will be blinded to study drug assignment for the duration of the study.

7.3. Measures of Treatment Compliance

Time on treatment (days) will defined, for each Part/Period, as (date of last dose - date of first dose + 1). Dose interruptions will be subtracted from this calculation.

Patients will strive for 100% compliance with the daily dosing schedule. Treatment compliance will be summarized as percent of planned dose received for each dosing regimen. Percent of planned dose received will be calculated for each Part/Period as follows:

- 100*(Tablets Dispensed-Tablets Returned)/(Tablets Expected)

Tablets Expected is defined as the time on treatment multiplied by the expected number of pills taken daily (x2 for the 12 mg BID group; x2 for the 8 mg BID group; x2 for the 4 mg BID group; x2 for the placebo group), where time on treatment is defined as above, but with dose interruptions being ignored in this calculation. Derived patient compliance, compliance per the eCRF (80% or higher versus less than 80%), and dosing exceptions will be listed in by-patient data listings.

8. ENDPOINT EVALUATION

8.1. Overview of Efficacy Analysis Methods

8.1.1. Multicenter Studies

Patients will be enrolled at up to approximately 25 sites; site identifiers will be included in by-patient listings.

8.1.2. Assessment Time Windows

The visit schedule for all study assessments is provided in Appendix 15.2, by Part. For scheduled visits, there will be no reassignment of the analysis visit based on date. Unscheduled visits and early termination visits will be reassigned based on the analysis windows in the below table and the schedule of events. Assessments in part B will be windowed counting from the part B treatment start date. Assessments may only be re-assigned to visits where they were to be collected per the schedule of events. The latest assessment in a window will be selected as the visit used in summaries, unless otherwise specified. All visits will be included in by-patient data listings.

Table 2: Analysis Windows for Unscheduled and Early Termination Visits

		Safety Analyses			Efficacy Analyses		
	Nominal Visit	Lower	Target	Upper	Lower	Target	Upper
Part A, Period 1	Screening	-28	-1	-1	-28	-1	-1
	Visit 2-Randomization	1	1	1	1	1	1
	Visit 3-Week 2	2	15	22	12	15	18
	Visit 4-Week 4	23	29	43	26	29	32
	Visit 5-Week 8	44	57	71	54	57	60
	Visit 6-Week 12	72	85	99	82	85	88
	Visit 7-Week 16	100	113	127	110	113	116
	Visit 8-Week 20	128	141	155	138	141	144
	Visit 9-Week 24	156	169	183	166	169	172
Part A, Period 2	Visit 10-Week 28 (PAP2 Week 4)	184	197	211	194	197	200
	Visit 11-Week 32 (PAP2 Week 8)	212	225	239	222	225	228
	Visit 12-Week 36 (PAP2 Week 12)	240	253	267	250	253	256
	Visit 13-Week 40 (PAP2 Week 16)	268	281	295	278	281	284
	Visit 14-Week 44 (PAP2 Week 20)	296	309	323	306	309	312
	Visit 15-Week 48 (PAP2 Week 24)	324	337	351	334	337	340
Part B	Visit B1-Day 1	1	1	1	1	1	1
	Visit B2-Week 2	2	15	22	12	15	18
	Visit B3-Week 4	23	29	43	26	29	32
	Visit B4-Week 8	44	57	71	54	57	60
	Visit B5-Week 12	72	85	99	82	85	88
	Visit B6-Week 16	100	113	127	110	113	116
	Visit B7-Week 20	128	141	155	138	141	144
	Visit B8-Week 24	156	169	183	166	169	172

8.1.3. Timing of Analyses

All final, planned analyses will be performed after the last patient has completed all study assessments in Part B, all relevant study data have been processed and integrated into the analysis database, and the database has been locked. Analyses for the abbreviated report for the NDA, focused on the primary efficacy for Part A and a safety analysis for Part A, will be performed after the last patient completes Part A and the database is frozen. PK analyses and the interim analysis (safety data for Part A Period 1) will be performed after the last patient completes Part A Period 1 and the database is frozen.

Any post hoc, exploratory analyses completed to support planned study analysis, which were not identified in this SAP, will be documented and reported in appendices to the applicable study reports. Any results from these unplanned analyses (post hoc) will also be clearly identified in the text of the applicable study reports.

8.1.4. Multiple Comparisons/Multiplicity

There will be no adjustment for multiple treatment group comparisons in this Phase 2 study.

8.2. Primary Endpoints

Part A:

This study is designed to be exploratory and descriptive in nature and no formal hypothesis testing is planned. Therefore, descriptive statistics will be used to summarize the results regarding dose modification following successful hair regrowth for each dose group. In Part A, Period 1, a Responder is defined as having an absolute SALT score ≤20 at Week 24 of the Treatment Period. Only Responders will enter into Part A, Period 2 (Dose Modification) for the primary efficacy analysis. For Part A of the study, there are two co-primary efficacy endpoints. The first co-primary efficacy endpoint is the percentage of patients achieving LOM criteria (SALT >20) compared to the percentage of patients maintaining treatment success (SALT ≤ 20) for each of the following dose reduction conditions (Period 2 ONLY):

- 12 mg BID reduced to 8 mg BID
- 8 mg BID reduced to 4 mg BID

The second co-primary efficacy analysis is the percentage of patients achieving LOM criteria compared to the percentage of patients maintaining treatment success for each of the following drug discontinuation conditions (Period 2 ONLY):

- 12 mg BID to Placebo
- 8 mg BID to Placebo

Part B:

For Part B of the study, the primary efficacy endpoint is the percentage of patients by dose group achieving ROR, defined as an absolute SALT score of ≤ 20 at Week 24 of re-treatment. The following treatment sequences will be compared:

- Dose reduction in Period 2
    - 12 mg BID reduced to 8 mg BID increased to 12 mg BID
    - 8 mg BID reduced to 4 mg BID increased to 8 mg BID

- Drug discontinuation in Period 2
  - 12 mg BID to placebo to 12 mg BID
  - 8 mg BID to placebo to 8 mg BID

8.2.1. Computation of the Primary Endpoints

The SALT is a measure of hair loss that quantifies the amount of scalp surface without hair in a pre-specified quadrant of the scalp (right side, top, left side, back), that is further summed after applying a quadrant-specific multiplier indicative of scalp surface area contribution, to provide an overall score of total hair loss. An example of the SALT assessment can be found in Appendix 18.2 of protocol.

The primary endpoints for each Part of the study consist of deriving and categorizing the individual overall SALT scores (≤ 20 versus > 20).

Due to the variable time on study for each patient within Part A Period 2, the primary analysis visit will be the End of Part A Period 2, where the last observed non-missing SALT value is selected for each patient. Otherwise, missing data will not be imputed for this descriptive, exploratory study.

Patterns of missing values across visits will be listed and summarized with numbers and percentages by treatment and visit.

8.2.2. Primary Analysis of the Primary Endpoints

This study is designed to be exploratory and descriptive in nature and no formal hypothesis testing is planned. Therefore, descriptive statistics will be used to summarize the results for each Part/Period.

The observed number and percentage of patients with an absolute SALT score ≤ 20 versus those with an absolute SALT score >20, will be reported by treatment group with 95% confidence intervals (using the binomial approximation with a Wald continuity correction). This analysis will be completed for the Efficacy Population. The results may also be displayed graphically. No p-values will be reported.

8.2.3. Sensitivity Analyses of the Primary Analysis

No sensitivity analyses specified.

8.2.4. Secondary Analyses of the Primary Endpoint

No secondary analyses specified.

8.3. Key Secondary Endpoints

No key secondary endpoints specified.

8.4. Secondary Endpoints

Analyses for secondary endpoints will be performed using the Efficacy Population.

Missing values will not be imputed.

For the secondary endpoints of proportions or percentages of patients achieving specified improvement criteria (hereinafter, "secondary responder endpoints"), pairwise treatment group differences in percentages and 95% CIs will be calculated in Part A Period 1 only.

Observed counts and percentages of responders will be summarized by treatment group for each Part/Period. 95% confidence intervals for percentages of responders and/or non-responders will be calculated using the binomial approximation with a Wald continuity correction.

For the secondary endpoints of absolute or relative changes (hereinafter, "continuous secondary endpoints"), continuous secondary endpoints will be summarized with descriptive statistics only and no treatment differences will be calculated. Descriptive statistics will include the number of subjects with data, mean, standard deviation, median, minimum, and maximum.

For Part A Period 1 only, treatment differences for continuous secondary endpoints will be assessed with a mixed-effect model of repeated measures (MMRM). Baseline SALT score will be included as a model covariate. Treatment group comparisons at each visit will be based on least squares (LS) mean estimates. An unstructured covariance matrix will be used to model the within-subject errors. Should the model fail to converge, an alternative autoregressive covariance matrix will be used instead. The Kenward-Roger approximation will be used to estimate the denominator degrees of freedom. Assuming that the data are MAR, the estimates of the treatment differences calculated from the MMRM described above are unbiased. Standard descriptive statistics will be reported for each time point on the values and changes from baseline along with the LS means, standard errors, 95% CIs and differences between treatment groups reported with LS means, standard errors, and 95% CIs. P-values will not be displayed.

8.4.1. Secondary SALT Endpoints

The following secondary SALT responder endpoints will be assessed:

Part A

- Percentage of patients achieving LOM criteria (SALT > 20) for each *dose reduction* condition at Weeks 4, 8, 12, 16, 20, and 24 (Period 2 ONLY). Note that these timepoints in Period 2 are equivalent to Weeks 28, 32, 36, 40, 44, and 48, respectively.
- Percentage of patients achieving LOM criteria (SALT > 20) for each *drug discontinuation* condition at Weeks 4, 8, 12, 16, 20, and 24 (Period 2 ONLY). Note that these timepoints in Period 2 are equivalent to Weeks 28, 32, 36, 40, 44, and 48, respectively.
- Percentage of patients achieving an absolute SALT score ≤ 20 at Weeks 4, 8, 12, 16, 20, and 24 (Period 1 ONLY)
- Relative change in SALT scores from Baseline at Weeks 4, 8, 12, 16, 20, and 24 (Period 1 ONLY)

Part B:

- Percentage of patients achieving the ROR criteria (SALT ≤ 20) at Weeks 4, 8, 12, 16, and 20
- Relative change in SALT scores from Part B Baseline at Weeks 4, 8, 12, 16, 20, and 24

Secondary endpoints on percentage of patients achieving an absolute SALT score of ≤20 or SALT >20, will be assessed according to Section 8.4.

The continuous secondary SALT endpoint of relative change in SALT score from baseline at Weeks 4, 8, 12, 16, 20, and 24 in Part A Period 1 will be assessed with an MMRM, according to Section 8.4. The baseline SALT score will be as follows for each endpoint per Part:

Relative reduction is based on relative change from baseline.

Relative change in SALT score is derived as percent change of the follow-up SALT score, where baseline SALT score is the denominator (i.e. absolute change divided by the baseline score, multiplied by 100).

In addition, summary statistics for the mean, mean change, and mean relative change in total SALT score from Part A Period 1 baseline will be reported for Part A Period 1, Part A Period 2, and Part B. The mean and mean change in total SALT score from Part A Period 2 baseline will be reported for Part A Period 2 and Part B. Mean relative change from Part A Period 2 baseline will not be calculated as baseline values may be zero by design and would result in undefined relative changes. The mean, mean change, and mean relative change in total SALT score from Part B baseline will be reported for Part B.

8.4.2. Secondary SPRO Endpoints

The following secondary SPRO responder endpoints will be assessed:

- Percentage of responders (defined as “satisfied” or “very satisfied”) on the SPRO scale at Weeks 12, 16, 20, and 24 (Part A Period 1 ONLY)

The SPRO is a single item questionnaire answered by the patient, designed to measure how satisfied alopecia areata patients are with their hair at the time of the assessment. The SPRO responses are on a scale of 1-5, where 1 = very satisfied, 2 = satisfied, 3 = neither satisfied nor dissatisfied, 4 = dissatisfied, and 5 = very dissatisfied. An example of the SPRO assessment can be found in Appendix 18.4.1 of the protocol.

A responder is defined as patients with answers of “very satisfied” or “satisfied” at each post-treatment visit on the SPRO. No missing data will be imputed for this endpoint.

8.4.3. Clinical Global Impression of Improvement (CGI-I)

The CGI-I will be assessed by the Investigator at Weeks 12, 16, 20, and 24, in Part A Period 1 only. Compared to the patient’s alopecia areata prior to treatment at baseline, the patient’s current state of alopecia areata will be assessed according to the Investigator’s perceived change. The Investigator may select one of seven numeric choices representing “Very Much Worse” to “Very Much Improved”. To reduce variability, one rater should perform the CGI-I assessment for the patient for the duration of the study. An example of the CGI-I assessment can be found in Appendix 18.3.2 of the protocol.

The percentage of responders (defined as “much improved” or “very much improved”) using the CGI-I at Weeks 12, 16, 20, and 24 will be assessed per Section 8.4 in Part A Period 1 only. No missing data will be imputed for this endpoint.

8.4.4. Clinical Global Impression of Severity (CGI-S)

The CGI-S will be assessed by the Investigator and will consider the severity of the patient's alopecia areata at the time of assessment. The Investigator may select one of seven numeric choices representing "Among the most extreme hair loss" to "Normal, no hair loss". To reduce variability, one rater should perform the CGI-S assessment for the patient for the duration of the study. An example of the CGI-S assessment can be found in Appendix 18.3.1 of the protocol.

The continuous secondary endpoint of change from baseline in the CGI-S at Weeks 12, 16, 20, and 24 will be assessed per Section 8.4 in Part A Period 1 only. No missing data will be imputed for this endpoint.

8.4.5. Patient Global Impression of Improvement (PGI-I)

The PGI-I will be assessed by the patient at Weeks 12, 16, 20, and 24 in Part A Period 1 only. Compared to the patient's alopecia areata prior to treatment at baseline, the patient's current state of alopecia areata will be assessed according to his/her perceived change. The patient may select one of seven numeric choices representing "Very Much Worse" to "Very Much Improved". An example of the PGI-I assessment can be found in Appendix 18.3.4 of the protocol.

The secondary PGI-I responder endpoint of percentage of responders (defined as "much improved" or "very much improved") at Weeks 12, 16, 20, and 24 will be assessed per Section 8.4 in Part A Period 1 only. No missing data will be imputed for this endpoint.

8.4.6. Patient Global Impression of Severity (PGI-S)

The PGI-S will be assessed by the patient and will consider the severity of his/her alopecia areata at the time of assessment. The patient may select one of seven numeric choices representing "Among the most extreme hair loss" to "Normal, no hair loss". An example of the PGI-S assessment can be found in Appendix 18.3.3 of the protocol.

The continuous secondary endpoint of change from baseline in the PGI-S at Weeks 12, 16, 20, and 24 will be assessed per Section 8.4 in Part A Period 1 only. No missing data will be imputed for this endpoint.

8.4.7. Quality of Hair Patient Reported Outcome (QPRO)

The QPRO questionnaire is a 4-item assessment which provides additional details on key attributes of patient hair and helps provide context to the SPRO response. Like the SPRO, the QPRO responses are on a scale of 1-5, where 1 = very satisfied, 2 = satisfied, 3 = neither satisfied nor dissatisfied, 4 = dissatisfied, and 5 = very dissatisfied. An example of the QPRO assessment can be found in Appendix 18.4.2 of the protocol.

The continuous secondary endpoints of change from baseline for each individual item of QPRO at Weeks 12, 16, 20, and 24 will be assessed per Section 8.4 in Part A Period 1 only. No missing data will be imputed for this endpoint.

8.5. Other Endpoints

8.5.1. Time to First LOM (Part A only)

Time to first LOM (in weeks) will be summarized descriptively with Kaplan-Meier methodology for patients in the Efficacy Population who entered Part A Period 2. Treatment sequence across Period 1 and Period 2 (8 mg BID to 4 mg BID, 8 mg BID to placebo, 12 mg BID to 8 mg BID, and 12 mg BID to placebo) will be used as strata to present quantiles (25%, median, 75%), if estimable. Ninety-five percent confidence intervals for the median will be presented, if estimable, using the Brookmeyer and Crowley (1982) method. If KM statistics are not estimable, standard descriptive statistics for non-censored patients will be displayed.

First LOM is defined as the first date where a patient has an absolute SALT score >20 in Part A Period 2. Time in weeks will be calculated from the date of randomization in Part A Period 2, as

- (date of first LOM (or censored date) - date of Part A Period 2 randomization + 1)/7

Patients who do not experience LOM before completion of Part A Period 2 or otherwise prematurely discontinue from Part A Period 2 will be censored at their last study visit date where SALT was measured in Part A Period 2 of the study, or a maximum or 24 weeks.

A Kaplan-Meier plot over time will also be presented.

8.6. Examination of Subgroups

No subgroup analyses are planned.

9. SAFETY EVALUATION

9.1. Overview of Safety Analysis Methods

All safety summaries will be descriptive with no statistical hypothesis testing and based on the Safety Population. Patients will be summarized according to the study drug received (i.e., as treated), should it differ from the randomized treatment arm. Safety assessments will be summarized by treatment group and overall, for each Part/Period of the study. All safety endpoints will be listed in by-patient data listings.

9.2. Extent of Exposure

Study drug exposure will be summarized for each treatment group and overall for each Part/Period. The number of days on which study drug was dosed (at least partially), the number of days in the study exposed, and total cumulative dose will be summarized for each treatment group. The number and percentage of patients with at least one drug interruption will also be summarized.

The total number of days in the study exposed will include/ignore drug interruptions. The total number of days on study drug (excluding dose interruptions) and drug compliance will also be summarized, per Section 7.3.

9.3. Adverse Events

An adverse event is any untoward medical occurrence that may appear or worsen in a patient during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the patient's health, including laboratory test values, regardless of etiology. Any worsening (ie, any clinically significant adverse change in the frequency or intensity of a pre-existing condition) should be considered an adverse event. A diagnosis or syndrome should be recorded on the adverse event page of the eCRF rather than the individual signs or symptoms of the diagnosis or syndrome. A worsening of the condition under study, alopecia areata, will not be reported as an adverse event.

All patients will be monitored for adverse events during the study. Assessments may include monitoring of the following parameters: the patient's clinical symptoms, laboratory, physical examination findings, or findings from other tests and/or procedures.

Adverse events will be coded using MedDRA version 23.1, and summarized by treatment group, system organ class, and preferred term for each Part/Period of the study.

An adverse event reported after informed consent, but before the first dose of study drug (i.e., Day 1), will be considered a pre-treatment adverse event. TEAEs will be defined as any adverse event that occurs after administration of the first dose of study drug in each Part/Period (ie, on or after the day of the first dose in each Part/Period). Adverse events will further be considered treatment-emergent with respect to a given Part/Period if the adverse event occurred after administration of the first dose of study drug in that Part/Period and, if the patient continues onto a subsequent period part, prior to the first dose of study drug in the subsequent Part/Period. Adverse events will be limited to those collected within this protocol (ie, for rollover patients, AEs collected under the protocol of the rollover study but not in this study will not be in this

study). The number and percentage of patients who report TEAEs will be summarized by treatment group, system organ class, and preferred term.

Treatment emergent adverse events will also be summarized by intensity as well as relationship to study drug.

Partial dates will be imputed for the purposes of defining TEAEs as follows:

- For a missing start day where the month and year are present, the start day will be set to the first day of the month, unless 1) the first day of the month is before the date of administration of study drug and the month and year are the same as the month and year of the date of administration of study drug, and 2) the end date is on or after the date of administration of study drug or the end date is completely missing, in which case the start day will be set to the first day of administration of study drug.
- For a missing start day and month where the year is present, the start day and month will be set to January 1st, unless 1) January 1st is before the date of administration of study drug, and 2) the end date is on or after the date of administration of study drug or the end date is completely missing, in which case the start day and month will be set to that of the first date of administration of study drug.
- For an entirely missing start date (ie day, month, and year are missing), the start date will be set to the date of administration of study drug in Part A Period 1, unless 1) the stop date is prior to the date of administration of study drug in in Part A Period 1 which case the start date will be set to the stop date, or 2) the stop date is between the start date of Part A Period 2 and the end date of Part A Period 2, in which case, the date will be set to treatment start date of Part A Period 2, or 3) the stop date is between the start date of Part B and the end date of Part B, in which case, the date will be set to the treatment start date of Part B.
- For a missing end day where the month and year are present, the end day will be set to the last day of the month, unless the month and year are the same as the month and year of the last visit date for the patient, in which case the end day will be set to that of the patient's last visit date.
- For a missing end day and month where the year is present, the end day and month will be set to the patient's last visit date, unless the year of the patient's last visit date is greater than the end year, in which case the end day and month will be set to December 31st.
- For an entirely missing stop date (i.e. day, month, and year are missing), the stop date will be imputed as the patient’s last visit date.

Partial dates will be compared to the start and end dates of each Part/Period to determine the study drug administration date that will be used to be imputed.

Patients who report the same preferred term on multiple occasions will be counted once per Part/Period for the preferred term: under the highest severity when summarized by severity and under the closest relationship to study drug when summarized by relationship. Missing severity or relationship will not be imputed. If a patient reports multiple preferred terms for a system organ class, the patient will be counted only once for that system organ class.

The number and percentage of patients who experience TEAEs will be summarized by treatment group and overall for each Part/Period for the following:

- By system organ class and preferred term
- By severity/intensity, system organ class, and preferred term
- By relationship to study drug, system organ class, and preferred term
- Serious adverse events by system organ class and preferred term
- Serious adverse events by relationship to study drug, system organ class, and preferred term
- Adverse events resulting in discontinuation of study drug by system organ class and preferred term
- Adverse events that result in study drug dose interruption by system organ class and preferred term

The number of TEAEs (events) will also be reported. By-patient listings will include all adverse events. TEAEs will be flagged.

9.4. Deaths, Serious Adverse Events, and Other Significant Adverse Events

A serious adverse event is an adverse event that fulfills the following criteria:

- Is fatal (results in death);
- Is life-threatening (Note: the term "life-threatening" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event that could hypothetically have caused death had it been more severe);
- Requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization is defined as an inpatient admission, regardless of length of stay);
- Results in persistent or significant disability/incapacity (a substantial disruption of the patient's ability to conduct normal life functions);
- Is a congenital anomaly/birth defect; or
- Constitutes an important medical event that may jeopardize the patient or may require medical or surgical intervention to prevent one of the other outcomes listed above.

Serious adverse events will be summarized according to Section 9.3.

By-patient listings will be provided for any deaths, serious adverse events, and adverse events leading to discontinuation of treatment. TEAEs that result in dose interruption will also be identified in these listings.

9.5. Clinical Laboratory Evaluation

Clinical laboratory samples should be collected at the beginning of each clinic visit and just prior to a dose on all Study Visit Days and will be processed by a central laboratory. In the event a

patient is unable to attend an in-clinic visit due to COVID-19, clinical laboratory blood draws may be performed by a Home Health Care agency or a local laboratory.

Clinical laboratory variables will be presented in 4 main ways, for each Part/Period of the study. First, change from baseline to each scheduled visit. Only post-baseline values on treatment (i.e., on the same date or prior to last dose of study drug) will be eligible for change from baseline calculations. Summary statistics for the mean and mean change from Part A Period 1 baseline will be reported for Part A Period 1, Part A Period 2, and Part B. The mean and mean change from Part A Period 2 baseline will be reported for Part A Period 2 and Part B. The mean and mean change from Part B baseline will be reported for Part B

Second, treatment-emergent potentially clinically significant (PCS) laboratory values will be identified. Potentially clinically significant values are defined as those that meet Grade 3 or Grade 4 toxicity criteria from the CTCAE criteria (or Grade 2 or higher for platelets). Laboratory values will be graded using CTCAE version 5.0, for those values included. CTCAE grades will be based solely on numeric results and without regard to other symptoms based on clinical judgment. For laboratory parameters whose CTCAE grading is independent of baseline criteria, treatment-emergent PCS laboratory values are those in which the baseline value is not PCS and the post-baseline value is PCS. For laboratory parameters whose CTCAE grading is dependent upon baseline criteria, any post-baseline grading of Grade 3 or Grade 4 (or Grade 2 or higher for platelets) will be considered treatment-emergent. The number and percentage of patients with treatment-emergent PCS laboratory values will be summarized by treatment group and overall for each clinical laboratory variable patient to CTCAE grading. For this analysis, the visit with the highest CTCAE grade value within a window will be selected.

Third, box plots of hemoglobin, platelets, and neutrophils will also be provided with dose interruption limits included as reference lines (see Protocol Section 10.2.1).

Finally, the count and percentage of abnormal laboratory values per parameter, where applicable, will be provided. Additionally, a listing of patients with Abnormal laboratory values will be provided.

These analyses will be repeated for serum chemistry results, hematology results, and lipid results (where lipid tests include total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides). Laboratory results will also be listed. Reference ranges for each clinical laboratory parameter will also be summarized in a data listing.

Pregnancy test results will be listed only.

9.6. Vital Signs, Physical Findings, and Other Observations Related to Safety

9.6.1. Vital Signs

Vital signs will be measured after the patient has been in a supine or semi-supine position for at least 5 minutes and will include blood pressure, pulse rate, respiratory rate, and temperature.

Height will only be measured at the Screening Visit in Part A Period 1. Weight and vital signs will be measured according to the Schedule of Assessments (Appendix 15.2). Weight and height will be used to calculate the patient's body mass index at Screening.

The mean change from Part A Period 1 baseline to each scheduled assessment will be summarized descriptively by treatment group and overall for each vital sign variable specified in the protocol.

The number and percentage of patients with at least 1 PCS vital sign value, defined as for laboratory values in Section 9.5, will be summarized descriptively by treatment group and overall. A listing of vital signs by patient will also be provided.

9.6.2. Physical Examinations

A complete physical examination will consist of an examination of all major organ systems to include, but not be limited to, chest auscultation, abdominal auscultation and palpation, head, eyes, ears, nose and throat. An assessment for active signs and symptoms of infection including tuberculosis and skin examinations for non-melanoma skin cancers will be performed. Evaluation for progressive multifocal leukoencephalopathy symptoms such as facial droop, general weakness, clumsiness, trouble speaking, personality changes, memory problems, and vision changes will be assessed.

Additionally, an assessment for the presence or absence of nasal hair will be performed during complete physical exams. Presence or absence of nasal hair will be summarized at baseline, Week 24 (Part A Period 1), Week 48 (Part A Period 2), and Week 24 (Part B). The presence or absence of nasal hair will be summarized as counts and percentages by treatment group and visit for the Safety Population, for each Part/Period of the study.

Brief physical examinations will include assessment for active signs and symptoms of infection, including tuberculosis, skin examinations for non-melanoma skin, and an evaluation for PML symptoms such as facial droop, general weakness, clumsiness, trouble speaking, personality changes, memory problems, and vision changes. Brief physical examinations will be performed according the Schedule of Events (Appendix 15.2).

A listing of the date and type of physical examinations performed will be provided. The listing will include presence or absence of nasal hair. Deteriorations from baseline on physical examination will be coded as adverse events and summarized as such.

9.6.3. Other Safety Measures

9.6.3.1. 12-Lead Electrocardiogram

Twelve-lead electrocardiograms (ECG) will be performed according to the Schedule of Assessments (Appendix 15.2) after the patient has rested in a supine or semi-supine position for at least 5 minutes. Individual parameters including heart rate, PR, QT, QTcF (Frederica's correction), QRS, and RR intervals will be collected. If a patient is unable to attend an in-person clinic visit due to COVID-19, an ECG may not be performed. Missed assessments will be recorded in the eCRF as due to COVID-19.

The mean change from Part A Period 1 baseline to each scheduled assessment will be summarized descriptively by treatment group and overall for each ECG variable specified in the protocol, for each Part/Period of the study.

A listing of ECG results will be provided. A listing of abnormal ECG findings will also be provided.

10. PHARMACOKINETIC EVALUATION

Pharmacokinetic samples will be collected in Part A, Period 1 at the following time points to evaluate plasma concentrations of CTP-543:

- Day 1 (post-dose) and Weeks 12 and 24 (variable times post-dose)

The exact time of blood collection as well as the exact time of the preceding dose will be recorded. All attempts to adhere to the pharmacokinetic schedule should be made. However, the inability to follow the schedule or to obtain/process a sample will not be considered a protocol deviation.

Sparse PK sampling was performed in this study in order to contribute to a cross study population PK analysis. Covariates from this study and others will include age, gender, race, weight (or BMI), for the population PK analysis of CTP-543. Exposure-response relationships for both efficacy and safety parameters will also be assessed. This population PK analysis will be described in a separate analysis plan and a separate population PK report will be generated. The data will not be summarized in the CP543.2004 final clinical study report.

A by-patient listing of whether PK sampling was performed will be included in the final clinical study report.

11. OTHER ANALYSES

In light of the COVID-19 pandemic and recommendations in the FDA guidance document "Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency", the following additional listings and summaries will be provided:

- Listing of patients affected by COVID-19 related study disruption, defined as missed or remote visits or assessments indicated per the eCRF.
- Listing of dosing exceptions related to COVID-19.
- Summary and listing of protocol deviations related to COVID-19, per Section 7.1.
- Summary of TEAEs related to COVID-19 by system organ class and preferred term and TEAEs related to COVID-19 leading to study drug discontinuation by system organ class and preferred term, per Section 9.3. Relationship to COVID-19 will be determined using the Standard MedDRA Query for COVID-19 (Appendix 15.3) and may also include preferred terms related to vaccinations if the collected term indicates relation to COVID-19 (ex: Vaccination complication, Vaccination site pain). Terms may be reviewed by the sponsor prior to database lock to finalize the list of preferred terms.
- Listing of TEAEs related to COVID-19.
- Listing of prior and concomitant medications related to COVID-19, where relationship to COVID-19 is defined by the question "Related to COVID-19?" on the Prior and Concomitant Medications CRF page.
- Summary of number and percentage of randomized patients with missed visits due to COVID-19.

12. INTERIM ANALYSES AND DATA MONITORING

There is no data monitoring committee planned for this study.

The PK population analyses will be conducted at the end of Part A, Period 1 by the PK vendor. Details on the PK population analyses will be provided in a separate analysis plan.

See Section 13.5 of the protocol. An interim analysis to support regulatory activities related to an upcoming CTP-543 NDA submission will be conducted. The focus of the interim analyses will be on safety data and will occur following completion of Part A, Period 1, addressed in a separate Integrated Summary of Safety SAP.

Per protocol Section 8.1, the primary efficacy assessment for Part A will be conducted when all patients have completed Part A, Period 2. An analysis of safety data from Part A will also be conducted. These analyses will be submitted as the abbreviated report. The analyses described in this document to be included in the abbreviated report for the primary efficacy assessment for Part A and safety summary are indicated in the list of planned tables, listings, and figures in Appendix 15.4.

Site personnel and patients will remain blinded throughout the entirety of Part A and Part B. Dissemination of these results will be limited to the unblinded reporting team of the CRO and Sponsor management. The Sponsor and CRO personnel who are unblinded will be separate from the direct study team. The Sponsor and CRO will still maintain the blind for study team members who will be involved in daily study conduct, study management, safety and data monitoring through the completion of the study. There will be no impact on CP543.2004 study conduct, analysis, or reporting.

13. CHANGES TO THE ANALYSES PLANNED IN THE PROTOCOL

The following alterations were made to the original analyses planned in the protocol:

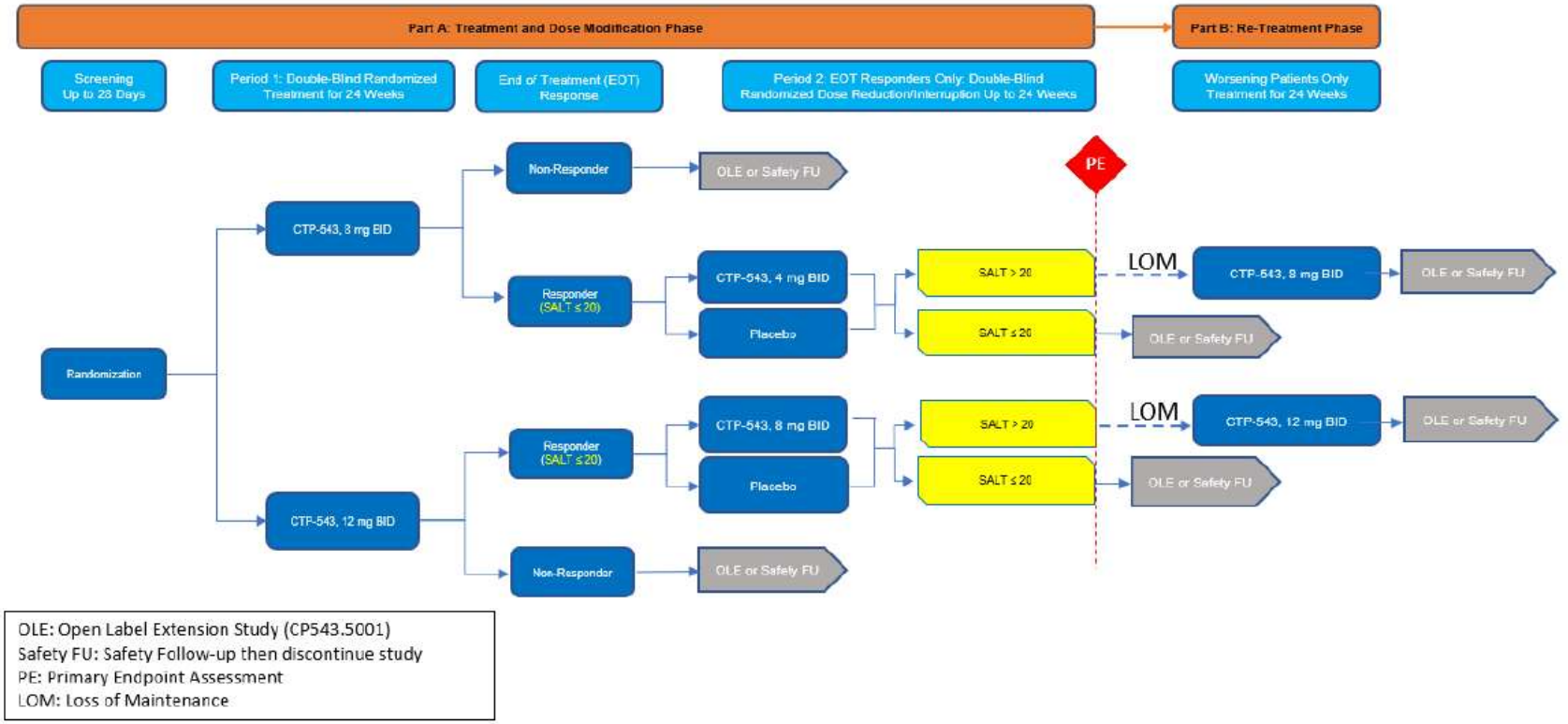
- An additional summary of percentage of patients achieving an absolute SALT score ≤ 20 at Week 4 was added for Part A Period 1.
- An additional summary of the presence or absence of nasal hair from physical examinations was added for each Part/Period of the study
- Details added to protocol definition for analysis populations in Section 13.3. The text "Patients will be summarized according to study drug dose received (i.e., as treated) should it differ from the randomized arm" was amended to add additional information in the event that a patient is given only a portion of the incorrect treatment.
- Analyses for COVID-19 were added in Section 11 of the SAP.

14. REFERENCES

Not applicable.

15. APPENDIX

15.1. Study Flow Chart



15.2. Schedule of Events

As copied from the Protocol

Table 1: Schedule of Assessments: Part A

Event	Screening	Part A, Period 1						Part A, Period 2					Safety Follow-Up[6]
	Day -28 to Day -1 (Visit 1)	Randomization[1,2] Day 1 (Visit 2)	Week 2 (Visit 3)	Week 4, 8 (Visit 4, 5)	Week 12 (Visit 6)	Week 16, 20 (Visit 7, 8)	Week 24[3,4] (Visit 9)	Week 28[5] (Visit 10)	Week 32 (Visit 11)	Week 36 (Visit 12)	Week 40, 44 (Visit 13, 14)	Week 48[4] (Visit 15)	Safety Follow-Up Visit
Informed consent	X												
Eligibility assessment	X	X											
Demographics	X												
Medical history	X	X											
Randomization		X					X[7]						
PE	X	X					X					X	X
Brief PE				X	X	X			X	X	X		
Height	X												
Weight	X	X		X	X	X	X		X	X	X	X	X
Pregnancy test[8]	X	X[9]		X	X	X	X	X	X	X	X	X	
Tuberculosis test	X												
Clinical laboratory testing[10, 11]	X[12]	X	X	X	X	X	X	X	X	X	X	X	X
Lipid assessment[13]		X			X		X			X		X	X
HBV and HCV test	X												
12-lead electrocardiogram	X	X			X		X			X		X	X
Vital signs	X	X		X	X	X	X		X	X	X	X	X
SALT assessment	X	X		X	X	X	X	X[14]	X[14]	X[14]	X[14]	X	
Photographs	X	X		X	X	X	X	X	X	X	X	X	
SPRO and QPRO		X			X	X	X						
CGI-S and PGI-S		X			X	X	X						
CGI-I and PGI-I					X	X	X						
Dispense study drug		X		X	X	X	X[7]	X[15]	X[15]	X[15]	X[15]		
Pharmacokinetic blood sampling[16]		X			X		X						
Study drug accountability				X	X	X	X		X	X	X	X	
Adverse events	X	X								X			X
Concomitant medications	X	X								X			X

PE = Physical Examination; HBV= hepatitis B virus; HCV = hepatitis C virus; SPRO = Satisfaction of Hair Patient Reported Outcome; QPRO = Quality of Hair Patient Reported Outcome; CGI-S = Clinical Global Impression of Severity; CGI-I = Clinical Global Impression of Improvement; PGI-S= Patient Global Impression of Severity; PGI-I = Patient Global Impression of Improvement;

[1] Day 1 (Visit 2) may occur any time after Screening laboratory results are available and reviewed by the Investigator.
[2] For Part A, Period 1, all subsequent visits and week increments should be based on the date of Visit 2. All visit windows are ±2 days.
[3] Week 24 from Part A, Period 1 will also serve as the Day 1 visit for Part A, Period 2 for those who meet criteria to continue into the Dose Modification Phase.
[4] Also serves as the Early Termination Visit for patient withdrawal in this period.
[5] For Part A, Period 2, all subsequent visits and week increments should be based on the date of Week 24 (Visit 9). All visit windows are ±2 days.
[6] The Safety Follow-Up Visit is intended as an Exit Visit for those subjects who discontinue the trial or for those who do not continue into the Open-label Extension study following completion of Part A, Period 1 or Part A, Period 2.
[7] Randomization and dispensation of study drug will occur on Week 24 **only** for those subjects who meet criteria and will continue into Part A, Period 2.
[8] Serum pregnancy test for females of childbearing potential only. Subjects who are surgically sterile or (hysterectomy or bilateral ligation) or post-menopausal (cessation of menses for at least 12 months prior to screening) need not be tested.
[9] Urine pregnancy test should be performed at the randomization visit.
[10] Includes hematology and serum chemistry, fasted.
[11] Collect pre-dose if subject is dosing in the clinic on study visit days.
[12] Will include thyroid stimulating hormone and hemoglobin A1c at Screening only.
[13] Includes total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides under fasted conditions.
[14] If SALT score >20 at any visit in Part A, Period 2, patient will enter into Part B of the study and return to their original 8 mg BID or 12 mg BID dose from Part A, Period 1. However, all safety assessments outlined in Part A, Period 2 should be performed prior to dispensing study drug in Part B.
[15] Dispensation in Part A, Period 2 will only occur for subjects whose SALT remains ≤ 20. If SALT >20, the subject should proceed to Day 1 (Visit B1).
[16] Day 1 (post-dose) and Weeks 12 and 24 (variable times post-dose)

Table 2: Schedule of Assessments: Part B

Event	Treatment Period						Safety Follow-Up[4]
	Day 1[1, 2] (Visit B1)	Week 2 (Visit B2)	Week 4, 8 (Visit B3, B4)	Week 12 (Visit B5)	Week 16, 20 (Visit B6, B7)	Week 24[3] (Visit B8)	Week 28 (Visit B-SFU)
Physical examination						X	X
Brief physical examination			X	X	X		
Weight			X	X	X	X	X
Pregnancy test[5]			X	X	X	X	
Clinical laboratory testing[6]		X	X	X	X	X	X
Lipid assessment[7]				X		X	X
12-lead electrocardiogram				X		X	X
Vital signs			X	X	X	X	X
SALT assessment			X	X	X	X	
Photographs			X	X	X	X	
Dispense study drug	X[8]		X	X	X		
Study drug accountability			X	X	X	X	
Adverse events	X						X
Concomitant medications	X						X

[1] All subsequent visits and week increments should be based on the date of Visit B1. All visit windows are ±2 days.
[2] As Day 1 occurs on the same day as the last visit from Part A, Period 2, eligible subjects for Part B will not have assessments repeated.
[3] Also serves as the Early Termination Visit for patient withdrawal in this period or any patient meeting ROR criteria and entering OLE.
[4] The Safety Follow-Up Visit is intended as an Exit Visit for those patients who do not roll over into an open-label extension and for patients who have been discontinued from the study and completed the Early Termination Visit (Week 24).
[5] Serum pregnancy test for females of childbearing potential only. Subjects who are surgically sterile or (hysterectomy or bilateral ligation) or post-menopausal (cessation of menses for at least 12 months prior to screening) need not be tested.
[6] Includes hematology and serum chemistry, fasted.
[7] Includes total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides under fasted conditions.
[8] Any patient from Part A, Period 2 meeting the LOM criteria will enter into Part B of the study and return to their original 8 mg BID or 12 mg BID dose from Part A, Period 1.

15.3. Standardized MedDRA Query Values for COVID-19

Scope	Preferred Term	Preferred Term Code
Narrow	Asymptomatic COVID-19	10084459
Narrow	Coronavirus infection	10051905
Narrow	Coronavirus test positive	10070255
Narrow	COVID-19	10084268
Narrow	COVID-19 immunisation	10084457
Narrow	COVID-19 pneumonia	10084380
Narrow	COVID-19 prophylaxis	10084458
Narrow	COVID-19 treatment	10084460
Narrow	Exposure to SARS-CoV-2	10084456
Narrow	Multisystem inflammatory syndrome in children	10084767
Narrow	Occupational exposure to SARS-CoV-2	10084394
Narrow	SARS-CoV-2 antibody test positive	10084491
Narrow	SARS-CoV-2 carrier	10084461
Narrow	SARS-CoV-2 sepsis	10084639
Narrow	SARS-CoV-2 test false negative	10084480
Narrow	SARS-CoV-2 test positive	10084271
Narrow	SARS-CoV-2 viraemia	10084640
Narrow	Suspected COVID-19	10084451
Broad	Antiviral prophylaxis	10049087
Broad	Antiviral treatment	10068724
Broad	Coronavirus test	10084353
Broad	Coronavirus test negative	10084269
Broad	Exposure to communicable disease	10049711
Broad	Pneumonia viral	10035737

Broad	SARS-CoV-2 antibody test	10084501
Broad	SARS-CoV-2 antibody test negative	10084509
Broad	SARS-CoV-2 test	10084354
Broad	SARS-CoV-2 test false positive	10084602
Broad	SARS-CoV-2 test negative	10084273

15.4. List of Planned Tables, Listings, and Figures

Type	Number	Title	Population	For abbreviated report?
Table	14.1.1.1	Summary of Patient Disposition and Reasons for Discontinuation — Part A Period 1	All Screened Patients	Y
Table	14.1.1.2	Summary of Patient Disposition and Reasons for Discontinuation — Part A Period 2	All Randomized Patients	Y
Table	14.1.1.3	Summary of Patient Disposition and Reasons for Discontinuation — Part B	All Randomized Patients	
Table	14.1.2.1	Summary of Randomized Patients by Site — Part A Period 1	All Randomized Patients	Y
Table	14.1.2.2	Summary of Randomized Patients by Site — Part A Period 2	All Randomized Patients	Y
Table	14.1.2.3	Summary of Randomized Patients by Site — Part B	All Randomized Patients	
Table	14.1.3.1.1	Summary of Protocol Deviations — Part A Period 1	All Randomized Patients	Y
Table	14.1.3.1.2	Summary of Protocol Deviations — Part A Period 2	All Randomized Patients	Y
Table	14.1.3.1.3	Summary of Protocol Deviations — Part B	All Randomized Patients	
Table	14.1.3.2.1	Summary of Protocol Deviations Related to COVID-19 — Part A Period 1	All Randomized Patients	Y
Table	14.1.3.2.2	Summary of Protocol Deviations Related to COVID-19 — Part A Period 2	All Randomized Patients	Y
Table	14.1.3.2.3	Summary of Protocol Deviations Related to COVID—19 — Part B	All Randomized Patients	
Table	14.1.4.1	Summary of Demographics — Part A Period 1	All Randomized Patients	Y
Table	14.1.4.2	Summary of Demographics — Part A Period 2	All Randomized Patients	Y
Table	14.1.4.3	Summary of Demographics — Part B	All Randomized Patients	
Table	14.1.5.1	Summary of Baseline Characteristics — Part A Period 1	All Randomized Patients	Y
Table	14.1.5.2	Summary of Baseline Characteristics — Part A Period 2	All Randomized Patients	Y
Table	14.1.5.3	Summary of Baseline Characteristics — Part B	All Randomized Patients	

Type	Number	Title	Population	For abbreviated report?
Table	14.1.6	Summary of Medical History by System Organ Class and Preferred Term	Safety Population	
Table	14.1.7.1	Summary of Study Drug Administration and Compliance by Treatment Group — Part A Period 1	Safety Population	Y
Table	14.1.7.2	Summary of Study Drug Administration and Compliance by Treatment Group — Part A Period 2	Safety Population	Y
Table	14.1.7.3	Summary of Study Drug Administration and Compliance by Treatment Group — Part B	Safety Population	
Table	14.1.8.1	Summary of Prior Medications	Safety Population	
Table	14.1.8.2.1	Summary of Concomitant Medications — Part A Period 1	Safety Population	Y
Table	14.1.8.2.2	Summary of Concomitant Medications — Part A Period 2	Safety Population	Y
Table	14.1.8.2.3	Summary of Concomitant Medications — Part B	Safety Population	
Table	14.2.1.1	Part A Period 2 Co-Primary Endpoints: Patients with Loss of Regrowth Maintenance (SALT Score >20) versus Responders (SALT Score ≤20)	Efficacy Population	Y
Table	14.2.1.2	Part B Primary Endpoint: Patients with Restoration of Regrowth (SALT Score ≤20) at Week 24	Efficacy Population	
Table	14.2.2.1	Patients with Absolute SALT Score ≤20 at Weeks 4, 8, 12, 16, 20, and 24 — Part A Period 1	Efficacy Population	Y
Table	14.2.2.2	Patients with Loss of Regrowth Maintenance (SALT Score >20) or Response (SALT Score ≤20) at Weeks 4, 8, 12, 16, 20, and 24 — Part A Period 2	Efficacy Population	Y
Table	14.2.2.3	Patient with Restoration of Regrowth (SALT Score ≤20) at Weeks 4, 8, 12, 16, 20, and 24 — Part B	Efficacy Population	

Type	Number	Title	Population	For abbreviated report?
Table	14.2.2.4	Mixed Model for Repeated Measures Analysis of Relative Change from Part A Period 1 Baseline in Total SALT Scores by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.2.6.1	Mean, Mean Change, and Mean Relative Change from Part A Period 1 Baseline in Total SALT Scores by Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.2.6.2	Mean, Mean Change, and Mean Relative Change from Part A Period 1 Baseline in Total SALT Scores by Visit — Part A Period 2	Efficacy Population	Y
Table	14.2.2.6.3	Mean and Mean Change from Part A Period 2 Baseline in Total SALT Scores by Visit — Part A Period 2	Efficacy Population	Y
Table	14.2.2.6.4	Mean, Mean Change, and Mean Relative Change from Part A Period 1 Baseline in Total SALT Scores by Visit — Part B	Efficacy Population	
Table	14.2.2.6.5	Mean and Mean Change from Part A Period 2 Baseline in Total SALT Scores by Visit — Part B	Efficacy Population	
Table	14.2.2.6.6	Mean, Mean Change, and Mean Relative Change from Part B Baseline in Total SALT Scores by Visit — Part B	Efficacy Population	
Table	14.2.2.7.1	Summary of Missing SALT Scores by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.2.7.2	Summary of Missing SALT Scores by Treatment Group and Visit — Part A Period 2	Efficacy Population	Y
Table	14.2.2.7.3	Summary of Missing SALT Scores by Treatment Group and Visit — Part B	Efficacy Population	
Table	14.2.3.1	Satisfaction of Hair Patient Reported Outcome (SPRO) Responders by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.3.2	Clinician Global Impression of Improvement (CGI-I) Responders by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y

Type	Number	Title	Population	For abbreviated report?
Table	14.2.3.3	Patient Global Impression of Improvement (PGI-I) Responders by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.3.4	Mixed Model for Repeated Measures Analysis of Change from Baseline in Clinician Global Impression of Severity (CGI-S) by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.3.5	Mixed Model for Repeated Measures Analysis of Change from Baseline in Patient Global Impression of Severity (PGI-S) by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.3.6	Mixed Model for Repeated Measures Analysis of Change from Baseline in Quality of Hair Patient Reported Outcome (QPRO) Items by Treatment Group and Visit — Part A Period 1	Efficacy Population	Y
Table	14.2.4.1	Time to First Loss of Regrowth Maintenance (SALT Score >20) Kaplan-Meier Estimates — Part A	Efficacy Population	Y
Table	14.3.1.1.1	Summary of Treatment-Emergent Adverse Events — Part A Period 1	Safety Population	Y
Table	14.3.1.1.2	Summary of Treatment-Emergent Adverse Events — Part A Period 2	Safety Population	Y
Table	14.3.1.1.3	Summary of Treatment-Emergent Adverse Events — Part B	Safety Population	
Table	14.3.1.2.1	Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.2.2	Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.2.3	Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term — Part B	Safety Population	
Table	14.3.1.3.1	Summary of Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term — Part A Period 1	Safety Population	Y

Type	Number	Title	Population	For abbreviated report?
Table	14.3.1.3.2	Summary of Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.3.3	Summary of Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term — Part B	Safety Population	
Table	14.3.1.4.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.4.2	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.4.3	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term — Part B	Safety Population	
Table	14.3.1.5.1	Summary of Treatment-Emergent Adverse Events Resulting in Study Dose Interruption by System Organ Class and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.5.2	Summary of Treatment-Emergent Adverse Events Resulting in Study Dose Interruption by System Organ Class and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.5.3	Summary of Treatment-Emergent Adverse Events Resulting in Study Dose Interruption by System Organ Class and Preferred Term — Part B	Safety Population	
Table	14.3.1.6.1	Summary of Treatment-Emergent Adverse Events by Severity/Intensity, System Organ Class, and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.6.2	Summary of Treatment-Emergent Adverse Events by Severity/Intensity, System Organ Class, and Preferred Term — Part A Period 2	Safety Population	Y

Type	Number	Title	Population	For abbreviated report?
Table	14.3.1.6.3	Summary of Treatment-Emergent Adverse Events by Severity/Intensity, System Organ Class, and Preferred Term — Part B	Safety Population	
Table	14.3.1.7.1	Summary of Treatment-Emergent Adverse Events by Relationship, System Organ Class, and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.7.2	Summary of Treatment-Emergent Adverse Events by Relationship, System Organ Class, and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.7.3	Summary of Treatment-Emergent Adverse Events by Relationship, System Organ Class, and Preferred Term — Part B	Safety Population	
Table	14.3.1.8.1	Summary of Serious Treatment-Emergent Adverse Events by Relationship, System Organ Class, and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.8.2	Summary of Serious Treatment-Emergent Adverse Events by Relationship, System Organ Class, and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.8.3	Summary of Serious Treatment-Emergent Adverse Events by Relationship, System Organ Class, and Preferred Term — Part B	Safety Population	
Table	14.3.1.9.1	Summary of Treatment-Emergent Adverse Events Related to COVID-19 by System Organ Class and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.9.2	Summary of Treatment-Emergent Adverse Events Related to COVID-19 by System Organ Class and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.9.3	Summary of Treatment-Emergent Adverse Events Related to COVID-19 by System Organ Class and Preferred Term — Part B	Safety Population	

Type	Number	Title	Population	For abbreviated report?
Table	14.3.1.10.1	Summary of Treatment-Emergent Adverse Events Related to COVID-19 Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term — Part A Period 1	Safety Population	Y
Table	14.3.1.10.2	Summary of Treatment-Emergent Adverse Events Related to COVID-19 Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term — Part A Period 2	Safety Population	Y
Table	14.3.1.10.3	Summary of Treatment-Emergent Adverse Events Related to COVID-19 Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term — Part B	Safety Population	
Table	14.3.4.1.1	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Hematology — Part A Period 1	Safety Population	Y
Table	14.3.4.1.2	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Hematology — Part A Period 2	Safety Population	Y
Table	14.3.4.1.3	Mean and Mean Change from Part A Period 2 Baseline of Clinical Laboratory Values: Hematology — Part A Period 2	Safety Population	Y
Table	14.3.4.1.4	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Hematology — Part B	Safety Population	
Table	14.3.4.1.5	Mean and Mean Change from Part A Period 2 Baseline of Clinical Laboratory Values: Hematology — Part B	Safety Population	
Table	14.3.4.1.6	Mean and Mean Change from Part B Baseline of Clinical Laboratory Values: Hematology — Part B	Safety Population	
Table	14.3.4.2.1	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Serum Chemistry — Part A Period 1	Safety Population	Y
Table	14.3.4.2.2	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Serum Chemistry — Part A Period 2	Safety Population	Y

Type	Number	Title	Population	For abbreviated report?
Table	14.3.4.2.3	Mean and Mean Change from Part A Period 2 Baseline of Clinical Laboratory Values: Serum Chemistry — Part A Period 2	Safety Population	Y
Table	14.3.4.2.4	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Serum Chemistry — Part B	Safety Population	
Table	14.3.4.2.5	Mean and Mean Change from Part A Period 2 Baseline of Clinical Laboratory Values: Serum Chemistry — Part B	Safety Population	
Table	14.3.4.2.6	Mean and Mean Change from Part B Baseline of Clinical Laboratory Values: Serum Chemistry — Part B	Safety Population	
Table	14.3.4.3.1	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Lipids — Part A Period 1	Safety Population	Y
Table	14.3.4.3.2	Mean and Mean Change from Part A Period 1 Baseline of Clinical Laboratory Values: Lipids — Part A Period 2	Safety Population	Y
Table	14.3.4.3.3	Mean and Mean Change from Part A Period 2 Baseline of Clinical Laboratory Values: Lipids — Part A Period 2	Safety Population	Y
Table	14.3.4.3.4	Mean and Mean Change from Baseline of Clinical Laboratory Values: Lipids — Part B	Safety Population	
Table	14.3.4.3.5	Mean and Mean Change from Part A Period 2 Baseline of Clinical Laboratory Values: Lipids — Part B	Safety Population	
Table	14.3.4.3.6	Mean and Mean Change from Part B Baseline of Clinical Laboratory Values: Lipids — Part B	Safety Population	
Table	14.3.4.4.1	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Hematology — Part A Period 1	Safety Population	Y
Table	14.3.4.4.2	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Hematology — Part A Period 2	Safety Population	Y

Type	Number	Title	Population	For abbreviated report?
Table	14.3.4.4.3	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Hematology — Part B	Safety Population	
Table	14.3.4.5.1	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Serum Chemistry — Part A Period 1	Safety Population	Y
Table	14.3.4.5.2	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Serum Chemistry — Part A Period 2	Safety Population	Y
Table	14.3.4.5.3	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Serum Chemistry — Part B	Safety Population	
Table	14.3.4.6.1	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Lipids — Part A Period 1	Safety Population	Y
Table	14.3.4.6.2	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Lipids — Part A Period 2	Safety Population	Y
Table	14.3.4.6.3	Summary of Treatment-Emergent Potentially Clinically Significant Clinical Laboratory Values: Lipids — Part B	Safety Population	
Table	14.3.4.7.1	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Hematology — Part A Period 1	Safety Population	Y
Table	14.3.4.7.2	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Hematology — Part A Period 2	Safety Population	Y
Table	14.3.4.7.3	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Hematology — Part B	Safety Population	
Table	14.3.4.8.1	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Serum Chemistry — Part A Period 1	Safety Population	Y

Type	Number	Title	Population	For abbreviated report?
Table	14.3.4.8.2	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Serum Chemistry — Part A Period 2	Safety Population	Y
Table	14.3.4.8.3	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Serum Chemistry — Part B	Safety Population	
Table	14.3.4.9.1	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Lipids — Part A Period 1	Safety Population	Y
Table	14.3.4.9.2	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Lipids — Part A Period 2	Safety Population	Y
Table	14.3.4.9.3	Summary of Abnormal Clinical Laboratory Values by Treatment Group and Visit: Lipids — Part B	Safety Population	
Table	14.3.5.1.1	Vital Signs Summary — Part A Period 1	Safety Population	
Table	14.3.5.1.2	Vital Signs Summary — Part A Period 2	Safety Population	
Table	14.3.5.1.3	Vital Signs Summary — Part B	Safety Population	
Table	14.3.5.2.1	Presence or Absence of Nasal Hair by Treatment Group and Visit — Part A Period 1	Safety Population	Y
Table	14.3.5.2.2	Presence or Absence of Nasal Hair by Treatment Group and Visit — Part A Period 2	Safety Population	Y
Table	14.3.5.2.3	Presence or Absence of Nasal Hair by Treatment Group and Visit — Part B	Safety Population	
Table	14.3.5.3.1	12-Lead Electrocardiogram Summary — Part A Period 1	Safety Population	
Table	14.3.5.3.2	12-Lead Electrocardiogram Summary — Part A Period 2	Safety Population	
Table	14.3.5.3.3	12-Lead Electrocardiogram Summary — Part B	Safety Population	
Table	14.3.5.4.1	Summary of Missing or Remote Visits Related to COVID-19 by Treatment Group — Part A Period 1	Safety Population	
Table	14.3.5.4.2	Summary of Missing or Remote Visits Related to COVID-19 by Treatment Group — Part A Period 2	Safety Population	

Type	Number	Title	Population	For abbreviated report?
Table	14.3.5.4.3	Summary of Missing or Remote Visits Related to COVID-19 by Treatment Group — Part B	Safety Population	
Figure	14.1.1.1	Summary of Patient Disposition — CONSORT Diagram — Part A Overall	All Screened Patients	Y
Figure	14.1.1.2	Summary of Patient Disposition — CONSORT Diagram — Part A and Part B	All Screened Patients	
Figure	14.1.2.1	Kaplan-Meier Plot for Time to Treatment Discontinuation — Part A Period 1	Safety Population	Y
Figure	14.1.2.2	Kaplan-Meier Plot for Time to Treatment Discontinuation — Part A Period 2	Safety Population	Y
Figure	14.1.2.3	Kaplan-Meier Plot for Time to Treatment Discontinuation — Part B	Safety Population	
Figure	14.2.1.1	Patients Achieving Loss of Regrowth Maintenance (SALT Score >20) or Response (SALT Score ≤20) by Treatment at End of Part A Period 2 — Part A Period 2	Efficacy Population	Y
Figure	14.2.2.1.1	Responders (SALT Score ≤20) by Treatment across Time — Part A Period 1	Efficacy Population	Y
Figure	14.2.2.1.2	Loss of Regrowth Maintenance (SALT Score >20) by Treatment across Time — Part A Period 2	Efficacy Population	Y
Figure	14.2.2.1.3	Responders (SALT Score ≤20) by Treatment across Time — Part A Period 2	Efficacy Population	Y
Figure	14.2.2.1.4	Restoration of Regrowth (SALT Score ≤20) by Treatment across Time — Part B	Efficacy Population	
Figure	14.2.2.2.1	SALT Scores by Treatment across Time — Part A Period 1	Efficacy Population	Y
Figure	14.2.2.2.2	SALT Scores by Treatment across Time — Part A Period 2	Efficacy Population	Y
Figure	14.2.2.2.3	SALT Scores by Treatment across Time — Part B	Efficacy Population	

Type	Number	Title	Population	For abbreviated report?
Figure	14.2.2.3.1	Mean Change from Part A Period 1 Baseline in Total SALT Scores by Treatment across Time — Part A Period 1	Efficacy Population	Y
Figure	14.2.2.3.2	Mean Change from Part A Period 1 Baseline in Total SALT Scores by Treatment across Time — Part A Period 2	Efficacy Population	Y
Figure	14.2.2.3.3	Mean Change from Part A Period 2 Baseline in Total SALT Scores by Treatment across Time — Part A Period 2	Efficacy Population	Y
Figure	14.2.2.3.4	Mean Change from Part A Period 1 Baseline in Total SALT Scores by Treatment across Time — Part B	Efficacy Population	
Figure	14.2.2.3.5	Mean Change from Part A Period 2 Baseline in Total SALT Scores by Treatment across Time — Part B	Efficacy Population	
Figure	14.2.2.3.6	Mean Change from Part B Baseline in Total SALT Scores by Treatment across Time — Part B	Efficacy Population	
Figure	14.2.2.4.1	Relative Change in Total SALT Scores by Treatment across Time — Part A Period 1	Efficacy Population	Y
Figure	14.2.2.4.2	Relative Change from Part B Baseline in Total SALT Scores by Treatment across Time — Part B	Efficacy Population	
Figure	14.2.4.1	Kaplan-Meier Plot for Time to First Loss of Regrowth Maintenance (SALT Score >20) — Part A Period 2	Efficacy Population	Y
Figure	14.3.4.1	Key Clinical Laboratory Values: Hematology Parameters — Part A Period 1	Safety Population	Y
Figure	14.3.4.2	Key Clinical Laboratory Values: Hematology Parameters — Part A Period 2	Safety Population	Y
Figure	14.3.4.3	Key Clinical Laboratory Values: Hematology Parameters — Part B	Safety Population	
Listing	16.1.1	Randomization Codes	All Randomized	Y
Listing	16.1.10.1	Clinical Laboratory Reference Range		Y
Listing	16.2.1.1	Patient Disposition	All Randomized	Y

Type	Number	Title	Population	For abbreviated report?
Listing	16.2.1.2	Screen Failures		Y
Listing	16.2.1.3.1	All Patient Visits — Part A	All Randomized	Y
Listing	16.2.1.3.2	All Patient Visits — Part B	All Randomized	
Listing	16.2.1.4.1	Patients with Missed or Remote Visits Related to COVID-19 — Part A	All Randomized	Y
Listing	16.2.1.4.2	Patients with Missed or Remote Visits Related to COVID-19 — Part B	All Randomized	
Listing	16.2.2.1.1	Protocol Deviations — Part A	All Randomized	Y
Listing	16.2.2.1.2	Protocol Deviations — Part B	All Randomized	
Listing	16.2.2.2.1	Protocol Deviations Related to COVID-19 — Part A	All Randomized	Y
Listing	16.2.2.2.2	Protocol Deviations Related to COVID-19 — Part B	All Randomized	
Listing	16.2.3	Analysis Sets	All Randomized	Y
Listing	16.2.4.1	Patient Demographic and Baseline Characteristics	All Randomized	Y
Listing	16.2.4.2	Medical History	All Randomized	Y
Listing	16.2.4.3.1	Prior and Concomitant Medications — Part A	All Randomized	Y
Listing	16.2.4.3.2	Prior and Concomitant Medications — Part B	All Randomized	
Listing	16.2.4.4.1	Prior and Concomitant Medications Related to COVID-19 — Part A	All Randomized	Y
Listing	16.2.4.4.2	Prior and Concomitant Medications Related to COVID-19 — Part B	All Randomized	
Listing	16.2.5.1.1	Overall Study Drug Administration and Treatment Compliance — Part A	Safety Population	Y
Listing	16.2.5.1.2	Overall Study Drug Administration and Treatment Compliance — Part B	Safety Population	
Listing	16.2.5.2.1	Study Drug Administration and Treatment Compliance by Visit — Part A	Safety Population	Y
Listing	16.2.5.2.2	Study Drug Administration and Treatment Compliance by Visit — Part B	Safety Population	

Type	Number	Title	Population	For abbreviated report?
Listing	16.2.5.3.1	Dosing Exceptions — Part A	Safety Population	Y
Listing	16.2.5.3.2	Dosing Exceptions — Part B	Safety Population	
Listing	16.2.5.4.1	Dosing Exceptions Related to COVID-19 — Part A	Safety Population	Y
Listing	16.2.5.4.2	Dosing Exceptions Related to COVID-19 — Part B	Safety Population	
Listing	16.2.6.1.1	SALT Score — Part A	Efficacy Population	Y
Listing	16.2.6.1.2	SALT Score — Part B	Efficacy Population	
Listing	16.2.6.1.3	SALT Scores over Time for Part A Period 2 Patients	Efficacy Population	Y
Listing	16.2.6.2.1	Missing SALT Scores — Part A	Efficacy Population	Y
Listing	16.2.6.2.2	Missing SALT Scores — Part B	Efficacy Population	
Listing	16.2.6.3.1	Photographs — Part A	Efficacy Population	
Listing	16.2.6.3.2	Photographs — Part B	Efficacy Population	
Listing	16.2.6.4	CGI-I and PGI-I	Efficacy Population	Y
Listing	16.2.6.5	CGI-S and PGI-S	Efficacy Population	Y
Listing	16.2.6.6	Satisfaction of Hair Patient Reported Outcome (SPRO)	Efficacy Population	Y
Listing	16.2.6.7	Quality of Hair Patient Reported Outcome (QPRO)	Efficacy Population	Y
Listing	16.2.7.1.1	All Adverse Events — Part A	All Randomized	Y
Listing	16.2.7.1.2	All Adverse Events — Part B	All Randomized	
Listing	16.2.7.2.1	Adverse Events Related to COVID-19 — Part A	All Randomized	Y
Listing	16.2.7.2.2	Adverse Events Related to COVID-19 — Part B	All Randomized	
Listing	14.3.2.1.1	Serious Adverse Events — Part A	All Randomized	Y
Listing	14.3.2.1.2	Serious Adverse Events — Part B	All Randomized	
Listing	14.3.2.2.1	Adverse Events Related to Study Drug — Part A	All Randomized	Y
Listing	14.3.2.2.2	Adverse Events Related to Study Drug — Part B	All Randomized	
Listing	14.3.2.3.1	Adverse Events Leading to Study Drug Discontinuation — Part A	All Randomized	Y

Type	Number	Title	Population	For abbreviated report?
Listing	14.3.2.3.2	Adverse Events Leading to Study Drug Discontinuation — Part B	All Randomized	
Listing	16.2.7.3.1	Adverse Events Leading to Study Drug Interruption — Part A	All Randomized	Y
Listing	16.2.7.2.2	Adverse Events Leading to Study Drug Interruption — Part B	All Randomized	
Listing	14.3.2.4.1	Adverse Events Leading to Death — Part A	All Randomized	Y
Listing	14.3.2.4.2	Adverse Events Leading to Death — Part B	All Randomized	
Listing	16.2.8.1.1	Clinical Laboratory Data: Hematology — Part A	All Randomized	Y
Listing	16.2.8.1.2	Clinical Laboratory Data: Hematology — Part B	All Randomized	
Listing	16.2.8.2.1	Clinical Laboratory Data: Serum Chemistry — Part A	All Randomized	Y
Listing	16.2.8.2.2	Clinical Laboratory Data: Serum Chemistry — Part B	All Randomized	
Listing	16.2.8.3.1	Clinical Laboratory Data: Lipids — Part A	All Randomized	Y
Listing	16.2.8.3.2	Clinical Laboratory Data: Lipids — Part B	All Randomized	
Listing	16.2.8.4.1	Pregnancy Test Results — Part A	All Randomized	
Listing	16.2.8.4.2	Pregnancy Test Results — Part B	All Randomized	
Listing	16.2.8.5.1	Positive Pregnancy Tests — Part A	All Randomized	
Listing	16.2.8.5.2	Positive Pregnancy Tests — Part B	All Randomized	
Listing	16.2.10.1.1	Vital Signs Results — Part A	All Randomized	
Listing	16.2.10.1.2	Vital Signs Results — Part B	All Randomized	
Listing	16.2.10.2.1	12-Lead Electrocardiogram Results — Part A	All Randomized	
Listing	16.2.10.2.2	12-Lead Electrocardiogram Results — Part B	All Randomized	
Listing	16.2.10.3.1	Abnormal 12-Lead Electrocardiogram Findings — Part A	All Randomized	
Listing	16.2.10.3.2	Abnormal 12-Lead Electrocardiogram Findings — Part B	All Randomized	
Listing	16.2.10.4.1	Physical Examinations — Part A	All Randomized	Y
Listing	16.2.10.4.2	Physical Examinations — Part B	All Randomized	
Listing	16.2.10.5	Pharmacokinetic Sampling Visits — Part A Period 1	All Randomized	Y

16. ATTACHMENTS

Not applicable.