STATISTICAL ANALYSIS PLAN - TEXT

Title: **A Randomized, Double-blind, Vehicle-controlled Multicenter Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ATI-50002 Topical Solution Administered Twice-Daily for 28 Days in Adult Subjects with Alopecia Universalis and Alopecia Totalis with a 12-Month Long-term Open-label Extension**

Protocol: ATI-50002-AA-202

Study Drug: ATI-50002

Sponsors: Aclaris Therapeutics,Inc.

Version (Date): Text 1.0 (10 December 2018)

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INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide a description of the statistical analyses performed for the Phase 2 protocol, ATI-50002-AA-202, V2.0 (14Aug2018).

1. STUDY OBJECTIVES

1.1 Primary Objective

To assess safety, tolerability, pharmacokinetics and pharmacodynamics of ATI-50002 Topical Solution, 0.46% compared to vehicle in subjects with alopecia universalis (AU) and alopecia totalis (AT).

1.2 Secondary Objectives

To assess the efficacy of ATI-50002 Topical Solution, 0.46% for the treatment of scalp hair loss and eyebrow in subjects with AU or AT.

To assess subject satisfaction following treatment with ATI-50002 Topical Solution, 0.46% for the treatment of scalp hair loss in subjects with AU or AT.

2. STUDY DESIGN

In the double-blind period, this Phase 2, multicenter, randomized study is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of ATI-50002 Topical Solution in subjects with AU and AT. Subjects will be required to have a clinical diagnosis of stable, clinically typical AU or AT for a duration of at least six months up to and including seven years. A total of 12 subjects will be randomized.

During the screening period, subjects will be assessed for eligibility into the study. Subjects who meet all the entry criteria will be randomized 2:1 to ATI-50002 Topical Solution, 0.46% or Vehicle Topical Solution and will apply a minimum of 1.5 mLs up to a maximum of 4 mLs of study medication to the entire scalp twice-a-day for 28 days. On Day 1 (Visit 2) and Day 28 (Visit 6), and Day 196 (1 day prior to Visit 13), subjects will apply study medication once-a-day.

Blood samples for concentrations of ATI-50002will be collected from the first 6 subjects enrolled into the study on Day 1 (Visit 2), and Day 28 (Visit 6) at pre-application and 1, 2, 4, 8 hours post application and on Day 2 (Visit 3) and Day 29 (Visit 7), 24 hours post-application. Blood samples for immunology will be collected on Day 1 (Visit 2) before study medication application, and on Day 29 (Visit 7), 24 hours after study medication application on Day 28 (Visit 6). A 4-mm punch biopsy of the scalp will be obtained to determine the concentration of ATI-50002 in the scalp skin on Day 2 (Visit 3) 24 hours after study medication application on Day 1 (Visit 2) and on Day 29 (Visit 7), 24 hours

after study medication application on Day 28 (Visit 6). A 4-mm punch biopsy will be obtained to determine histology and immunology prior to study medication application on Day 1 (Visit 2) and on Day 29 (Visit 7) and Day 197 (Visit 13), 24 hours after study medication application on Day 28 (Visit 6) and Day 196. Safety and tolerability will be evaluated at each study visit by assessment of adverse events and vital signs, and at select visits, ECGs and clinical laboratory tests will be completed.

On Day 29 (Visit 7) subjects who complete Visit 7, continue to meet the entry criteria and have no clinically significant AEs or tolerability issues will be eligible to enter a 12-month open-label extension. In the open-label extension, safety, tolerability and efficacy will be assessed. All subjects enrolled in the open-label extension will apply ATI-50002 Topical Solution, 0.46% to the entire scalp, twice daily for 52 weeks (12 months). In addition, subjects with eyebrow loss may apply a thin film of study medication to the affected eyebrow(s) twice-daily for 52 weeks (12 months). Subjects will be followed monthly for safety, tolerability and efficacy as detailed in Section 7.3. Subjects who decline or are not eligible for the open-label extension should be seen for suture removal, if applicable per Section 7.3 and Visit 16 (Post-treatment) 30 days ± 3 days following the Day 28 (Visit 6). Subjects enrolled in the initial 6-month Open Label Extension outlined by Protocol Amendment 1 (dated 06Feb2018) must be re-consented under Protocol Amendment 2 (dated 14AUG2018) in order to continue for an additional 6 months of Open Label treatment.

3. SCHEDULE OF ASSESSMENTS

The study schedule of assessments can be found in Table 1.A.

Schedule of Assessments

	Screening	Baseline	Double Blind Treatment						
	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Call	Visit 6	Visit 7	Optional Visit (Suture Removal)
Week		0	0	1	2	4	4	4	6
Treatment Day	-30 to 0	1	2	8	15	27	28	29	43
Treatment Window(days)	N/A	N/A		± 3	± 3	-3	-3	-3	± 3
Informed consent[1]	X							X[17]	
Inclusion/exclusion criteria	X	X							
Physical exam[2]	X							X	
Demographics & medical history	X								
Alopecia Areata History	X								
Vital signs[3]	X	X	X	X	X		X	X	X
Clinical laboratory sampling[4]: CBC, Chemistry with lipids, Virology, Serum Pregnancy, Urinalysis	X[4]	X			X			X	
Urine pregnancy test (WOCBP)[5]		X					X		
ECG	X	X			X			X	
SALT Score (prior to ALODEX)[6]		X						X	
ALODEX Score (after SALT)[7]		X						X	
Clinician Eyebrow Assessment								X[18]	
Subject Eyebrow Assessment								X[18]	
Subject Global Impression of Treatment Satisfaction (SGIS)									
Photography[8]		X						X	
Subject randomization		X							
Subject instructions[9]		X	X	X	X	X	X	X[17]	
Biopsy for PK[10]			X					X	
Biopsy for PD[11]		X						X	
Blood sample for PK[12]		X	X				X	X	
Blood for immunologic studies[13]		X						X	
Dispense, collect, weigh study medication bottles[14]		X	X	X	X		X	X[17]	
In office study medication application[9,14]		X					X		
Suture removal, if applicable[15]					X				X
Telephone Call[16]						X			
Concomitant therapies		X		X	X	X	X	X	X
Adverse events		X	X	X	X	X	X	X	X

	Open-Label Treatment	Post-Treatment[17]

	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Call	Visit 13	Optional Visit (Suture Removal)	Visit 14	Visit 15	Visit 16
Week	8	12	16	20	24	28	28	30	40	52	56
Treatment Day[17]	57 (OLE 28)	85 (OLE 56)	113 (OLE 84)	141 (OLE 112)	169 (OLE 140)	196 (OLE 167)	197 (OLE 168)	211 (OLE 182)	281 (OLE 252)	365 (OLE 336)	59/ 393 (OLE 364)
Treatment Window(days)	± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 7	+7	± 3/± 7
Informed consent[1]											
Inclusion/exclusion criteria											
Physical exam[2]											X
Demographics & medical history											
Alopecia Areata History											
Vital signs[3]	X	X	X	X	X		X	X	X	X	X
Clinical laboratory sampling[4]: CBC, Chemistry with lipids, Virology, Serum Pregnancy, Urinalysis		X					X		X	X	X
Urine pregnancy test (WOCBP)[5]	X	X	X	X	X		X		X	X	X
ECG		X					X				X
SALT Score (prior to ALODEX)[6]	X	X	X	X	X		X		X	X	X
ALODEX Score (after SALT)[7]	X	X	X	X	X		X		X	X	X
Clinician Eyebrow Assessment	X	X	X	X	X		X		X	X	X
Subject Eyebrow Assessment	X	X	X	X	X		X		X	X	X
Subject Global Impression of Treatment Satisfaction (SGIS)	X	X	X	X	X		X		X	X	
Photography[8]	X	X	X	X	X		X		X	X	
Subject randomization											
Subject instructions[9]	X	X	X	X	X		X		X	X	
Biopsy for PD[11]							X				
Blood for immunologic studies[13]							X				

	Open-Label Treatment										Post-Treatment[17]
	Visit 8	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**	**Call**	**Visit 13**	**Optional Visit (Suture Removal)**	**Visit 14**	**Visit 15**	Visit 16
Week	8	12	16	20	24	28	28	30	40	52	56
Treatment Day[17]	57 (OLE 28)	85 (OLE 56)	113 (OLE 84)	141 (OLE 112)	169 (OLE 140)	196 (OLE 167)	197 (OLE 168)	211 (OLE 182)	281 (OLE 252)	365 (OLE 336)	59/ 393 (OLE 364)
Treatment Window(days)	± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 7	+7	± 3/± 7
Dispense, collect, weigh study medication bottles[14]		X	X	X	X	X	X		X	X	
In office study medication application[9,14]		X									
Suture removal, if applicable[15]								X		X	
Telephone Call[16]						X					
Concomitant therapies		X	X	X	X	X	X	X	X	X	X
Adverse events		X	X	X	X	X	X	X	X	X	X

[1]A written signed ICF must be obtained from each subject prior to performing any study related procedure (i.e., prior to performing vital signs, standardized photography, biopsies, clinical laboratory sampling, or UPT).

[2]A physical exam includes: General appearance, examination of head, eyes, ears, nose and throat, respiratory, cardiovascular, abdominal, neurological, musculoskeletal, lymphatic and skin assessment.

[3] Vital signs include oral or ear temperature, blood pressure, heart rate, respiration rate (height and weight at Baseline only).

[4] Clinical laboratory sampling includes: CBC, Chemistry with lipids, Urinalysis, at each visit and **At Screening only:** Quantiferon Gold, TIBC, Serum iron, Serum Ferritin, Serum pregnancy, T3, T4, and TSH.

[5] UPT must be performed prior to randomization at Visit 2 and prior to study medication application at Day 28 (Visit 6) and at each OLE visit. UPT must be negative for the subject to continue in the study. WOCBP must have a negative serum pregnancy test at screening and a negative UPT at baseline prior to randomization.

[6]SALT is performed prior to ALODEX score using device provided.

[7] ALODEX is performed after SALT score using device provided.

[8] Photography should be performed on Day 1 (prior to application of study medication application) and on Day 29 & Day 197 prior to the scalp biopsy.

[9]Subjects must be instructed to apply the study medication according to the instructions in Appendix 1. Subjects will apply the first dose of study medication on the morning of Day 1 (Visit 2) and the last application of study medication on the morning of Day 28 (Visit 6), under the instruction and supervision of the study staff. Study medication at these visits should be applied in the morning to allow the 8-hour post dose assessments to occur at a reasonable time. On Day 1 (Visit 2) and Day 29 (Visit 7) subjects will only apply study medication once-a-day in the office.

[10] PK: A 4mm punch biopsy must be obtained on Day 2 (Visit 3) and Day 29 (Visit 7) 24 hours (± 30 minutes) after study medication application on Day 1 (Visit 2) and Day 28 (Visit 6).

[11] PD: A 4mm punch biopsy must be obtained on Day 1 (Visit 2) before application of first dose of study medication and Day 29 (Visit 7) 24 hours (± 30 minutes) after study medication application. Subjects that choose to continue in to open-label extension treatment will also have a 4mm punch biopsy collected on Day 197 (Visit 13).

	Open-Label Treatment										Post-Treatment[17]
	Visit 8	**Visit 9**	**Visit 10**	**Visit 11**	**Visit 12**	**Call**	**Visit 13**	**Optional Visit (Suture Removal)**	**Visit 14**	**Visit 15**	**Visit** 16
Week	8	12	16	20	24	28	28	30	40	52	56
Treatment Day[17]	57 (OLE 28)	85 (OLE 56)	113 (OLE 84)	141 (OLE 112)	169 (OLE 140)	196 (OLE 167)	197 (OLE 168)	211 (OLE 182)	281 (OLE 252)	365 (OLE 336)	59/ 393 (OLE 364)
Treatment Window(days)	± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 7	+7	± 3/± 7

[12]PK: The first 6 subjects enrolled in the study will have the blood PK testing performed. Blood for PK sampling will be obtained on Day 1 (Visit 2) and Day 28 (Visit 6), just prior to study medication application (predose), and 1, 2, 4, 8 hours post dose and on Day 2 (Visit 3) and Day 29 (Visit 7), 24 hours after study mediation application (on Day 1 (Visit 2) and Day 28 (Visit 6). See Section 9.3.2 for PK sample draw time windows.

[13] Blood for immunology will be obtained prior to administration of study medication on Day 1 (Visit 2) and on Day 29 (Visit 7) 24 hours (± 30 min) after study medication application on Day 28 (Visit 6). Subjects that choose to continue in to open-label extension treatment will also have blood for immunology collected on Day 197 (Visit 13).

[14] On Day 1 (Visit 2) and Day 28 (Visit 6) the study medication bottle should be weighed and then dispensed to the subject for the initial application under the supervision of study staff in the office. After the initial application on Day 1, the study medication bottle should be collected, weighed and dispensed to the subject after the 24-hour post-dose blood draw on Day 2 (Visit 3). For Visits 3 -6, each study medication bottle (with the cap) must be weighed before dispensing to the subject and at the time of return using the scale provided by Aclaris. On Day 28 (Visit 6), the study medication bottle should be weighed after subject applies the study medication in the office and not redispensed.

[15] The investigator or designee will remove the sutures approximately 14 days after scalp biopsy, unless an absorbable suture is used.

[16] On Day 27 or the day prior to Day 28 (Visit 6), the study staff will call the subject to remind them not to apply study medication on the morning of Day 28 (Visit 6) and to bring both used and unused study medication bottles to the visit. Study medication will be applied in the office under the supervision of the study staff. On Day 196 or the day prior to Week 28 (Visit 13) the study staff will call the subject to remind them not to apply study medication in that evening and on the morning of Week 28 (Visit 13), and to bring both used and unused study medication bottles to the visit. The scalp biopsy at Week 38 (Visit 13) should be performed 24 hours (±30 minutes) post the last study medication application.

[17]On Day 29 (Visit 7) subject may be given the option to move into open-label extension treatment.

- If the subject declines the open-label extension, she/he should be seen for the Visit 16 (Post-treatment) assessments 30 days following the date of Day 29 (Visit 7).
- If the subject chooses to continue in to the open-label extension, she/he must sign an ICF prior to being dispensed open-label drug and receiving continued study medication application instructions.
- If the subject enrolls in open-label treatment after Day 29 (Visit 7), an unscheduled visit will be conducted in order to obtain consent, review drug application instructions, and dispense drug. This will be considered the official date that the subject initiated open-label extension treatment and the scheduling of subsequent visits 8-16 should be based off of this date as referenced by (OLE xxx) in the treatment day schedule header above.

[18]Subjects who are eligible and consent to enter the open-label extension will have a baseline CEA and SEA completed at Visit 7 or the unscheduled Visit.

4. STATISTICAL METHODS

In general summaries will be presented according to double-blind treatment group and additionally for the subset of patients entering open-label. Other than baseline data (ie data collected prior to the first application of double-blind medication), the data summarized corresponds to the period of collection (ie during double-blind or during open-label). For those entering open-label, the open label period begins at the application of open-label medication. Additional details are provided in the data handling and programming specifications document. No imputation of missing data was performed other than completely or partially missing dates as described in the Data Handling and Programming Specifications document.

All Data listings are sorted by double-blind treatment group and patient ID.

4.1 Study Populations, Disposition, Baseline Characteristics, Medical History Concomitant Medications, Exposure and Protocol Violations

4.1.1 Analysis Populations

The efficacy and safety populations will be defined as follows:

- As-Treated population (AS): This population includes all patients with at least one application of study treatment. This population will be used for pharmacodynamics and safety analyses. All analyses using this population will be based on the treatment actually received.
- Blood Pharmacokinetic (PK1) population: This population includes patients participating in the PK assessment who had evaluable blood plasma measurements with no significant protocol deviations that may impact the data.
- Scalp Pharmacokinetic (PK2) population: This population includes patients participating in the PK assessment who had evaluable scalp biopsy measurements with no significant protocol deviations that may impact the data.
- Pharmacodynamic (PD) population: This population includes all randomized patients who had at least 1 evaluable pharmacodynamic measurement.

4.1.2 Patient Disposition

The number of patients in each population is presented together with the study completion status and the reasons for discontinuation. Patents entering open-label are considered to have completed the study with regard to double-blind medication.

4.1.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics are presented in the data listings. Descriptive summary statistics (n, mean, standard deviation, median, minimum, and maximum) and/or frequency distributions, as appropriate, are generated for the AS population.

4.1.4 History of Alopecia

The type of Alopecia (AT or AU) and prior therapies for alopecia will be summarized by frequency distributions. The time since onset of the current episode of alopecia at entry will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum, and maximum). Summaries will be generated for the AS population. Histological/Cytologic information will be tabulated.

4.1.5 Prior and Concomitant Medications, Therapies and Procedures

Medications are coded using the WHO Drug Reference. Prior and concomitant medications are listed only. The period(s) in which the medications were administered are flagged.

4.1.6 Exposure to Study Medication and Study Medication Administration

Exposure will be summarized and listed for the AS population with separate summaries from double-blind and open-label periods. Additionally, the combined exposure to ATI-50002 from the double-blind and open-label periods will be tabulated.

The duration of treatment, total weight, total volume, and average volume per application will be summarized using descriptive statistics (n, mean, SD, median, minimum and maximum).

4.1.7 Major Protocol Violations

Protocol violations will be identified to measure adherence to key aspects the protocol. Prior to unblinding the sponsor will assess the data and identify all major and minor protocol deviations. Specific data fields that will be examined to identify protocol deviations include entrance inclusion/exclusion criteria and prohibited prior and concomitant medications as well as all deviations identified by the investigator. All protocol violations will be listed, and major protocol violations will be summarized (n and percent) by randomized treatment group for all violations during the double-blind period.

4.2 Pharmacokinetic Endpoints

4.2.1 Blood Levels of ATI-50002

The blood levels of ATI-5002 will be listed only.

4.2.2 Scalp Biopsy Levels of ATI-50002

Scalp biopsy levels of ATI-50002 will summarized with descriptive statistics for each schedule collection visit. Levels that are BLQ will not be included but will be accounted for categorically.

4.3 Pharmacodynamic Endpoints

The baseline scores for SALT and ALODEX will be the last non-missing value collected ≤ the date of the first application of double-blind study medication. This baseline will be used also for calculating changes during open-label for these variables. For the eyebrow assessments (CEA and SEA), the value collected at V7 will be used as the baseline for calculating changes during subsequent visits.

4.3.1 SALT and ALODEX Scores

For both SALT and ALODEX the mean and mean change from baseline will be tabulated by visit and treatment group. Change will be assessed both as an absolute percentage difference (timepoint percentage score – baseline percentage score) as well as relative percent regrowth (absolute percentage difference divided by baseline percentage * -1). In addition, the proportion of patients that have ≥25%, ≥50% and ≥75% regrowth will be tabulated for both SALT and ALODEX.

4.3.1 ALADIN Scores

The analysis of ALADIN scores will be detailed in a separate document.

4.3.2 Eyebrow Assessments during Open-Label

For patients entering open-label, mean Percent hair loss, CEA and SEA scores mean and mean change from baseline will be provided by visit. At entry into open-label, V7, summary statistics will be provided by double-blind treatment group as well as for all patients entering open-label. Where applicable, each patient's scores for the left and right eyebrows will be averaged prior to summarization. Individual scores for the left and right eyebrows will be provided in the data listings.

4.3.3 Subject Global Impression of Treatment Satisfaction (SGIS)

For patients entering open-label, descriptive statistics (N, mean, SD, median, minimum

and maximum) of the SGIS will be provided by visit. Additionally, the number of percentage of patents recording each of the 7 possible SGIS scores will be provided categorically.

4.4 Safety Analyses

The comprehensive safety analysis is based on all patients in the AS population.

The following sections detail the summaries performed on the safety data. Additional data handling rules including those for imputation of partially missing dates are provided in a separate SAP document pertaining to data handling and programming specifications.

The baseline scores for vital signs, laboratory assessments and ECGs will be the last non-missing value collected ≤ the date of the first application of double-blind study medication. This baseline will be used also for calculating changes during open-label for these variables.

4.4.1 Adverse Events

Adverse events are coded using the MedDRA dictionary and are categorized by system organ class (SOC) and preferred term (PT). Only treatment emergent adverse events are included in summary tabulations and include the following groupings: Double-Blind ATI-5002, Double-Blind Placebo, Open-Label ATI-5002 and Total ATI-50002 (Double-Blind + Open-Label). All adverse events are included in the data listings including those that are not considered treatment emergent.

To allow differentiation as to which study period an Adverse Event occurred, four categories are defined based upon onset date. Adverse Events that had onset dates prior to the first application of study medication are considered "prior". Adverse events with onset dates on or after the first application of double-blind study medication, prior to entry into open label (first application of open-label study medication) and within 30 days following the last application of study medication are considered "on double-blind therapy" or equivalently "treatment emergent". Events with onset dates on or after the first application of open-label study medication and within 30 days of the last application of study medication are consider "on-open-label therapy" and also considered "treatment emergent". Events with onset dates more than 30 days after the last application of study medication, be it double-blind or open label, are considered as "post-therapy".

Frequency tabulations are presented by MedDRA SOC and preferred term, for all adverse events; study treatment-related, adverse events resulting in discontinuation of study treatment, serious adverse events and adverse events by maximum severity. Adverse events resulting in discontinuation are those with 'action taken' recorded as 'drug withdrawn'.

4.4.2 Physical Examinations

Physical examination findings will be listed for each patient.

4.4.3 Vital Signs

Systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate and temperature are summarized using descriptive statistics for each visit. Both actual values and changes from baseline are summarized.

4.4.4 ECG assessments

The core laboratory's interpretation of the ECGs are summarized as "shift" from baseline to "worst" overall interpretation recorded after baseline where the order of severity of the interpretations from best to worst are "Normal", "Abnormal, NCS" and "Abnormal, CS". Separate summaries are used for post baseline data collected during double-blind and during open-label. If applicable, follow-up visits are included in the post-baseline data dependent upon entry into open-label (ie included in double-blind assessment if a patient did not enter open-label and in open-label assessment if they did).

4.4.5 Laboratory Evaluations

Shift tables showing changes in relationship to the normal reference range grade from baseline to the "worst" relationship recorded post-baseline are tabulated. In the event a patient had both "low" and "high" post-baseline values the patient will be counted under both "low" and "high". As such the percentages of the cells in the shift table may add to more than 100%.

Chemistry and Hematology parameters are summarized using descriptive statistics for each visit. Both actual values and changes from baseline are summarized.

The number and percentage of patients meeting criteria for hepatobiliary abnormalities and for potential renal impairment are provided for Double-Blind ATI-50002, Double-Blind Placebo, Open-Label ATI-50002 and Total ATI-50002 (Double-Blind + Open-Label).

4.5 Pharmacokinetic Analyses

Levels of ATI-50002 in the scalp biopsy is summarized for V3 (Day 2) and V7 (Day 29) using simple descriptive statistics. Only values that are quantifiable are included in the mean, SD, etc.; however, a separate summary of the number and percentage of patients with value that were BLQ (below limit of quantification) is provided.

4.6 Interim Analyses

An interim assessment of blood and scalp PK was performed in the first N=6 patients. For this analysis, the following steps were taken to ensure that unblinded review of PK / PD

parameters did not affect the blinded creation, collection, review or verification of any clinical study data. No PK / PD unblinded reviews were undertaken until all relevant subjects have had all data through Visit 7 verified by source document review and were determined to have all data complete and accurate. Additionally, data from visits through Visit 7 were locked in the EDC system by CRAs, to prevent any changes without permission from the Sponsor. As such, the EDC system audit trail will capture all data activity before and after this Visit 7 lock. All clinical evaluations through Visit 7 for the applicable subjects were done without knowledge of treatment group assignment.

4.7 Sample Size

Since this is the first multicenter study of ATI-50002 Topical Solution in subjects with stable alopecia universalis and alopecia totalis, sample size considerations were based upon feasibility factors and not on a formal power computation.

4.8 Changes in/ Clarifications to the Conduct of the Study or Planned Analysis

The Chi-square statistic was not created to compare the incidence of adverse events

Details of analyses of ALADIN scores and immunologic evaluation of blood T-cells will be provided in a separate document.

Scalp biopsy histology will not be analyzed due to limited samples.

5. STATISTICAL SOFTWARE

All data summaries and listings will be performed using SAS® Version 9.2 or higher, under Windows operating system.