

NCT02781311

Study ID: 1922-201-002

Title: MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED,
PHASE 2A STUDY OF SETIPIPRANT TABLETS IN ANDROGENETIC ALOPECIA IN
MALES

Statistical Analysis Plan Amendment 2 Date: 25-Jul-2018


1. Title Page

STATISTICAL ANALYSIS PLAN

**MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED,
PHASE 2A STUDY OF SETIPIPRANT TABLETS IN ANDROGENETIC ALOPECIA IN
MALES**

Original: 2017-APR-17

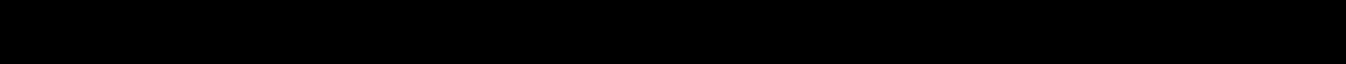
Amendment 2: 2018-JUL-25

Protocol Number: 1922-201-002
Development Phase: 2A
Product Name: Setipiprant Tablets
Study Statistician: 
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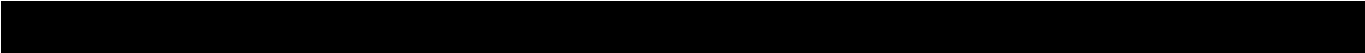
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2.2 List of Figures



3. List of Abbreviations and Definition of Terms

Table 3-1 Abbreviations and Definitions of Terms

| Term/Abbreviation | Definition |
|----------------------|---|
| AE | adverse event |
| AGA | androgenetic alopecia |
| █ | █ |
| ALT | alanine aminotransferase |
| ANCOVA | analysis of covariance |
| ASA | Alopecia Symptom Assessment |
| AST | aspartate aminotransferase |
| █ | █ |
| █ | █ |
| █ | █ |
| AUC _{0-inf} | area under the concentration-time curve from time 0 to infinity |
| BID | twice daily |
| bpm | beats per minute |
| █ | █ |
| CMH | Cochran-Mantel-Haenszel |
| █ | █ |
| █ | █ |
| CSR | Clinical Study Report |
| █ | █ |
| eCRF | electronic case report form |
| █ | █ |
| █ | █ |
| █ | █ |
| █ | █ |
| LOCF | last observation carried forward |
| mITT | modified intent-to-treat |
| NHS | Norwood-Hamilton Hair Loss Scale |
| █ | █ |
| PT | preferred term |
| █ | █ |
| █ | █ |
| █ | █ |
| █ | █ |

| | |
|------------|-------------------------|
| [REDACTED] | [REDACTED] |
| [REDACTED] | [REDACTED] |
| SOC | system organ class |
| SSA | Subject Self-Assessment |
| [REDACTED] | [REDACTED] |
| TAHC | target area hair count |
| [REDACTED] | [REDACTED] |
| [REDACTED] | [REDACTED] |
| TBL | total bilirubin |
| [REDACTED] | [REDACTED] |
| ULN | upper limits of normal |
| WBC | white blood cell |

4. Introduction

This document details the planned analysis for Study 1922-201-002, a phase 2A study to evaluate the safety, tolerability and efficacy of oral administration of setipiprant tablets 1000 mg twice daily (BID) in males with androgenetic alopecia (AGA) who are 18 to 49 years old and in generally good health. Specifications of tables, figures, and data listings are contained in a separate document. [REDACTED]

The statistical analysis will be conducted after all subjects have completed or exited the study and after database lock.

4.1 Primary Study Objectives and Design

The objectives of this study are to evaluate the safety, tolerability, and efficacy of oral administration of setipiprant tablets 1000 mg BID in males with androgenetic alopecia (AGA), [REDACTED]

[REDACTED] Male subjects aged 18 to 49 years (inclusive) at baseline, who are in general good health, have androgenetic alopecia with vertex patterns IIIv, IV, or V on the NHS, and are dissatisfied with [REDACTED]

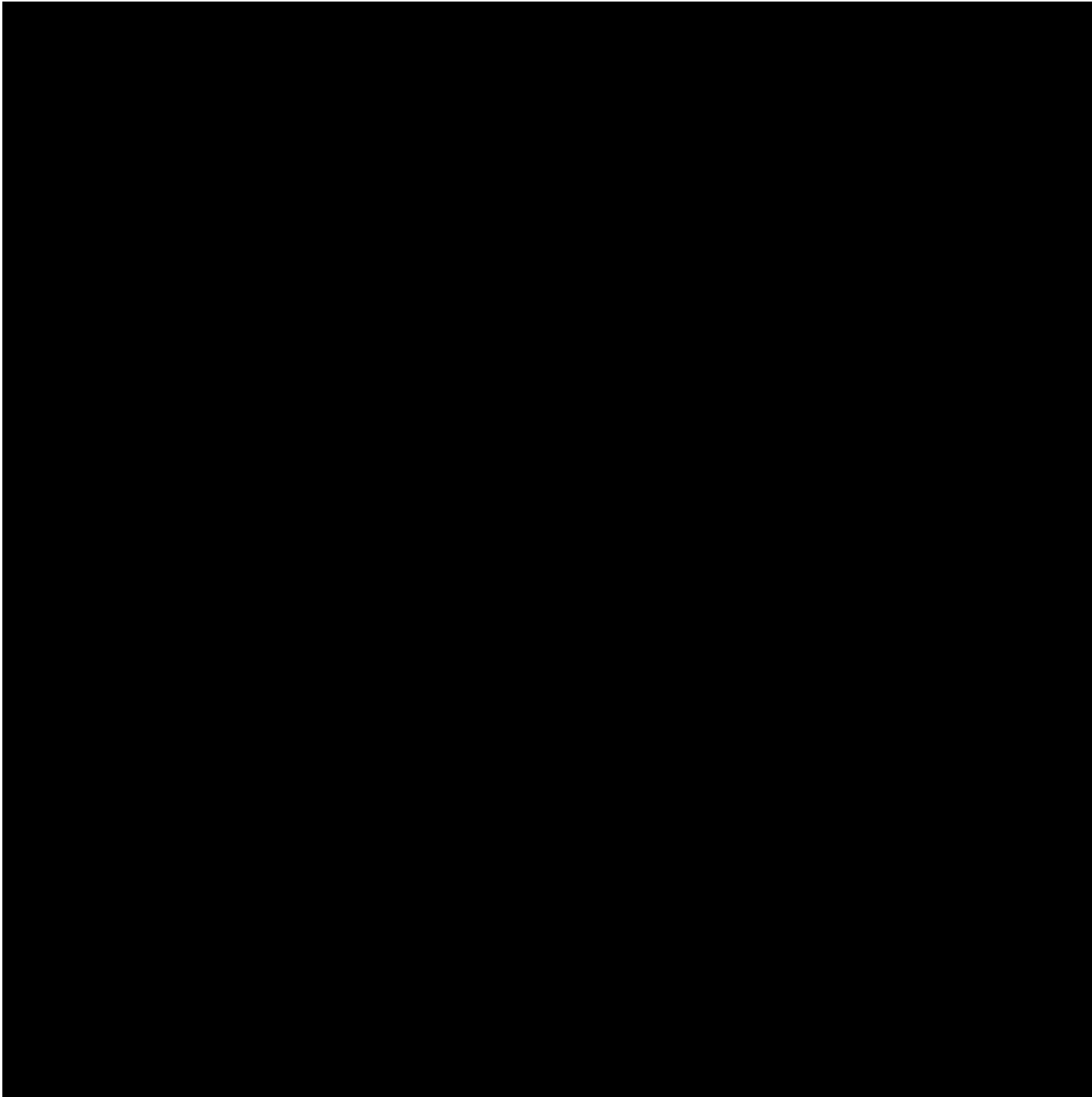
[REDACTED] will be screened for eligibility for enrollment into the study.

This is a multicenter, randomized, double-blind, placebo-controlled study designed to determine the effect of treatment with setipiprant tablets 1000 mg BID on scalp hair growth as assessed by objective (ie, imaging-based) and subjective [REDACTED] - and subject-reported) measures.

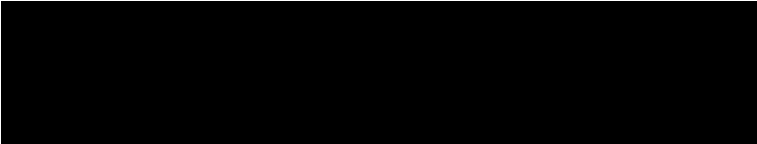
All investigators, site staff, and subjects will be blinded to whether subjects receive setipiprant or matching placebo during the study.

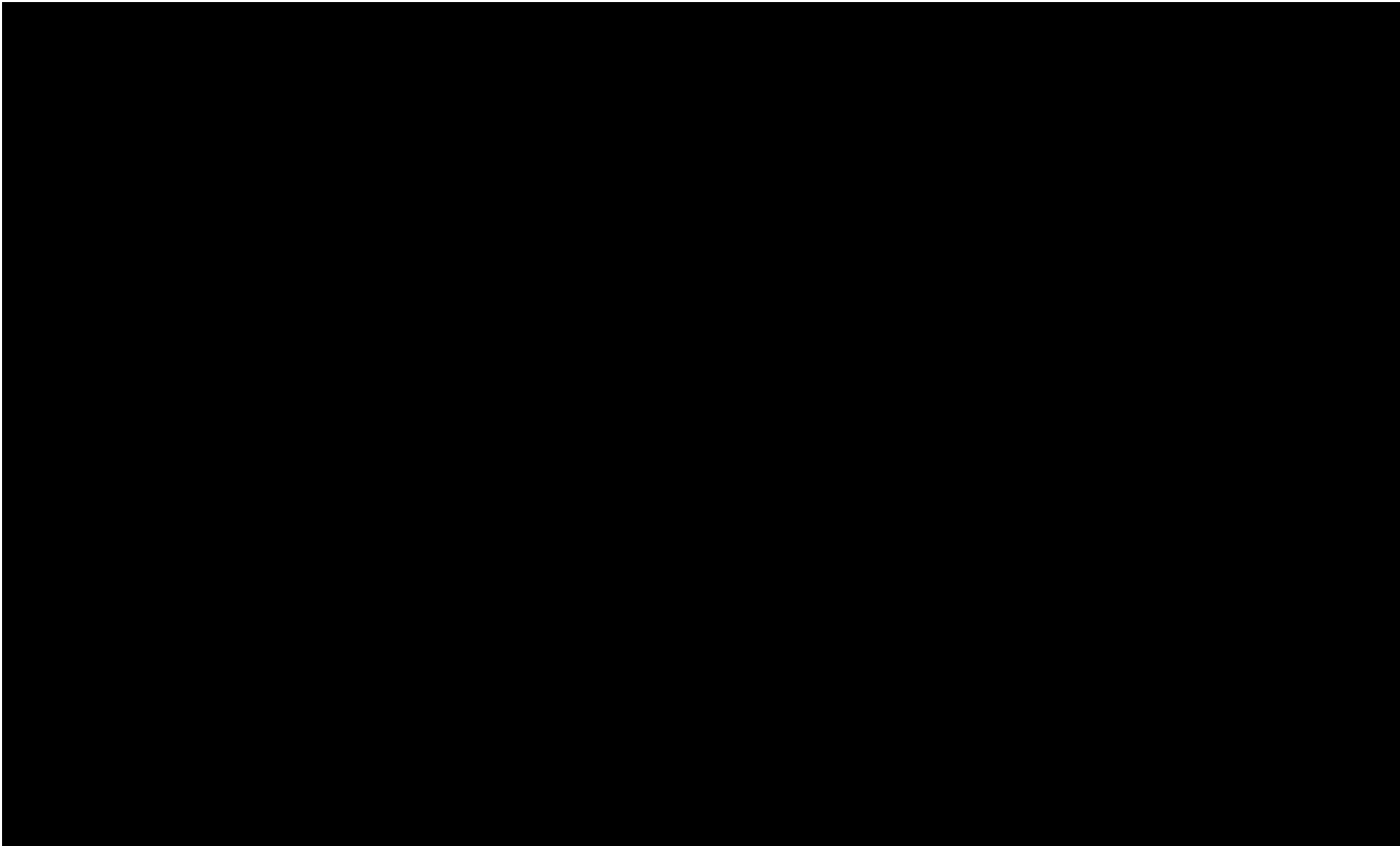
Approximately 152 subjects will be enrolled in up to 20 US sites. On Day 1, 140 eligible [REDACTED] subjects will be randomly assigned to 1 of 2 treatment groups in a 1:1 ratio to receive setipiprant tablets 1000 mg BID (hereafter referred as Setipiprant), or placebo BID (hereafter referred as Placebo), and [REDACTED]

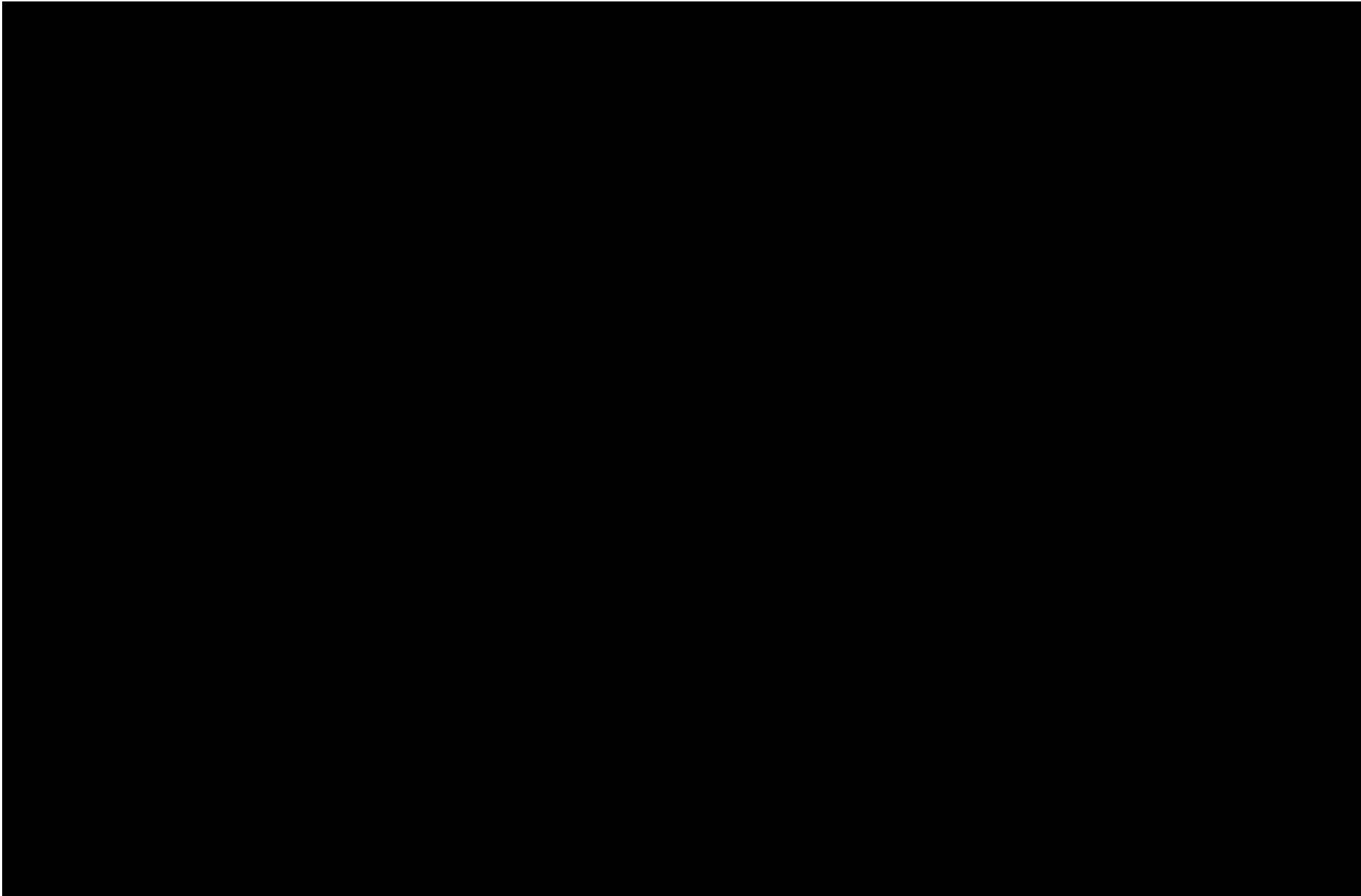
[REDACTED] will be stratified by baseline age group (< 35 and \geq 35 years). Overall, the number of subjects enrolled into the setipiprant and placebo groups will be about 80 and 72, respectively (Figure 4-1).

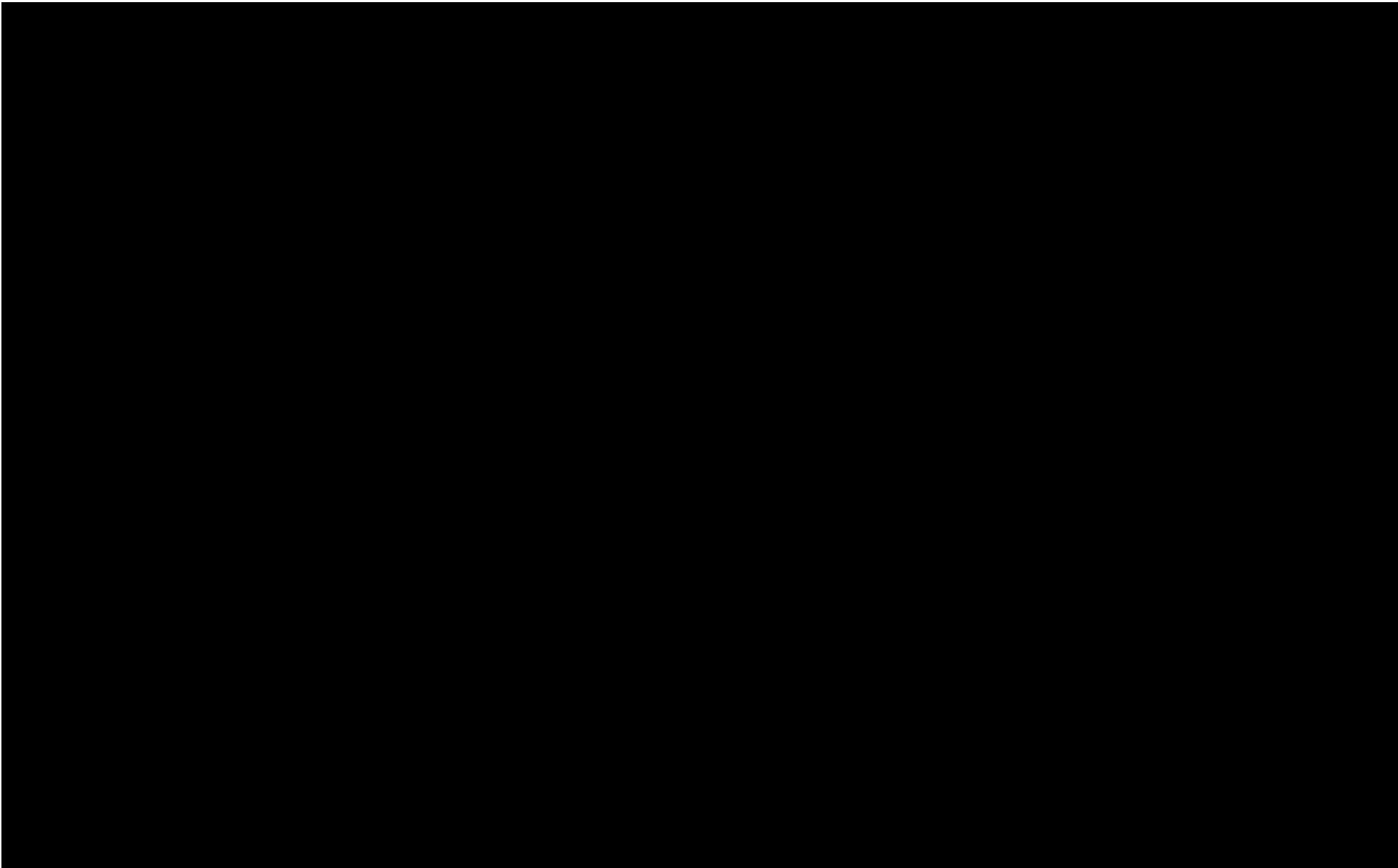


This SAP is based on the Amendment 1 of the protocol. The original protocol had three treatment arms – Setipiprant 1000 mg BID, Placebo BID and Finasteride 1 mg QD. The Finasteride 1 mg QD was removed from Amendment 1 of the protocol. Data in the Finasteride group will be summarized but not compared with the other treatment groups.









5. Statistical Methodology and Study Endpoints

5.1 Statistical Methods Planned in the Protocol and Determination of Sample Size

This statistical analysis plan (SAP) will be approved prior to database lock. The SAP expands the statistical section of the protocol and contains a detailed description of methods to analyze data collected in the study. The text portion of the SAP will be included in the CSR report as Appendix 16.1.9. [REDACTED]

5.1.1 Statistical and Analytical Plans

Statistical analyses will be conducted using [REDACTED]

5.1.1.1 Common Conventions

5.1.1.1.1 Analysis Populations

Two populations will be used in the analysis: modified intent-to-treat (mITT) and safety.

The mITT population, consisting of all randomized subjects who have a baseline and at least 1 postbaseline measurement for 1 of the coprimary efficacy measures, will be used for analyses of efficacy data based on the randomized treatment group. All efficacy variables will be summarized and analyzed using the mITT population. Demographic and baseline characteristics will also be based on mITT population.

The safety population, consisting of all subjects who receive at least 1 dose of study drug (ie, all treated subjects), will be used for analyses of all safety data based on the actual treatment received.

5.1.1.1.2 Study Treatments

The following treatment groups are defined for this study.

- Setipiprant
- Placebo
- Finasteride: enrolled under the original protocol, data will be summarized but not included in any data analysis models.

They will be labeled as “Setipiprant”, “Placebo” and “Finasteride” in the data summary tables/listings.

5.1.1.1.3 Statistical Methodology

The methodologies defined below apply as specified to individual endpoints defined in this SAP. Finasteride subjects enrolled prior to Protocol Amendment 1 will be summarized alone and will not be included in the analysis models. All statistical testing will be based on 2-sided hypothesis tests with a statistical significance of $p \leq 0.05$, unless specified otherwise.

- Descriptive statistics include the sample size (N), mean, standard deviation (SD), median, minimum (Min), and maximum (Max) for continuous/ordinal data, and the sample size (N), frequency count, and percentage for categorical data.
- For the analysis of ordinal-scaled categorical data, unless specified otherwise, Cochran-Mantel-Haenszel (CMH) row mean scores test stratified by age group (< 35 and ≥ 35 years) will be used.
- Change from baseline (CFB) will be analyzed using an analysis of covariance (ANCOVA) model with treatment as a fixed effect and age and baseline value as covariates (if applicable). The treatment difference (Setipiprant versus Placebo) will be constructed based on the ANCOVA model, along with the 2-sided p-value and 95% confidence intervals (CI). The type III sums of squares will be used for all ANCOVA models.

5.1.1.1.4 Other Common Conventions

- The baseline value of an assessment will be the last value recorded prior to the subject receiving the first dose of study medication (day 1), except for TAHC. [REDACTED] For these parameters, the baseline value is based on the nominal Visit 2 (baseline) macrophotography, which may include photos taken after the first dose of study drug when a reshoot was required to obtain evaluable baseline measurements. [REDACTED]
[REDACTED]
[REDACTED]
- In general, change from baseline is calculated as follow-up minus baseline. Between-group differences will be calculated for Setipiprant minus Placebo.
- Clinical laboratory system will be presented with Standard International (SI) units.
- Medical Dictionary of Regulatory Activities (MedDRA) nomenclature will be used to code diagnosis or symptoms from medical histories, adverse events (AEs), indications for prestudy and concomitant medications. In addition, the Drug Dictionary Enhanced (DDE) preferred drug names from World Health Organization (WHO) Drug Dictionary will be used to classify all prestudy and concomitant medications by drug class and drug names.

5.1.1.2 Demographics and Other Baseline Characteristics

Disposition and exit status, demographics and baseline characteristics will be performed on the mITT population.

5.1.1.2.1 Disposition and Exit Status

Subject disposition and exit status will be summarized overall and by treatment group using frequency distributions at the primary efficacy endpoint of week 24 as well as at the end of the study.

Reasons for early termination include AEs, lack of efficacy as determined by investigator, lost to follow-up, personal reasons, protocol violation, and other reasons. Subjects who discontinue prematurely will be listed along with the corresponding reason(s) for their early termination.

5.1.1.2.2 Protocol Deviations

Significant (major) protocol deviations will be summarized using standard text by treatment group, and data listing will be presented.

5.1.1.2.3 Demographics

Demographic data will include age, sex, race, and ethnicity. Age will be summarized with descriptive statistics by treatment group and overall (ie, all treatment groups combined). In addition, age will be classified into categories of < 35 and ≥ 35 years, and race will be classified as White and non-White. Age group, sex, race and ethnicity will be summarized with frequency distribution by treatment group and overall, respectively.

5.1.1.2.4 Baseline Characteristics

Body mass index (BMI) is defined as weight (kg) / height (m)². Weight, height, and BMI will be summarized with descriptive statistics by treatment group and overall.

Baseline TAHC (terminal hairs/cm²), [REDACTED] will be summarized by left circular areas of 1 [REDACTED], and right circular areas of 1 [REDACTED]. In addition, TAHC will be summarized within the area of [REDACTED]. The summary will be presented with descriptive statistics by treatment group and overall.

Distribution of subject's score of modified Norwood-Hamilton Scale of male-pattern baldness at baseline, Fitzpatrick skin type, Hair Loss history, and the Hair Satisfaction Assessment scale (HSA) will be presented with frequency distributions by treatment group and overall, respectively.

A subject listing with demographics and baseline characteristics will be presented.

5.1.1.2.5 Medical History

Medical and surgical history will be analyzed on the mITT population.

Medical history, encompassing abnormalities and surgeries reported as occurring before the Screening Visit, will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1 or newer. Unique subjects who report medical history events will be summarized by the primary system organ class (SOC) and preferred term (PT) (per MedDRA definition) for each treatment group and overall using frequency distributions.

5.1.1.2.6 Prior and Concomitant Medications

Prior and concomitant medications will be analyzed on the mITT population.

Prior medications include all medications with a start date before the day 1 date, whether or not medication is continuing beyond the baseline visit.

Concomitant medications encompass all non-study medications that the subject was taking prior to day 1 visit that are ongoing at the visit, in addition to all medications that have a start date on or after baseline (day 1) visit date.

Medications will be coded using the World Health Organization (WHO) Drug Dictionary, version March 2016 or newer. Unique subjects who reported medications will be summarized by Anatomical Therapeutic Chemical (ATC) 4 class and PT in total and by treatment group in mITT population. No statistical comparisons will be performed.

5.1.1.3 Efficacy Analyses

Efficacy analyses will be based on the mITT Population. Hypothesis testing will be 2-tailed with a significance level of 0.05, unless specified otherwise. Treatment comparison will be made for Setipiprant versus Placebo. For all efficacy analyses, no adjustment of significance levels will be made for multiplicity of treatment comparisons.

5.1.1.3.1 Collection and Derivation of Primary and Other Efficacy Measurements

The coprimary efficacy variables will be based on the following 2 measures: TAHC within a 1 cm² circular area on the left side of the scalp and SSA.

- The TAHC is a standardized objective quantification of each subject's number of terminal hairs (hair width $\geq 30 \mu\text{m}$) within a 1 cm² target circular area on the left side located at the anterior leading edge of the vertex thinning area of the scalp using digital image analysis.

- The SSA score is the subject's assessment of change of hair growth, scored on a 7-point scale (-3 = greatly decreased, -2 = moderately decreased, -1 = slightly decreased, 0 = remained the same, +1 = slightly increased, +2 = moderately increased, and +3 = greatly increased). The analyses of the SSA from the blinded photograph assessments will be based on the actual change from the screening photographs (ie, if the postbaseline photograph is used as Photo A, the assessment score will be reversed for analyses).

The coprimary efficacy endpoints based on the measurements of TAHC and SSA (blinded) are the following.

- Change from baseline in TAHC within a 1 cm² target circular area on the left side located at the anterior leading edge of the vertex thinning area of the scalp at Week 24
- Subject Self-Assessment of change from baseline in hair growth as viewed on the subject's paired (before and after presented in a blinded fashion) global photographs of the vertex target area at Week 24 and measured by the distribution of SSA scores

Postbaseline evaluations of TAHC and SSA will be made at Week [REDACTED] 24 and 32, with the primary analysis timepoint being Week 24. For SSA, if the postbaseline photograph is used as Photo A, then the assessment score will be reversed for analyses.

For each of the 2 coprimary measures (TAHC and SSA), missing data will be imputed up to Week 24 using last observation carried forward (LOCF) method.

[REDACTED]

[REDACTED]

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[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

5.1.1.3.2 Primary Efficacy Analyses

For analyses of TAHC, the following set of hypotheses will be used to compare setipiprant tablets 1000 mg BID versus placebo BID:

- Null hypothesis: There is no difference between setipiprant tablets 1000 mg BID and placebo BID in increasing TAHC (terminal hairs in a 1 cm² circular area) as measured by the change from baseline at Week 24 using digital image analysis.
- Alternative hypothesis: There is a difference between setipiprant tablets 1000 mg BID and placebo BID in increasing TAHC (terminal hairs in a 1 cm² circular area) as measured by the change from baseline at Week 24 using digital image analysis.

For analyses of the SSA, the following set of hypotheses will be used to compare setipiprant tablets 1000 mg BID versus placebo BID:

- Null hypothesis: There is no difference between setipiprant tablets 1000 mg BID and placebo BID in SSA (blinded) of hair growth from baseline at Week 24.
- Alternative hypothesis: There is a difference between setipiprant tablets 1000 mg BID and placebo BID in SSA (blinded) of hair growth from baseline at Week 24.

Change from baseline in TAHC at Week 24 and SSA of the change of hair growth from baseline at Week 24 will be analyzed using an analysis of covariance (ANCOVA) model with treatment as a fixed effect and age and baseline value as covariates (if applicable). The treatment difference for setipiprant tablets 1000 mg BID versus placebo BID will be constructed based on this ANCOVA model, along with the 2-sided p-value.

[Redacted text block containing multiple paragraphs of information, all obscured by black bars.]



5.1.1.4 Safety Analyses

All safety analyses will be performed on the safety population. All analyses will be based on observed cases without imputation.

5.1.1.4.1 Study Treatment Exposure

Subjects' exposure to the study medication will be characterized by duration of treatment exposure.

Duration of subject exposure to study treatment (days) will be calculated as the study treatment end date minus study treatment start date +1. Duration of treatment exposure will be summarized with descriptive statistics by treatment group.

5.1.1.4.2 Adverse Events

An AE is defined as any untoward medical occurrence in a subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. Adverse events are collected both for the screening/baseline period pretreatment (which are referred to as pretreatment AEs) and for the follow-up period after treatment is initiated (which are referred to as postbaseline AEs). Adverse events will be summarized using the concept of treatment-emergent adverse events (TEAEs). TEAE is a postbaseline AE where:

- a) there is no pretreatment AE of the same MedDRA primary system organ class (SOC) and preferred term (PT); or
- b) the maximum severity during the postbaseline period is greater than the maximal severity of any pretreatment AE of the same MedDRA primary SOC and preferred term during the screening/baseline period; or
- c) the AE reports as a serious AE (SAE) during the postbaseline period

Analysis of the incidence of TEAEs will be performed over the entire study period, and the incidence of TEAEs will be presented and summarized as follows:

- (1) Overall AE, treatment related TEAE, serious AE, deaths, AEs leading to discontinuation and Non-scalp hair growth.
- (2) TEAEs by primary SOC in alphabetical order, PT and severity (maximum severity). The maximum severity of a TEAE experienced by a subject is determined by the greatest severity recorded on the eCRFs for the subject’s given TEAE.
- (3) Common ($\geq 2\%$) TEAEs by Preferred Term
- (4) Treatment related TEAEs by primary SOC in alphabetical order, and preferred term.
- (5) Treatment-emergent serious AEs (SAE) by SOC in alphabetical order, and preferred term.
- (6) TEAEs leading to treatment discontinuation by SOC in alphabetical order, and preferred term
- (7) Treatment-emergent SAE with fatal outcome by primary SOC in alphabetical order, and preferred term. Subject listings will be generated for all AEs, SAE, Deaths, and AEs leading to study discontinuation.

Participant listings will be provided for all AEs, SAEs, AEs leading to study treatment discontinuation, and death (if occurred).

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5.1.1.4.6 Other Analyses

5.1.1.4.6.1 Nonscalp Hair Growth

Starting at Week 8, subjects will be queried at each visit whether they have noticed any hair growth in nonscalp areas (yes/no) and this response will be captured in the eCRF. If judged by the investigator as clinically significant, nonscalp hair growth may be reported as an AE.

The nonscalp hair growth will be summarized separately with a frequency distribution by treatment group.

5.1.1.5 Subgroup Analyses

Subgroup analyses are not planned but might be performed as Ad hoc analyses after database lock.

5.1.1.6 Interim Analyses

Not applicable.

[REDACTED]



5.2 Changes in the Conduct of the Study or Planned Analyses

5.2.1 Changes in the Conduct of the Study

Not applicable.

5.2.2 Changes to Analyses Prior to Database Lock

Not applicable.

6. Data Handling and Analysis Conventions

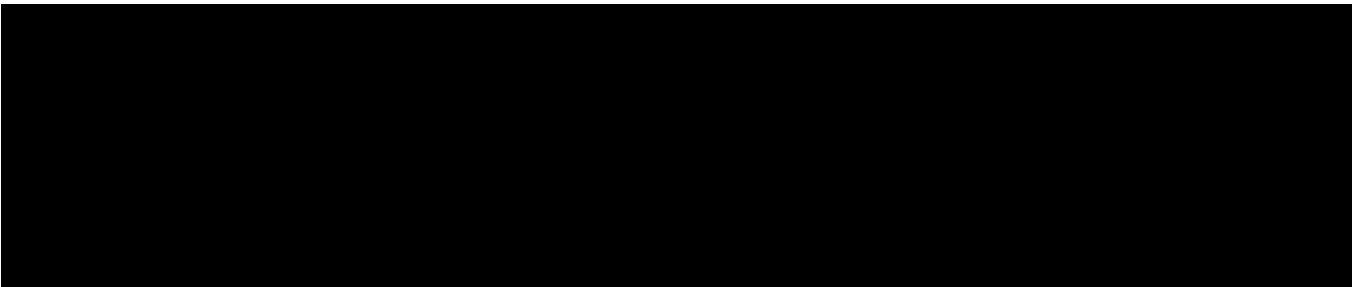
6.1 Study Treatment Conventions

6.1.1 Analysis Days

- Study days will be calculated as visit date – baseline date (day 1) + 1 if visit date is on or after baseline date; otherwise it will be calculated as visit date -baseline date (day 1).
- Treatment period is defined as days between the date of study treatment start and the date of the study treatment end.

6.1.2 Missing/Incomplete Treatment End Date

If the investigator is unable to provide the treatment end date, treatment end date will be imputed to the last treatment application, or early exit, or week 24 visit, whichever is the first.



6.3 Missing Date Information for Adverse Events

Partial AE dates will be imputed using the below methods.

Partial AE onset date will be imputed as follows:

- 1) If day is missing but month is not, impute the date as the first day of the month;
- 2) If both day and month are missing, impute the date as 01 Jan;
- 3) If imputed onset date is before the first treatment, yet the corresponding AE was not observed pre-treatment, then impute the onset date as the first treatment date.

Imputed partial AE onset date will only be used to determine the AE onset cycle.

Partial AE stop date will be imputed as follows:

- 1) If day is missing but month is not, impute the date as the last day of the month;
- 2) If both day and month are missing, impute the date as 31 Dec.

The date of first increase in severity to moderate, if a partial date, will be imputed as follows:

The date of first increase in severity (to moderate or severe), if a partial date, will be imputed as follows:

- 1) If day is missing but month is not, impute the date as the 15th of the month;

- 2) If both day and month are missing, impute the date as 15 June;
- 3) If imputed partial date is before the first treatment, and the corresponding AE was observed during treatment study period, then impute the date as the first treatment date;
- 4) If imputed partial date is before the onset date or the date of first increase in severity, then impute the partial date as the later of these two dates.

Imputed partial AE dates will only be used to determine treatment-emergent AE (TEAE). All partial dates will be listed “as is” in the data listings.

6.4 **Missing/Incomplete Date for Prior and Concomitant Medications**

For prior or concomitant medications, including rescue medications, incomplete (ie, partly missing) start dates and/or stop dates will be imputed. When the start date and the stop date are both incomplete for a patient, the start date will be imputed first. If the stop date is complete (or imputed) and the imputed start date is after the stop date, the start date will be imputed using the stop date. Imputed partial medication start/stop dates will only be used to determine prior or concomitant medication. All partial dates will be listed “as is” in the data listings.

6.4.1 **Missing/Incomplete Start Date**

The following rules will be applied to impute the missing numeric fields for an incomplete prior or concomitant medication start date.

- **Missing month and day**

- 1) If the year of the incomplete start date is the same as the year of the first dose of study treatment, the month and day of the first dose of study treatment will be assigned to the missing fields;
- 2) If the year of the incomplete start date is before the year of the first dose of study treatment, December 31 will be assigned to the missing fields;
- 3) If the year of the incomplete start date is after the year of the first dose of study treatment, January 1 will be assigned to the missing fields.

- **Missing month only**

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

- **Missing day only**

- 1) If the month and year of the incomplete start date are the same as the month and year of the first dose of study treatment, the day of the first dose of study treatment will be assigned to the missing day;

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

6.4.2 Missing/Incomplete End Date

The following rules will be applied to impute the missing numeric fields for an incomplete prior or concomitant medication stop date. If the date of the last dose of study treatment is missing, impute it as the method in the Section 6.1.2. If the imputed stop date is before the start date (imputed or nonimputed start date), the imputed stop date will be equal to the start date.

- **Missing month and day**

- 1) If the year of the incomplete stop date is the same as the year of the last dose of study treatment, the month and day of the last dose of study treatment will be assigned to the missing fields;
- 2) If the year of the incomplete stop date is before the year of the last dose of study treatment, December 31 will be assigned to the missing fields;
- 3) If the year of the incomplete stop date is after the year of the last dose of study treatment, January 1 will be assigned to the missing fields.

- **Missing month only**

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

- **Missing day only**

- 1) If the month and year of the incomplete stop date are the same as the month and year of the last dose of study treatment, the day of the last dose of study treatment will be assigned to the missing day;
- 2) If either the year of the incomplete stop date is before the year of the date of the last dose of study treatment or if both years are the same but the month of the incomplete stop date is before the month of the date of the last dose of study treatment, the last day of the month will be assigned to the missing day;

- 3) If either the year of the incomplete stop date is after the year of the date of the last dose of study treatment or if both years are the same but the month of the incomplete stop date is after the month of the date of the last dose of study treatment, the first day of the month will be assigned to the missing day.

6.5 Imputation of Primary Efficacy Measurements (TAHC and SSA)

Missing data of all TAHC endpoints and SSA (blinded and unblinded) will be imputed up to Week 24 using last observation carried forward (LOCF) as follows: when there is no observation in a particular visit window, the latest non-missing observation prior to that visit window will be carried forward and used for analysis for that particular window, whether from a scheduled or unscheduled visit. Imputation will be applied to postbaseline visits up to Week 24 only. If missing data occur at scheduled visit(s) immediately following baseline, the baseline value will be carried forward for imputation. Analyses of Week 32 data will be based on observed cases without data imputation.



6.7 Imputed Value Listing Conventions

In general, listings will present the actual partial or missing values rather than the imputed values that may be used in endpoint derivation. In instances where imputed values will be presented, imputed values will be flagged. Actual rules will be fully defined in the table, figure, and data listing specification document.

7. Data Collected but Not Analyzed

Some fields collected on the eCRF may be not analyzed (eg, photography consent, and subject privacy was signed) but will be listed.

8. References

Cotsarelis G, Zheng Y, Hsieh J. *Evaluation of DP-2 antagonists in promotion of hair growth*. Philadelphia: University of Pennsylvania; 2015a.

Harcha G, Martinez B, Tsai TF, et al. A randomized, active- and placebo-controlled study of the efficacy and safety of different doses of dutasteride versus placebo and finasteride in the

treatment of male subjects with androgenetic alopecia. *J Am Acad Dermatol*. 2014;70(3):489-498.

Olsen EA, Hordinsky M, Whiting D, et al. The importance of dual 5alpha-reductase inhibition in the treatment of male pattern hair loss: results of a randomized placebo-controlled study of dutasteride versus finasteride. *J Am Acad Dermatol*. 2006;55(6):1014-1023.

9. Amendment 1

The following amendments were made from the originally approved SAP/TFL shells.

- New analyses were specified in Sections 5.1.1.3.3, 5.1.1.4.2 and 5.1.1.4.3 with the following new tables and listings added

- [REDACTED]
- [REDACTED]

- Table 14.3-2.4 Number (%) of Participants with Common ($\geq 2\%$) Treatment-Emergent Adverse Events by Preferred Term
- Table 14.3-4.4 Potential Hy's Law Criteria: Number of Participants Meeting Criteria
- Figure 14.3-4.4-1 The maximum postbaseline TBL elevation vs the maximum postbaseline ALT elevation
- Figure 14.3-4.4-2 The maximum postbaseline TBL elevation vs the maximum postbaseline AST elevation
- Listing 14.3-4.5 Laboratory Parameters: Potential Hy's Law Criteria Findings
- Table 14.3-4.6 Shift from Baseline to End of Treatment in Hematology and Chemistry Parameters

- [REDACTED]

- Some TFLs were re-numbered in the shells due to deletion and addition of tables/listings

10. Amendment 2

The following updates were made relative to Amendment 1 of the SAP:

- Section 5.1.1.1.4: Text was added to clarify that the baseline values used for macrophotography (TAHC, [REDACTED]) may include photos taken after the first dose of study drug when a reshoot was required to obtain evaluable baseline measurements.

█ [REDACTED]
[REDACTED]
[REDACTED]

- Section 6.5: Clarification was made to indicate that the LOCF missing data imputation will be done for all TAHC endpoints and SSA (blinded and unblinded). In addition, more details of how the LOCF algorithm will be done are provided.

ALLERGAN

Analysis Plan for 1922-201-002 Amendment 2

Date (DD/MMM/YYYY)/Time (PT)

Signed by:

Justification

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]