STATISTICAL ANALYSIS PLAN

A PHASE 2, MULTICENTER STUDY OF ATR-101 FOR THE TREATMENT OF CONGENITAL ADRENAL HYPERPLASIA

Protocol Number:	ATR-101-201
Study Phase:	2
Product Name:	ATR-101
IND Number:	122745
NCT Number:	NCT02804178
Sponsor:	Millendo Therapeutics, Inc.
Current Protocol:	Amendment 1 / January 14, 2016
SAP:	V2.0 / September 6, 2017

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06 SEP 2017
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1 SUMMARY OF CHANGES

SAP Version History		
Version	**Date**	**Description of Changes**
1.0	June 19, 2017	Original Document
2.0	September 6, 2017	Modify TEAE to include all AEs starting on or after dosing by removing "or exist before but get worse in severity or relationship to study drug after first dose." Also urinalysis is only collected at Screening and Final Study Visit. Remove summaries by dose level for Day 1 and Day 15.

2 INTRODUCTION

This Statistical Analysis Plan (SAP) provides a description of the statistical and pharmacokinetic (PK) methods and procedures to be implemented for the analyses of data from Millendo Therapeutics Protocol ATR-101-201. Any deviations from this analysis plan will be substantiated by sound statistical/PK rationale and will be documented in the final clinical study report.

3 STUDY OBJECTIVES

3.1 Primary Objective

The primary objective of this study is to evaluate the efficacy and safety of orally administered ATR-101 in subjects with congenital adrenal hyperplasia (CAH).

3.2 Secondary Objectives

The secondary objectives of this study are:

- To evaluate the changes in adrenal cortical steroids and steroid intermediates
- To evaluate the changes to the hypothalamic-pituitary-adrenal axis (via adrenocorticotropic hormone [ACTH])
- To evaluate the PK of ATR-101

4 STUDY ENDPOINTS

4.1 Efficacy Assessment

Efficacy will be assessed by changes in adrenal steroids and steroid intermediates. 17-hydroxyprogesterone (17-OHP) will serve as the **primary outcome measure** as this adrenal steroid intermediate is used diagnostically and to aid in the management of exogenous glucocorticoid (GC) replacement therapy in clinical practice. However, absolute target values for 17-OHP or androgens do not currently exist in treatment guidelines put forth by any of the medical societies. The entry criterion for 17-OHP is set at ≥4x upper limit of normal (ULN) (ULN adjusted as needed for the menstrual cycle phase of subjects who are premenopausal women), which is intended to enroll subjects who are not optimally controlled while on exogenous steroid replacement therapy. It is anticipated that most subjects will enter with 17-OHP levels markedly higher than 4xULN. The primary efficacy outcome measure will be aligned to the clinical goal of achieving a mildly elevated 17-OHP level, which for this study is defined as ≤2xULN. However, given the high baseline 17-OHP levels anticipated, the percentage change in 17-OHP and changes in other key efficacy parameters in the androgen pathway (androstenedione, testosterone, dehydroepiandrosterone [DHEA], dehydroepiandrosterone sulfate [DHEA-S]) will also serve to define efficacy.

The majority of CAH subjects will enter the study on both GC and mineralocorticoid (MC) replacement (75% of classic CAH subjects have deficiencies in both pathways). Direct renin and aldosterone will be assessed to determine the potential impact on the MC pathway.

ACTH levels will be assessed to determine potential effects on the hypothalamic-pituitary-adrenal (HPA)-axis. GC replacement doses are expected to remain unchanged. Confirmation of low GC levels associated with decreases in 17-OHP and androgens with ATR-101 dosing will help to establish the pharmacodynamic effects of ATR-101. Increased GC levels, secondary to decreased hepatic metabolism (ATR-101 CYP3A effect), could potentially lead to decreased ACTH and subsequently decreased 17-OHP levels. This could potentially confound assessment of direct ATR-101 effects on adrenal steroid and steroid intermediate synthesis. Therefore, assessment of GC levels will also be done during the study.

4.2 Safety Assessment

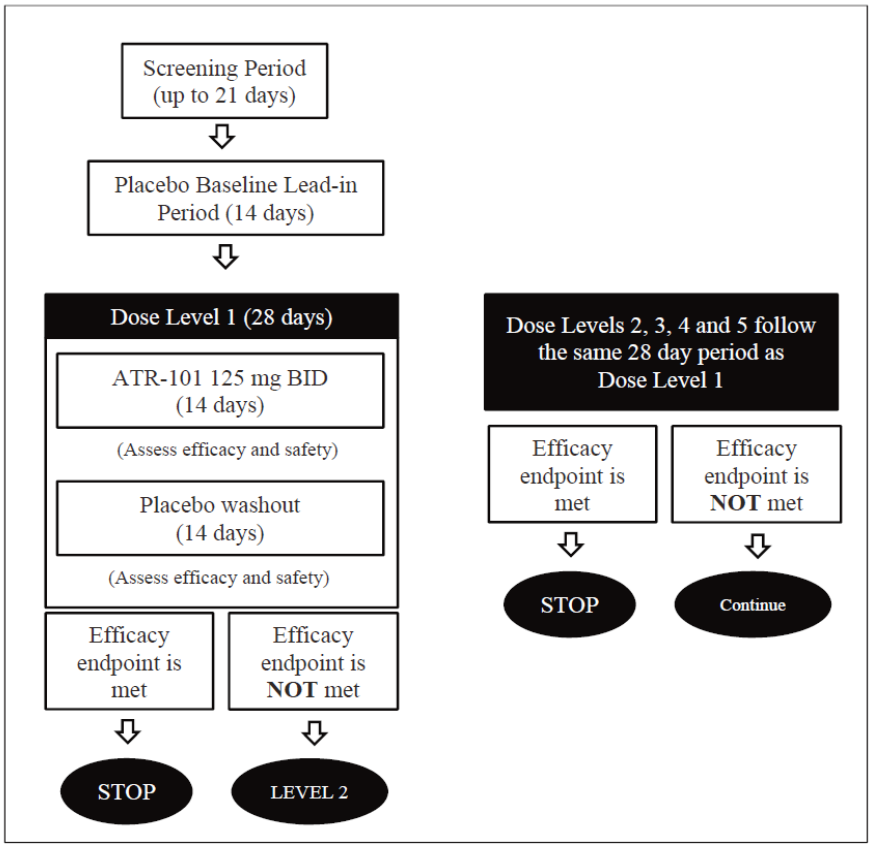
Safety will be assessed by monitoring adverse events (AEs), changes in physical examination (including vital signs), changes in electrocardiograms (ECGs), and changes in laboratory parameters. Safety assessments will take place every 2 weeks during study participation.

5 STUDY OVERVIEW

5.1 Study Design

This is a multicenter, single-blind, multiple dose study of ATR-101 with a placebo washout component. A minimum of nine subjects will be enrolled with the potential to add an additional eight subjects. The study design is presented in Figure 1 below.

Figure 1. ATR-101-201 Study Design



Each subject will complete a Screening Period of up to 21 days to assess inclusion and exclusion criteria. Baseline status will be established with a 14-day single-blind, placebo Lead-in Period. Exogenous GC and MC replacement therapy must be maintained throughout the duration of the study. Each dose level, comprised of ATR-101 administered for 14 days followed by a 14-day placebo washout, will last for a total of 28 days (see Figure 2 below). All subjects will start at Dose Level 1, ATR-101 125 mg twice daily (BID), for 14 days. Efficacy and safety will be assessed after the 14-day ATR-101 treatment period (on the morning of Day 15). Immediately after the completion of the ATR-101 treatment period, a 14-day single-blind, placebo Washout Period (placebo matching ATR-101 125 mg) will take place. The efficacy assessment obtained on Day 15 will be reviewed by the Principal Investigator (PI) or Sub-investiagor (SI) to determine whether the subject has met the

primary outcome measure or whether the subject should continue to the next dose level (if there are no safety issues).

Figure 2. Dosing Regimen per Dose Level

Subejcts will return to the study center after completion of the 14-day placebo Washout Period and will follow one of two actions based upon **Day 15** efficacy results:

- If the primary outcome measure is met (i.e., **17-OHP ≤ 2xULN**) the subject completes the Final Study Visit
- If the primary outcome measure is **not** met (i.e., **17-OHP > 2xULN**) the subject continues to the next dose level.

Table 1 below presents the 5 ATR-101 Dose Levels. Dose Levels 2, 3, 4, and 5 will follow the same procedures as Dose Level 1 (i.e., treatment with ATR-101 for 14 days, followed by the placebo Washout Period of 14 days). A subject may receive a minimum of one dose level (Level 1) or a maximum of 5 dose levels (Level 1-5), along with the corresponding placebo Washout Periods.

Table 1. ATR-101 Doses for Each Dose Level

Dose Level	ATR-101 Dose	Total Daily Dose
1	125 mg BID	250 mg
2	250 mg BID	500 mg
3	500 mg BID	1000 mg
4	750 mg BID	1500 mg
5	1000 mg BID	2000 mg

5.2 Treatments Administered and Blinding

During the 14-day Baseline Lead-in Period, placebo tablets that match the ATR-101 125 mg tablets will be administered BID.

Starting with Dose Level 1, each dose level will consist of a 28-day dosing regimen consisting of 14 days of ATR-101 treatment followed immediately by 14 days of matching placebo washout.

Subjects will be blinded to treatment beginning with the Baseline Lead-in Period, which will use placebo tablets that appear identical to ATR-101 125 mg. Dose levels 1 to 5 are split into two weeks of active treatment (ATR-101) followed by two weeks of treatment with matching placebo (Washout Period).

6 STATISTICAL METHODOLOGY

6.1 Sample Size Determination

Sample size considerations are based on a Simon 2-stage Minimax design with 1-sided alpha of 5% and 80% power.

Stage 1 consists of 9 completed subjects. The study will stop at Stage 1 if either of the following conditions are met:

- Futility criteria: defined as ≤2 of 9 (22%) subjects having a Day 15 17-OHP ≤ 2xULN or a negative mean percentage change (i.e., decrease) in 17-OHP from Day 1 to Day 15 for Dose Levels 1-5
- Success criteria: defined as ≥7 of 9 (78%) subjects having a Day 15 17-OHP ≤ 2xULN or a negative mean percentage change (i.e., decrease) in 17-OHP from Day 1 to Day 15 for Dose Levels 1-5

Stage 2 will commence if 3, 4, 5, or 6 of the 9 subjects meet the primary outcome measure. In this scenario, accrual will continue with up to 8 additional subjects for a total of no more than 17 subjects. Accrual may stop earlier with sufficient evidence for further development if a total of 7 or more subjects respond (minimum observed response rate of 7/17, 41%).

The study medical monitor along with the Sponsor may determine if a subject will be replaced in order to have a minimum of 9 evaluable subjects for Stage 1. Possible reasons for replacement include extreme noncompliance with study drug not related to an AE, and noncompliance with the protocol such as the use of prohibited medications that could confound results.

6.2 General Considerations

Unless otherwise specified, summaries will be presented by dose level where the first dose of ATR-101 defines the start of each dose level. In other words, each dose level consists of Day 1 – Day 28 (2 weeks of ATR-101 and 2 weeks of Placebo). Subjects may be counted in more than one dose level. Each subject will be counted once in each dose level according to sequential participation and once in the overall column.

In addition, summaries will be provided by last dose level. In other words, the results from the subject's last completed dose level will be carried forward.

6.3 Analysis Populations

6.3.1 Enrolled Population

The Enrolled Population will include all subjects who receive at least one dose of placebo during the Lead-in Period.

6.3.2 Safety Population

The Safety Population will include all subjects who receive at least one dose of ATR-101. For summaries by dose level, only subjects receiving at least one dose in the specified dose level will be included. For summaries by dose level and treatment, only subjects receiving at least one dose in the specified dose level treatment will be included.

6.3.3 Per Protocol Population

The Per Protocol Population will include all subjects who take at least 11 days of ATR-101 treatment at Dose Level 1 (the lowest dose level) and have at least one post-baseline efficacy assessment (i.e. 17-OHP) without having a significant protocol deviation. The Per Protocol Population will be identified per dose level. All subjects excluded from the Per Protocol Population will be identified after database lock.

6.3.4 Pharmacokinetic Population

The PK Population will include all subjects who receive at least one dose of ATR-101 and have any measurable level of ATR-101 or its metabolites.

6.4 Subject Disposition

Counts of subjects in each population, as well as counts and percentages of subjects who completed the study and who withdraw early from the study, with the reason for early withdrawal, will be presented by ATR-101 dose level and overall.

6.5 Demographic and Baseline Characteristics

Descriptive summaries of demographic and baseline characteristics will be presented by dose level and overall. Baseline measurements refer to data collected at Dose Level 1 Day 1 pre-dose. If a value at Dose Level 1 Day 1 pre-dose is not available, the last measurement prior to the first dose of study drug will be used as the baseline value.

Demographic and baseline characteristics include, but are not limited to: age at informed consent, sex, race, ethnicity, baseline glucocorticoids, baseline glucocorticoid dose, baseline mineralocorticoid dose, body weight, height, body mass index (BMI), body surface area, steroid hormones, and steroid intermediates. Continuous variables (age, glucocorticoid dose, mineralocorticoid dose, body weight, BMI, steroid hormones, and steroid intermediates) will be summarized by subject count, mean, standard deviation, median, minimum, and

maximum. Categorical variables (race, sex, ethnicity, and glucocorticoids) will be summarized by the number and percentage of subjects in the corresponding categories.

Body surface area will be calculated as:

$$\sqrt{\frac{Weight\ in\ kg \times Height\ in\ cm}{3600}}$$

Demographics and baseline characteristics will be summarized based on the Safety Population. If the Per Protocol Population and the PK Population differ from the Safety Population, the demographics and baseline characteristics will also be summarized based on these populations. Demographics and baseline characteristics will also be summarized for male and female subgroups and for men and postmenopausal women (excludes females <50 years in age).

All medical history will be listed.

6.6 Prior and Concomitant Medications

Prior and concomitant medications will be coded with the World Health Organization Drug Dictionary and listed. All concomitant medications taken after first dosing of study drug will be summarized for the Safety Population by dose level, treatment, and overall. All concomitant medications during the Placebo Lead-in Period will be summarized overall. All prior and concomitant medications will be listed.

6.7 Exposure and Compliance

Treatment duration within each dose level will be summarized with descriptive statistics for ATR-101 and placebo separately and overall. Treatment duration will be calculated as follows:

Treatment duration in days = last dose date – first dose date +1.

If the last dose date is not available within a dose level, the date prior to the first dose date of the next dose level will be used.

The number of tablets administered will be summarized within each dose level with descriptive statistics for ATR-101 and placebo separately and overall.

Number of tablets administered = number of tablets dispensed – number of tablets returned

Compliance within each dose level and overall will be summarized with descriptive statistics for ATR-101 and placebo separately. The percentage of subjects with compliance <80%, 80-120%, and >120% will also be tabulated.

Dose Levels 1, 2, and 3:

Compliance (%) = 100 x number of tablets administered / (treatment duration x 2).

Dose Levels 4 and 5:

Compliance (%) = 100 x number of tablets administered / (treatment duration x 4).

6.8 Primary Efficacy Analyses

The percentage of responders will be tabulated for the Safety Population overall. A responder is defined as a subject who meets the primary outcome measure of Day 15 17-OHP ≤ 2xULN (ULN adjusted as needed for the menstrual cycle phase of subjects who are premenopausal women) at any dose level.

The percentage of subjects showing "drug effect" will be tabulated for the Safety Population overall. A subject showing "drug effect" is defined as a subject who is a responder or who has a negative mean percentage change in 17-OHP from Day 1 to Day 15 for Dose Levels 1-5.

The percentage of responders and percentage of subjects showing "drug effect" will also be tabulated for the Per Protocol Population overall as a sensitivity analysis to test the robustness of the primary result.

The change and percentage change in 17-OHP will also be calculated from Day 15 to Day 1 of the next dose level as follows:

- Change and percentage change from Dose Level 1 Day 15 to *Dose Level 2 Day 1*
- Change and percentage change from Dose Level 2 Day 15 to *Dose Level 3 Day 1*
- Change and percentage change from Dose Level 3 Day 15 to *Dose Level 4 Day 1*
- Change and percentage change from Dose Level 4 Day 15 to *Dose Level 5 Day 1*
- Change and percentage change from Dose Level 5 Day 15 to *Final Study Visit (Visit Day 29)*

The percentage of placebo responders will be tabulated for the Safety Population overall. A placebo responder is defined as a subject who meets Day 1/Final Study Visit 17-OHP ≤ 2xULN at any dose level, i.e. the 17-OHP at the italicized visit above is ≤ 2xULN.

The percentage of subjects showing "placebo effect" will be tabulated for the Safety Population overall. A subject showing "placebo effect" is defined as a subject who is a placebo responder or who has a negative mean percentage change in 17-OHP from Day 15 to Day 1 of the next dose level.

6.9 Pharmacodynamic Analyses

All steroid hormones and steroid intermediates will be summarized for Day 1 and Day 15 by dose level. The change and percentage change from Day 1 to Day 15 within each dose level will be summarized. The change and percentage change from Day 15 to Day 1 of the next dose level will also be summarized. Summaries will also be provided for male and female subgroups and for men and postmenopausal women (excludes females <50 years in age).

Pharmacodynamic measures include:

- GC pathway: progesterone, cortisol
- MC pathway: 11-deoxycorticosterone (11-DOC), direct renin, aldosterone
- Androgens: androstenedione, free testosterone, DHEA, DHEA-S
- HPA-axis: ACTH

6.10 Pharmacokinetic Analyses

6.10.1 Sample Collections for Pharmacokinetic Analyses

Blood samples will be collected to profile the levels of ATR-101 and its metabolites on Day 1 of each Dose Level at pre-dose and 1, 2, 3, and 4 hours post-dose; on Day 15 of each Dose Level at pre-dose, and at the Final Study Visit or Early Termination Visit. A window of ±10 minutes is permitted around each sampling time point.

The exact time of each sample collection will be recorded. If the exact time (measured from dosing) is outside of the collection window for nominal time points, the corresponding concentration will be excluded from concentration versus time descriptive statistical summaries and plots, but will still be used in the calculations of PK parameter estimates.

6.10.2 Pharmacokinetic Variables

The PK parameters listed below will be calculated from the individual plasma concentration profiles by standard non-compartmental methods:

Table 2. PK Parameters to be Calculated

C_{max}	Maximum observed concentration
t_{max}	Time to reach the maximum observed concentration
$AUC_{0\text{-last}}$	Area under the concentration-time curve calculated from time zero to the last measurable concentration
$AUC_{0\text{-}4}$	Area under the concentration-time curve calculated from time zero to 4

	hours
Lambda z (λ_z)	Apparent first-order terminal elimination rate constant calculated by linear regression of the terminal linear portion of the log concentration vs. time curve (data permitting)
$t_{½}$	Apparent terminal half-life (data permitting)
$AUC_{0\text{-}inf}$	Area under the concentration-time curve from time zero to infinity (extrapolated) (data permitting)

6.10.3 Pharmacokinetic Variables Calculation

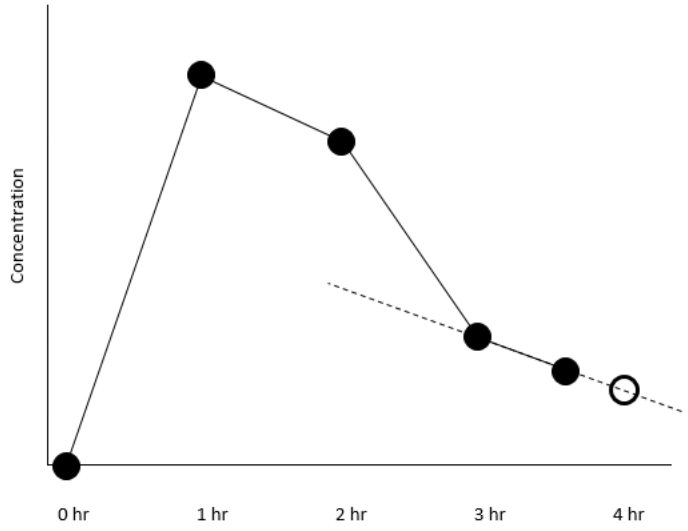
Actual collection times will be used in PK parameter calculations. The Linear Trapezoidal Linear Interpolation method will be used in the computation of all AUC values. The PK parameters λ_z, $t_{½}$, and $AUC_{0\text{-}inf}$ will not be presented for those subjects who do not exhibit a terminal elimination phase in their concentration versus time profiles. In order to estimate the apparent first-order terminal elimination constant, λ_z, linear regression of concentration in logarithm scale vs. time will be performed using at least 3 data points. Uniform weighting will be selected to perform the regression analysis to estimate λ_z. The constant λ_z will not be assigned if:

- the terminal elimination phase is not linear (as it appears on a semi-logarithmic scale)
- the terminal elimination rate constant indicates a positive slope ($\lambda_z > 0$)
- t_{max} is one of the 3 last data points
- the regression coefficient (R^2) is less than 0.8

If the percent extrapolated $AUC_{0\text{-}inf}$ is greater than 20%, the PK parameters will be reported but flagged in the appropriate listing. In cases where the λ_z interval is not assigned, the values of associated parameters (λ_z, $t_{½}$, $AUC_{0\text{-}inf}$) will not be calculated.

For the calculation of $AUC_{0\text{-}4}$ if the nominal (planned) time of the last observed measurable concentration is at 4 hours but the actual time of the last observed measurable concentration (t_{last}) is less than 4 hours (such as actual time = 3.9 hours), the concentration at 4 hours will be imputed. The imputed concentration is calculated using the linear extrapolation of the previous two records. If the extrapolated concentration is less than 0, then a value of 0 will be used. If the nominal time of the last observed measurable concentration is less than 4 hours, then $AUC_{0\text{-}4}$ will not be calculated. A visual aide for the imputation of the concentration at 4 hours is provided below in Figure 3.

Figure 3. Illustration of Imputation of Concentration at 4 Hours for Calculation of AUC_{0-4}



6.10.4 Pharmacokinetic Summary and Analysis

Day 1 PK concentration data, within the acceptable sampling window, will be summarized for each time point using descriptive statistics from the PK Population (i.e., Mean, SD, Min, Max, Median, %CV, Geometric Mean, Geometric %CV) for each dose level. Plots of mean Day 1 concentrations of plasma ATR-101 and its metabolites (with standard deviation bars) versus nominal time will be generated for each dose level. Individual ATR-101 and metabolite concentration versus actual time plots will also be provided.

The Day 1 PK parameters will be summarized by dose level using the PK Population. Actual sampling times will be used. Geometric mean and geometric coefficient of variation (CV%) will be added to the descriptive statistics for C_{max} and all AUCs.

PK/PD relationships may be explored graphically.

6.10.5 Handling Missing or Non-Quantifiable Data

Concentrations below the lower limit of quantitation (BLLOQ) before the first measurable concentration will be assigned a value of zero. A single BLLOQ value between measurable concentrations in a profile will be set to missing in the derivation of PK parameters, statistical analyses, and the individual subject plots. BLLOQ values that occur after the last measurable concentration will also be set to missing in the derivation of PK parameters and in the individual subject plots.

6.11 Safety Analyses

Safety data includes AEs, physical examinations, vital signs, ECGs, and clinical laboratory assessments. Safety data will be summarized and listed. No formal statistical analysis of the safety data will be conducted. All safety summaries will be based on the Safety Population. Safety summaries will be based on observed values only.

6.11.1 Adverse Events

AEs will be coded and classified by system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA). All AEs reported for enrolled subjects during the clinical study will be recorded on the electronic case report form (eCRF). All AEs, regardless of relationship to study drug or procedure, should be collected beginning from the time the subject signs the study consent. AEs in clinical investigation subjects include any change in the subject's condition. This includes symptoms, physical findings, or clinical syndromes.

TEAEs are defined as adverse events that happen for the first time on or after the first dose date (Dose Level 1 Day 1) of ATR-101.

An overview with counts of events and subjects will be provided by dose level and treatment at AE onset and overall for the incidence of AEs in the following categories:

- Any TEAE
- Maximum severity of TEAE
- Any study drug related TEAE
- Maximum severity of study drug related TEAE
- Any serious treatment-emergent SAE (TESAE)
- Any study drug related SAE
- Death due to AE
- AE leading to discontinuation from study
- Study drug related AE leading to discontinuation from study

The incidence of TEAEs will be summarized by dose level and treatment at AE onset and overall by system organ class and preferred term. System organ class will be sorted alphabetically and preferred term will be sorted by descending total frequency within system organ class. Similar summaries will be provided for TEAEs by maximum severity. The same summaries will be done for study drug related TEAEs.

The AE summaries will be provided by dose level and treatment at AE onset. In other words, AEs starting on or after ATR-101 and prior to the subsequent Placebo dose will be attributed

to ATR-101. AEs starting on or after Placebo and prior to the subsequent ATR-101 dose will be attributed to Placebo.

Listings will be provided for any SAEs, AEs leading to discontinuation from study, and AEs beginning in the Placebo Baseline Lead-In Period.

6.11.2 Clinical Laboratory Evaluations

Safety laboratory data (chemistry, hematology, and coagulation) will be summarized by dose level for Day 1 and Day 15 visits. Change from Day 1 to Day 15 will be summarized within each dose level. The change from Day 15 to Day 1 of the next dose level will also be summarized.

The number and frequency of subjects with laboratory abnormalities will be summarized by dose level. Shift tables from Day 1 to Day 15 will be presented for ALT and AST (>1xULN to ≤2xULN, >2xULN to ≤3xULN, >3xULN) and CK (>1xULN to ≤5xULN, >5xULN to ≤10xULN, >10xULN). Shift tables from Day 15 to Day 1 of the next dose level will also be presented.

Urinalysis will be summarized overall at Screening and the Final Study Visit.

6.11.3 Vital Signs

Vital signs including oral or tympanic temperature, systolic and diastolic blood pressure, pulse, and respiratory rate will be measured at Screening, at the start of the Baseline Lead-in Period, at Day 1 pre-dose and at 1, 2, and 4 hours post-dose for each dose level, at Day 15 pre-dose for each dose level, and at the Final Study Visit or Early Termination Visit. Body weight will be measured at Screening, at the start of the Baseline Lead-in Period, at Day 1 pre-dose for each dose level, at Day 15 pre-dose for each dose level, and at the Final Study Visit or Early Termination Visit.

Vital signs will be summarized by dose level for Day 1 pre-dose, 1, 2, and 4 hours post-dose and Day 15 visits. Change from Day 1 pre-dose will be summarized.

6.11.4 Electrocardiogram

All subjects will have 12-lead ECG assessments at Screening, Day 1 pre-dose and 2 hours post-dose for each dose level, Day 15 pre-dose for each dose level, and at the completion of the Placebo Washout Period on Day 29 (this ECG could serve as the pre-dose ECG, Day 1, if the subject is moving to the next dose level or as the ECG for the Final Study Visit or Early Termination Visit).

ECG measurements (heart rate, PR, QRS, QT, RR, QTcB, and QTcF) will be summarized by dose level for Day 1 pre-dose, 2 hours post-dose and Day 15 visits. Change from Day 1 pre-dose will be summarized.

ECG interpretations (normal, abnormal not clinically significant, abnormal clinically significant) will be tabulated by dose level for each time point.

6.11.5 Physical Examination

A complete physical examination will be obtained at Screening and the Final Study visit or Early Termination Visit. A targeted brief physical exam will be completed prior to the start of the Baseline Lead-in Period, prior to dosing on the first day of every Dose Level (active treatment), and prior to starting the placebo Washout Period at each Dose Level. Physical exam findings (normal, abnormal not clinically significant, abnormal clinically significant) will be tabulated by dose level for each visit.

6.11.6 Other Safety Parameters

All other safety data will be listed, such as urine pregnancy tests.

7 CHANGES FROM THE PLANNED ANALYSIS

Per Protocol, the study was to have been stopped at Stage 1 if either of the following conditions were met:

- Futility criteria: defined as ≤2 of 9 (22%) subjects meeting the primary outcome measure (17-OHP ≤ 2xULN)
- Success criteria: defined as ≥7 of 9 (78%) subjects meeting the primary outcome measure (17-OHP ≤ 2xULN)

From medical considerations, this has been modified as follows:

- Futility criteria: defined as ≤2 of 9 (22%) subjects having a Day 15 17-OHP ≤ 2xULN or a negative mean percentage change (i.e., decrease) in 17-OHP from Day 1 to Day 15 for Dose Levels 1-5
- Success criteria: defined as ≥7 of 9 (78%) subjects having a Day 15 17-OHP ≤ 2xULN or a negative mean percentage change (i.e., decrease) in 17-OHP from Day 1 to Day 15 for Dose Levels 1-5

8 GENERAL INFORMATION

The mock-ups for SAS-generated tables/figures/listings will be prepared in a separate document and finalized before database lock for the study.

8.1 Statistical Software

The creation of analysis datasets and all statistical analyses will be done using SAS® version 9.3. The PK parameters will be determined using Phoenix™ WinNonlin® version 6.4 or

higher. The Medpace standard operating procedures will be followed for the validation of all SAS programs and outputs.