Statistical Analysis Plan

Sponsor: Resolve Therapeutics, Inc.

Protocol Number: 132-03

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Protocol Title: A Phase 2a, Double Blind, Placebo Controlled Study of RSLV-132 in Subjects with Systemic Lupus Erythematosus (SLE)

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TABLE OF CONTENTS

1. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

ADA	Anti-drug antibodies
AE	Adverse event
ATC	Anatomical Therapeutic Chemical Classification
BILAG	British Isles Lupus Activity Group
bpm	Beats per minute
°C	Celsius
CLASI	Cutaneous Lupus Erythematosus Disease Area and Severity Index
CRF	Case report form
CRO	Contract Research Organization
CSR	Clinical study report
DBP	Diastolic blood pressure
eCRF	Electronic case report form
°F	Fahrenheit
FACIT	Functional Assessment of Chronic Illness Therapy
FAS	Full analysis set
HIV	Human immunodeficiency virus
IR	Incidence rate of the adverse event
ITT	Intent-to-Treat analysis set
IV	Intravenous
IWRS	Interactive Web Response System
LOCF	Last observation carried forward
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mg/kg	Milligram per kilogram
mm	Millimeter
mm Hg	Millimeter of mercury
OCS	Oral Corticosteroids

PGA	Physician's global assessment
PK	Pharmacokinetic
PT	Preferred term
RNA	Ribonucleic acid
RR	Respiratory rate
SAE	Serious adverse event
SAP	Statistical analysis plan
SAS	Safety analysis set
SBP	Systolic blood pressure
SD	Standard deviation
SELENA	Safety of estrogens in lupus erythematosus national assessment
SLE	Systemic lupus erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index SELENA Modification
SOC	System organ class
TEAE	Treatment Emergent Adverse Event
WHO	World Health Organization

2. INTRODUCTION

This document presents the statistical analysis plan (SAP) for Resolve Therapeutics, Inc. based on protocol 132-03: A Phase 2a, Double Blind, Placebo Controlled Study of RSLV-132 in Subjects with Systemic Lupus Erythematosus. The analyses described in this document will be performed for the final clinical study report (CSR). Any deviations from the statistical analysis plan will be described and a justification given in the final CSR.

All analyses will be conducted using SAS version 9.3 or higher.

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective of the study is:

- to assess the impact of 13 intravenous (IV) infusions of RSLV-132 on cutaneous lupus disease activity using the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score comparing Baseline with Day 85 and Day 169 among the drug-treated and placebo groups.

2.1.2. Secondary Objectives

The secondary objectives of the study are:

At Days 85 and 169:

- to assess disease activity using Systemic Lupus Erythematosus Disease Activity Index SELENA (safety of estrogens in lupus erythematosus national assessment) Modification (SLEDAI-2K), British Isles Lupus Activity Group (BILAG-2004) and physician's global assessment (PGA);
- to evaluate the immunogenicity of RSLV-132 in subjects with systemic lupus erythematosus;
- to assess improvement in tender or swollen joint count;
- to assess improvement in patient reported outcomes using the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale;
- to assess the proportion of subjects achieving a 50% improvement in CLASI activity score.

At Day 169:

- to assess the ability of subjects to reduce oral steroids at Day 169 relative to Day 85;
- to evaluate the safety and tolerability of 22 weeks of RSLV-132 exposure.

2.1.3. Exploratory Measures

The exploratory measures of the study are:

- to evaluate the impact of RSLV-132 treatment on gene expression profile;
- to evaluate the impact of RSLV-132 treatment on autoantibody and complement profiles;
- to evaluate the impact of RSLV-132 on serum protein levels;
- to assess the impact of RSLV-132 on the CLASI damage score.

2.2. Endpoints

2.2.1. Efficacy Endpoints

2.2.1.1. Primary Efficacy Endpoints

- Compare the treatment group difference in the mean improvement from Baseline to Day 85 in CLASI Activity scores of those in the efficacy analysis set receiving RSLV-132 and those receiving placebo.
- Compare the treatment group difference in the mean improvement from Baseline to Day 169 in CLASI Activity scores of those in the efficacy analysis set receiving RSLV-132 and those receiving placebo.

2.2.1.2. Secondary Efficacy Endpoints

Compare the treatment group difference on the following endpoints:

- Improvements (from baseline to Day 85 and Day 169) in the SLEDAI-2K, BILAG-2004, and PGA scores
- Improvement (from Baseline to Day 85 and Day 169) in the FACIT-Fatigue scale
- Improvements (from Baseline to Day 85 and Day 169) in tender or swollen joint count
- Reduction in oral steroids at day 169 relative to Day 85

- The proportion of subjects achieving a 50% improvement in CLASI Activity score

2.2.1.3. Exploratory Efficacy Measures

- Evaluate the differences on the gene expression profiles between the two treatment groups
- Evaluate the difference on the autoantibody and complement profiles between the two treatment groups
- Evaluate the difference on the serum protein levels between the two treatment groups
- Compare the mean improvement (from Baseline to Day 85; or Baseline to Day 169) in CLASI damage scores of those randomized to be treated with RSLV-132 and those randomized to receive placebo.

2.2.2. Safety Measures

- Reported adverse events
- Changes in laboratory values and vital signs from baseline
- Evaluate the immunogenicity of RSLV-132 as measured by the presence of RSLV-132 antibodies

2.3. Study Design

2.3.1. Study Population

This is a Phase 2a, multi-center, double-blind, placebo-controlled study to evaluate the impact of 13 intravenous infusions of RSLV-132 in subjects with Systemic Lupus Erythematosus. The study population will be 18 to 70 years male or female with SLE, including cutaneous manifestations of SLE and a CLASI score of ≥10 at Screening, and elevated levels of any one of the Ro-52/60, La, Sm, SmRNP, U1 RNP A/68 autoantibodies at Screening (local or central laboratory).

Approximately 50 subjects will be enrolled at approximately 15-20 clinical centers in the United States. Study subjects who are eligible for enrollment and have provided written informed consent will be randomized 2:1 (Active:Placebo) to receive 13 infusions of 10 milligram per kilogram (mg/kg) of RSLV-132 or Placebo.

2.3.2. Treatment Groups and Dosing

Following Baseline evaluations on Day 1, randomized subjects will receive their first infusion of RSLV-132 or Placebo. RSLV-132 or Placebo will be administered intravenously at 10 mg/kg at baseline, then weekly for two weeks and then once every 2 weeks for the next 20 weeks (13 administrations) to subjects with SLE.

RSLV-132 shall be prepared for each subject from individual stock vials provided by Sponsor. Details of dilution, dose preparation, and administration instructions will be provided in the Study Drug Reference Manual. The dose for each individual shall be based on the subject's baseline body weight.

2.3.3. Study Visits and Assessments

Potential subjects will be screened to assess their eligibility to enter the study within 28 days prior to study entry (i.e., prior to Baseline visit). Following Baseline evaluations on Day 1, randomized subjects will receive their first intravenous infusion of RSLV-132 or Placebo. Subjects will return to the research unit for additional visits as described in Table 1 Study Procedures.

Subject participation duration: 28 days of screening followed by 22 weeks of treatment and 8 weeks of follow up (approximately 34 weeks total). The duration of the study from Baseline visit to End of Study visit, excluding the screening period is approximately 30 weeks for each subject. Study assessments are outlined in Table 1.

Table 1: Study Procedures

Study Procedures	Screen (-28 to -1)	Baseline Day 1	Day 8	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85	Day 99	Day 113	Day 127	Day 141	Day 155	Day 169 (EOT)	Day 215 (EOS)
Acceptable Visit Window (days)			±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±5	±5
Informed Consent	X															
Inclusion/exclusion	X	X[a]														
Demographics	X															
Weight, height	X															
Hepatitis, HIV tests	X															
Physical exam	X	X[b]			X[b]		X[b]		X[b]		X[b]		X[b]		X[b]	X[b]
Pregnancy tests	X[c]	X[d]														X[c]
AE assessment		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Medical/medication history	X	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chem-20, CBC, UA	X	X			X		X		X		X		X		X	X

Study Procedures	Screen (-28 to -1)	Baseline Day 1	Day 8	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85	Day 99	Day 113	Day 127	Day 141	Day 155	Day 169 (EOT)	Day 215 (EOS)
Acceptable Visit Window (days)			±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±5	±5
SLEDAI, BILAG, PGA, joint count		X			X		X		X		X		X		X	
CLASI	X	X			X		X		X	X	X	X	X	X	X	
Photographs of cutaneous disease	X	X							X						X	
FACIT index		X							X						X	
Serum for study drug concentration		X			X				X						X	X
Serum for protein analysis		X							X						X	
Serum for RNase activity		X			X				X						X	X
Whole blood for gene expression		X			X				X						X	X
Serum for autoantibody, C3, C4 profile	X	X			X		X		X		X		X		X	

Study Procedures	Screen (-28 to -1)	Baseline Day 1	Day 8	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85	Day 99	Day 113	Day 127	Day 141	Day 155	Day 169 (EOT)	Day 215 (EOS)
Acceptable Visit Window (days)			±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±5	±5
Serum for ADA		X		X	X				X							X
Study Drug administration		X[f]	X	X[f]	X[f]	X[f]	X[f]	X[f]	X[f]	X[f]	X[f]	X[f]	X[f]	X[f]		

[a] CLASI activity and damage score and confirm no changes in SLE medications only

[b] directed physical exam

[c] serum pregnancy test for women of childbearing potential (6.5)

[d] urine pregnancy test for women of childbearing potential (6.5)

[e] interim medical/medication history only

[f] RSLV-132 or placebo shall be administered according to the infusion rate and time set forth in the Study Drug Reference Manual

2.3.4. Concomitant Medications

Subjects entering the study who had no changes to their SLE medications in the previous 30 days prior to the Baseline visit shall remain on the background medications at the same doses throughout the study. With the exception of decreases in Oral Corticosteroids (OCS), no changes in lupus medications shall be permitted during the study, including the addition of topical steroids or topical tacrolimus, except for the rescue of a lupus flare.

2.3.4.1. Steroid Tapering

One of the objectives of the study is to evaluate the potential steroid sparing effects of RSLV-132. Steroid doses should remain stable through Day 85. Therefore, Investigators shall decrease the use of oral corticosteroids beginning on Day 85 using the guidance below. No further steroid decreases should occur from Day 141 through Day 169.

- Subjects receiving >7.5 milligram (mg) of prednisone or equivalent daily AND demonstrating a clinical improvement in the cutaneous manifestations of lupus as measured by a decrease in the CLASI activity by 50% compared with Baseline shall decrease oral corticosteroids as follows:
    - Decrease prednisone (or equivalent) by 2.5 mg/day
    - If the prednisone dose (or equivalent) remains greater than 7.5 mg/day AND cutaneous disease activity remains improved (CLASI activity score decreased by 50% compared with baseline) AND prednisone has been stable for 2 weeks, reduce prednisone by an additional 2.5 mg; repeat after 2 more weeks.
    - If prednisone reduced to 7.5 mg, see below,
    - If after a decrease in prednisone, the CLASI is no longer decreased (compared to baseline) by 50%, the investigator may increase the prednisone to the previous daily dose (not to exceed the baseline dose)
- Subjects receiving ≤7.5 mg/of prednisone or equivalent daily AND demonstrating clinical improvement in the cutaneous manifestations of lupus as measured by a decrease in the CLASI activity score by 50% compared with baseline, the investigator may, at his/her discretion, decrease prednisone by no greater than 2.5 mg/day every other week.

2.3.4.2. Treatment of Flares

Investigators should treat lupus flares as they deem appropriate with the minimum amount of corticosteroid necessary and should return the subject to baseline steroid dose as quickly as medically reasonable. Should a subject require more than steroids for a lupus flare, investigators should treat as necessary and notify the medical monitor.

2.3.5. Subject Withdrawal

Subjects will be informed that they are free to withdraw from the study at any time and for any reason. The Investigator may remove a subject from investigational treatment if, in the Investigator's opinion, it is not in the best interest of the subject to continue. Notification of discontinuation of investigational treatment will be made immediately to the Sponsor. In case of premature discontinuation of investigational treatment, efforts will be made to perform all End of Treatment (EOT) assessments and an End of Study (EOS) visit outlined in SAP Section 2.3.3 Table 1.

If a subject wishes to withdraw from the study, the site staff should confirm whether the subject is agreeable to continue the assessments without the investigational treatment or if they wish no further involvement in the study. In the latter case no further study-related evaluations will be performed and no additional data will be collected.

The date and the reason for discontinuation of investigational treatment or withdrawal from the study will be recorded on the subject's Case Report Form (CRF). Subjects that withdraw after receiving study drug will not be replaced.

2.3.6. Randomization and Blinding

This will be a double-blind, placebo-controlled study. As such, except for the specifically designated unblinded study site pharmacist, the investigator, sponsor, and remaining study site clinical staff will be blinded as to treatment. Ongoing drug accountability will be monitored by an unblinded monitor.

A randomization code will be computer-generated by a contract research organization (CRO) Axio Research LLC. Subjects meeting the study entry criteria will be randomized via an interactive web response system (IWRS). Subjects will be randomized in a 2:1 ratio to either RSLV-132 or Placebo. The randomization schedule will be generated by the randomization statistician at Axio Research (who is not on the project team) or designee and maintained in a secure and limited-access location separate from the study investigator and members of the project team. The study subject, investigative staff, the Sponsor, the Sponsor study team (includes contractors and vendors), excluding the unblinded study site pharmacist and unblinded monitor mentioned above, will be blinded to treatment assignments during the study.

Except in a medical emergency, the investigator or designee and blinded study site clinical staff will remain blinded during the conduct of the study and until database lock.

If any other unblinding event occurs in addition to the ones mentioned above, it will be documented in a separate document other than this SAP.

2.3.7. Sample Size and Power

The sample size of approximately 50 subjects chosen for this study was based upon precedent set by other studies of similar nature and was not based on power calculations. Therefore no formal hypothesis testing will be performed.

P-values obtained from the analyses, if they are generated, will be used for obtaining information only and will be evaluated at the two-sided alpha level of 0.05.

3. GENERAL CONSIDERATION FOR DATA ANALYSES

3.1. Analysis Sets

3.1.1. Intent-to-Treat Analysis Set

The Intent-to-Treat (ITT) Analysis Set is defined as all subjects who were randomized, regardless of whether the subject actually received any study drug (RSLV-132 or Placebo). The subject will be included in the treatment group to which they were randomized.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) is a modified ITT and is defined as all subjects randomized who received at least one dose of study drug (RSLV-132 or Placebo). The subject will be included in the treatment group to which they were randomized. The Full Analysis Set is equivalent to the Efficacy Analysis Set defined in the study protocol and can be used interchangeably. For the purpose of generating the summary tables and by subject listings under the description of this SAP, the term of Full Analysis Set will be used.

3.1.3. Safety Analysis Set

The Safety Analysis Set (SAS) is defined as all subjects who received any treatment with either RSLV-132 or placebo.

Randomized subjects that receive the incorrect therapy from that intended will be summarized in the group according to the therapy actually received. Subjects who are not randomized but who receive treatment or placebo will also be included and summarized according to the therapy actually received. In the unlikely event of a subject commencing one study therapy and crossing over to the other, the data for that subject will be included in summaries and analyses with the original group.

3.2. Statistical Analysis Issues

3.2.1. Strata and Covariates

There is no stratification and covariate analysis planned for this study. However, if there is any stratification and covariate analysis performed in an ad hoc exploratory nature, it will be noted in the final CSR.

3.2.2. Examination of Subject Subsets

There is no subgroup analysis planned for this study. However, if there is any subgroup analysis performed in an ad hoc exploratory nature, it will be noted in the final CSR.

3.2.3. Multiple Comparisons

No formal hypothesis testing and no multiple comparisons will be conducted for this study.

3.2.4. Multi-center Studies

The study will be conducted from approximately 15-20 centers in the United States. Randomization to the treatment groups will not be stratified by study site due to small sample size. Subjects from all centers will be pooled for summaries.

3.2.5. Missing Data and Outliers

Every attempt will be made to capture all study data. For subjects whose visit value is missing, the last observation will be carried forward (LOCF) for the efficacy analyses. Any missing, unused, or spurious data will be noted in the final CSR.

3.2.6. Data Conventions and Transformations

Laboratory numeric data may be recorded with a '<' or '>' sign (i.e. < 0.1 or > 0.1). In order to summarize the data, the original value will be converted to 0.09 in the case of < 0.1 and to 0.11 in the case of > 0.1. The same principle will be used if the data has additional extended significant digits. The actual values will be presented in the data listings.

3.2.7. Study Baseline and Study Day

Baseline is defined as the last assessment prior to the first dose of study drug (RSLV-132 or Placebo) at Day 1. Measurements that are obtained after the first dose of study drug will be considered post-baseline values. Change from baseline is defined as post-baseline assessment minus baseline assessment.

Study day for events on or after the date of the first dose will be defined as the number of days from the date of the first dose of study drug, plus 1 day, so that the date of the first dose will be defined as Day 1. For events before the date of the first dose, study day will be calculated as the difference in days between the date of the first dose and the date of interest. Thus, the day before the date of the first dose will be defined as Day -1.

3.2.8. Visit Windows

The case report form nominal visits and visit windows will be used in the summaries. In general, unscheduled visits will not be summarized unless otherwise noted.

4. INTERIM ANALYSIS AND DATA MONITORING COMMITTEE

There is no interim analysis and data monitoring committee planned for this study.

5. GENERAL ANALYSIS METHODS

Continuous variables will be summarized using descriptive statistics including number of subjects (n), mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized using frequencies and percentages. Percentages will be calculated using the total number of subjects in each treatment group for each applicable population and/or subpopulation, unless otherwise noted.

Number of subjects, minimums, and maximums will be calculated to the same number of decimal places as the source data. Means, standard deviations and quartiles will be calculated to one more decimal place than the source data. Percentages will be calculated to one decimal place. Zero count cells will be displayed as "0" with percentage of (0%). Unless otherwise noted, summaries will be performed by the treatment group (Placebo and RSLV-132 10 mg/kg).

If statistical tests are performed, the tests will be done at the two-sided, 5% significance level to compare Placebo vs. RSLV-132 10 mg/kg, unless otherwise specified. The point estimate and 95% confidence interval (CI) for the treatment differences may be displayed along with the p-value for the treatment comparison. P-values will be presented to three decimal places. P-values < 0.0005 will be presented as < 0.001. P-values greater than 0.999 will be presented as > 0.999.

In the absence of any predefined hypotheses in this study, the general strategy of the analysis will be to examine the data summaries for any trends amongst the treatment groups. No formal hypothesis testing will be carried out. P-values obtained from statistical testing of the analyses will be used for descriptive purposes only.

All data collected in the clinical database will be included in the data listings, as appropriate. Subjects who were randomized and never treated will be accounted for in the data listings.

6. SUBJECT DISPOSITION

6.1. Enrollment and Disposition of Subjects

Subjects' enrollment and disposition will be summarized by treatment group on two different analysis sets. The reasons for discontinuation will be listed in the order as they appear on the electronic case report form (eCRF).

Summary based on the ITT analysis set will include all randomized subjects and will be summarize for the following. The percentages will be calculated based on the number of subjects randomized in each of the treatment group.

- Number and percentage of subjects randomized
- Number and percentage of subjects randomized and discontinued prior to treatment
- The reason for discontinuation prior to treatment

Summary based on the FAS will include all randomized and treated subjects and will be summarize for the following. The percentages will be calculated based on the number of subjects randomized and treated in each of the treatment group.

- Number and percentage of subjects randomized and treated (Placebo or RSLV-132 10 mg/kg)
- Number and percentage of subjects randomized and treated who completed the study
- Number and percentage of subjects randomized and treated who discontinued from the study
- The reasons for study discontinuation
- Number and percentage of randomized and treated subjects included in each analysis set

6.2. Extent of Exposure

RSLV-132 or Placebo will be administered intravenously at 10 mg/kg at baseline, then weekly for two weeks and then once every 2 weeks for the next 20 weeks (13 administrations) to subjects with SLE.

Total duration of study drug dosing (Days), total number of infusions, total duration of infusion (Hours), total volume infused (mL) and total duration of study drug exposure will be summarized by treatment group on SAS. The number and percentage subjects with overall

infusion status (completed, interrupted or terminated) during the treatment period and the reason for interrupted or terminated will be summarized by treatment group on SAS. The percentages will be calculated based on the number of subjects in each treatment group of the SAS.

Total duration of study drug dosing will be calculated as the total number of days from the first dose date to the last dose date plus 1 regardless of temporarily dose interruptions. Total number of infusions will be calculated as the sum from each infusion segment (if the infusion was interrupted and then started again). Total duration of infusion in hours will be calculated as the total minutes from each infusion segment (if the infusion was interrupted and then started again) start time to end time.

Overall infusion completed is defined as a subject without any infusion interruptions or terminations during the study.

Total duration of study drug exposure (Days) is defined as the sum of (study Day 1 to the last visit date plus 1).

6.3. Protocol Deviations

Deviations from the protocol will be documented on an ongoing basis on the protocol deviations eCRF throughout the study. Major protocol deviations will be determined prior to the database lock. The number and percentage of subjects within each major deviation category will be summarized by treatment group on the FAS. The percentages will be calculated based on the number of subjects in each treatment group of the FAS. The deviations collected on the eCRF will be listed.

Inclusion and exclusion criteria data will be listed for all subjects.

7. BASELINE DATA

7.1. Demographic and Baseline Characteristics

Demographic (age [years], gender, race, ethnicity, height [cm], weight [kg], BMI [kg/m^2]) and baseline characteristics (CLASI activity score, Number and percentage subjects with oral corticosteroids dose [Overall mean, 0 mg/day, >0 and ≤7.5 mg/day, >7.5 mg/day]) will be summarized descriptively by treatment group on the FAS. For categorical parameters, the percentages will be calculated based on the number of subjects in each treatment group of the FAS.

7.2. Medical History

Number and percentage of subjects with medical history body systems will be summarized by treatment group for the FAS.

A subject with multiple occurrence of the same body system will be counted only once. Medical history body systems will be sorted alphabetically. The percentages will be calculated based on the number of subjects in each treatment group of the FAS.

8. PRIOR AND CONCOMITANT MEDICATIONS

8.1. Medications

Prior and concomitant medications will be coded using the World Health Organization (WHO) drug dictionary for anatomical therapeutic chemical classification (ATC) and preferred drug name. The most current version of dictionary available will be used for the coding. Number and percentage of subjects with each of the coded medications will be summarized by treatment group on the FAS. A subject who used multiple medications will be counted only once for each ATC and preferred drug name. ATC and preferred drug name within each ATC will be sorted alphabetically. The percentages will be calculated based on the number of subjects in each treatment group of the FAS. Prior and concomitant medications will be summarized separately. No inferential statistics will be performed.

Prior medications are defined as any medications that started and stopped prior to the date of first dose of study drug (RSLV-132 or Placebo). Concomitant medications are defined as any medications that started or were ongoing at or after the date of first dose of study drug (RSLV-132 or Placebo). Where a medication recorded with a partially or fully missing start/stop date or time, and it is unclear as to whether the medication is concomitant, it will be assumed that it is concomitant.

9. EFFICACY ANALYSES

Efficacy analyses include assessing improvement in disease activity using CLASI, SLEDAI-2K, BILAG-2004, PGA, and FACIT-Fatigue scores; tender or swollen joint count; oral steroids use; as well as evaluating the autoantibody and complement profiles.

Each assessment will be summarized descriptively by treatment group on the FAS for all study visits at which the data were collected. No statistical testing will be performed, unless otherwise specified.

All data will be listed.

9.1. Analysis of Primary Efficacy Endpoints

The primary efficacy endpoints are the improvements from Baseline (Day 1) to Day 85 and Baseline to Day 169 CLASI Activity scores.

CLASI Activity assessment will be performed for each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. The assessment includes each anatomical location. The total score of the Activity subsection (defined as the sum of the scores from each anatomical location) will be used in the summary. The improvements from Baseline (Day 1) to Day 85 and from Baseline (Day 1) to Day 169 in the total activity score will be evaluated as part of the primary efficacy endpoints. Lower score represents less disease activity.

Summary of observed values: Observed values of total Activity score and the change and percent change from baseline at each scheduled visit will be summarized. In addition to the LOCF imputation described below, the primary endpoints (change from Baseline on observed values) will be analyzed using Mixed effect Model Repeat Measurement (MMRM) method. The MMRM model will include the fixed categorical effects of treatment, random effect visit, and treatment-by-visit interaction, as well as continuous fixed covariates of baseline score and baseline score-by-visit interaction. An unstructured covariance structure of random effect will be used for modeling the within-subject errors.

Summary of imputed values: LOCF imputed values and the change and percent change from Baseline (Day 1) in the CLASI Activity total score at Days 85 and 169 and at each scheduled visit will also be analyzed. The two-sample t-test will be used for the treatment group comparison on the change from Baseline.

Summary of non-censored values: Non-censored values and LOCF imputed non-censored values as well as the change and percent change from Baseline (Day 1) in the CLASI Activity total score at Days 85 and 169 and at each scheduled visit will also be analyzed. The two-sample t-test will be used for the treatment group comparison on the change from Baseline. The following values will be censored based on blinded review before database lock:

a. Values obtained within 60 days of a steroid (systemic/oral/topical but not ophthalmic or inhaled) dose that is increased above baseline for more than one day
b. Addition of other systemic agents for lupus (such as antimalarials, methotrexate, rituximab, dapsone)

9.2. Analysis of Secondary Efficacy Endpoints

The secondary efficacy endpoints are including the following:

- Improvements (from baseline to Day 85 and Day 169) in the SLEDAI-2K, BILAG-2004, PGA, and FACIT-Fatigue scores
- Improvements in tender or swollen joint count (from baseline to Day 85 and Day 169)
- Reduction in oral steroids at Day 169 relative to Day 85
- The proportion of subjects achieving a 50% improvement in CLASI Activity score (from baseline to Day 85 and Day 169)

9.2.1. SLEDAI-2K

Systemic Lupus Erythematosus Disease Activity Index SELENA Modification will be performed for each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. The total score (defined as the sum of weights next to descriptors marked present) will be summarized. The improvements from Baseline (Day 1) to Day 85 and from Baseline (Day 1) to Day 169 in SLEDAI-2K total scores will be evaluated as part of the secondary efficacy endpoints. Lower score represents less disease activity.

Summary of observed values: Observed values of total score and the change from baseline at each scheduled visit will be summarized. In addition to the LOCF imputation described below, the change from Baseline on observed values will be analyzed using Mixed effect Model Repeat Measurement (MMRM) method as described in the SAP Section 9.1.

Summary of imputed values: Imputed values and the change from Baseline (Day 1) in the SLEDAI-2K total score at each scheduled visit will also be analyzed. The two-sample t-test will be used for the treatment group comparison on the change from Baseline. LOCF will be used to impute missing values on the FAS.

9.2.2. BILAG-2004

BILAG-2004 Index Assessment will be performed for each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. The assessment includes subsections of Constitutional, Mucocutaneous, Neuropsychiatry, Musculoskeletal, Cardiorespiratory, Gastrointestinal, Ophthalmic, Renal and Hematological. Each subsection will be scored with Category of Zero or Non-Zero for analysis. Any category checked other than "Not Present" or "Not Done" will be treated as the Non-Zero category except for the Renal and Hematology panels. The category of Zero or Non-Zero will be presented in the summary. The improvements from Baseline (Day 1) to Day 85 and from Baseline (Day 1) to Day 169 in BILAG-2004 Index Assessment category of Zero or Non-Zero will be evaluated as part of the

secondary efficacy endpoints. Zero category represents no disease activity present for the body system. The detailed specifications of Zero or Non-Zero category rules for the Renal and Hematology panels will be stated in the analysis dataset specification document rather than in this SAP".

Summary of observed values: Observed values of the Zero and Non-Zero categories and the change from baseline at each scheduled visit (indicated by a shift from the baseline category) will be summarized for each subsection. The percentages will be calculated based on the actual number of subjects at each visit in each treatment group of the FAS. No statistical testing will be performed.

Summary of imputed values: Imputed values of the Zero and Non-Zero categories and the change from Baseline (Day 1) for the BILAG-2004 Index Assessment at each scheduled visit (indicated by a shift from the baseline category) will be summarized for each subsection. LOCF will be used to impute missing values on the FAS. No statistical testing will be performed.

9.2.3. PGA

Physicians Global Assessment will be performed for each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. The assessment is measured on a 0 to 100 Millimeter (mm) scale with score 0 to be No Disease Activity and score 100 to be the most Severe Disease Activity. The improvements from Baseline (Day 1) to Day 85 and from Baseline (Day 1) to Day 169 in PGA scores will be evaluated as part of the secondary efficacy endpoints.

Summary of observed values: Observed values and the change from baseline at each scheduled visit will be summarized. In addition to the LOCF imputation described below, the change from Baseline will be analyzed using Mixed effect Model Repeat Measurement (MMRM) method as described in the SAP Section 9.1.

Summary of imputed values: Imputed values and the change from Baseline (Day 1) in the PGA score at each scheduled visit will also be analyzed. The two-sample t-test will be used for the treatment group comparison on the change from Baseline. LOCF will be used to impute missing values on the FAS.

9.2.4. FACIT-Fatigue Scale

FACIT-Fatigue Scale assessment is a subject reported outcome. It will be performed by each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. The improvements from Baseline (Day 1) to Day 85 and from Baseline (Day 1) to Day 169 in

FACIT-Fatigue assessment total scores will be evaluated as part of the secondary efficacy endpoints.

FACIT-Fatigue assessment has 13 questions and is measured with scores of 0 (Not at all), 1 (A little bit), 2 (Somewhat), 3 (Quite a bit) or 4 (Very much). All FACIT-Fatigue scales are scored so that a higher score is better. As each of the 13 items of the FACIT-Fatigue scale ranges from 0-4, the range of possible scores is 0-52, with 0 being the worst possible score and 52 the best. To obtain the 0-52 score, each negatively-worded item response is recoded so that 0 is a bad response and 4 is good response. All responses are added with equal weight to obtain the total score. In cases where some answers may be missing, a total score is prorated from the scores of answered items, as long as more than 50% of the items (i.e., at least 7 of 13) were answered.

If there are missing items, subscale scores can be prorated. This is done by multiplying the sum of the subscale by the number of items in the subscale, then dividing by the number of items actually answered. This can be done by using the formula below:

Prorated subscale score = [Sum of item scores] x [N of items in subscale] / [N of items answered]

A computer program written in SAS for the FACIT-Fatigue Scale scoring is available in Appendix I of the SAP.

Summary of observed values: Observed values of total score and the change from baseline at each scheduled visit will be summarized. In addition to the LOCF imputation described below, the change from Baseline on observed values will be analyzed using Mixed effect Model Repeat Measurement (MMRM) method as described in the SAP Section 9.1.

Summary of imputed values: Imputed values and the change from Baseline (Day 1) in the FACIT-Fatigue Scale total score at each scheduled visit will also be analyzed. The two-sample t-test will be used for the treatment group comparison on the change from Baseline. LOCF will be used to impute missing values on the FAS.

Summary of non-censored values: Non-censored values and LOCF imputed non-censored values as well as the change and percent change from Baseline (Day 1) in the FACIT-Fatigue Scale total score at Days 85 and 169 and at each scheduled visit will also be analyzed. The two-sample t-test will be used for the treatment group comparison on the change from Baseline. The following values will be censored based on blinded review before database lock:

a. Values obtained within 60 days of a steroid (systemic/oral/topical but not ophthalmic or inhaled) dose that is increased above baseline for more than one day

b. Addition of other systemic agents for lupus (such as antimalarials, methotrexate, rituximab, dapsone)

9.2.5. Tender and Swollen Joint Count

Tender and swollen joint count assessment will be performed for each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. Tender and swollen joint count assessment includes total of 28 joints (left and right metacarpalphalangeal joints and proximal interphylangeal joints, wrist, elbow, shoulder and knee). The total Tender and Swollen Joint Count will be summarized. The improvements from Baseline (Day 1) to Day 85 and from Baseline (Day 1) to Day 169 in tender and swollen total joint count will be evaluated as part of the secondary efficacy endpoints. Lower joint count represents less disease activity.

Summary of observed values: Observed values of total tender and swollen joint count and the change from baseline at each scheduled visit will be summarized. In addition to the LOCF imputation described below, the change from Baseline on observed values will be analyzed using Mixed effect Model Repeat Measurement (MMRM) method as described in the SAP Section 9.1.

Summary of imputed values: Imputed values and the change from Baseline (Day 1) in the tender and swollen total joint count at each scheduled visit will also be analyzed. The two-sample t-test will be used for the treatment group comparison on the change from Baseline. LOCF will be used to impute missing values on the FAS.

9.2.6. Oral Steroids Tapering

One of the objectives of the study is to evaluate the steroid sparing effects of RSLV-132. The Investigators shall decrease the use of oral corticosteroids beginning on Day 85 using the guidance stated under SAP Section 2.3.4.1. No further steroid decreases should occur from Day 141 through Day 169. The reduction in oral steroids at Day 169 relative to Day 85 will be evaluated as part of the secondary efficacy endpoints.

Summary of observed values: (1) For those who were on any oral corticosteroids at Day 85, observed of corticosteroids dose values and the change from Day 85 at Day 169 will be summarized. (2) For those who were on any oral corticosteroids with >7.5 mg/day at Day 85, observed of corticosteroids dose values and the change from Day 85 at Day 169 will be summarized.

The summary of (1) or (2) will only be performed if there are 25% or more of the subjects in the RSLV-132 group were on any oral corticosteroids at Day 85 or were on any oral corticosteroids with >7.5 mg/day at Day 85 respectively. No statistical testing will be performed.

Dose equivalence to Prednisone:

Medication	Dose Equivalence to 10 mg	Dose Equivalence to 7.5 mg
Oral Prednisone	10 mg	7.5 mg
Cortisone	50 mg	37.5 mg
Hydrocortisone	40 mg	30 mg
Methylprednisolone	8 mg	6 mg
Prednisolone	10 mg	7.5 mg
Betamethasone	1.2 mg	0.9 mg
Dexamethasone	1.5 mg	1.125 mg
Budesonide	2.25 mg	1.6875 mg
Deflazacort	12 mg	9 mg

9.2.7. CLASI Activity Score Improvement

CLASI Activity assessment will be performed for each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. The assessment includes each anatomical location. Proportion of subjects achieving a 50% improvement (decrease) in CLASI total Activity score (defined as the sum of the scores from each anatomical location) will be evaluated as part of the secondary efficacy endpoints.

Summary of observed values: The number and percentage of subjects achieving a 50% improvement in CLASI Activity subsection score from baseline at each scheduled visit will be summarized. The percentages will be calculated based on the actual number of subjects at each visit in each treatment group of the FAS. No statistical testing will be performed.

Summary of imputed values: The number and percentage of subjects achieving a 50% improvement in CLASI Activity subsection score from baseline at each scheduled visit will also be analyzed on the imputed values. Fisher's exact test will be used for the treatment group comparison. LOCF will be used to impute missing values on the FAS.

Summary of non-censored values: Non-censored values and LOCF imputed non-censored values will be used to summarize the number and percentage of subjects achieving a 50% improvement in CLASI Activity subsection score from baseline at each scheduled visit. Fisher's exact test will be used for the treatment group comparisons. The following values will be censored based on blinded review before database lock:

a. Values obtained within 60 days of a steroid (systemic/oral/topical but not ophthalmic or inhaled) dose that is increased above baseline for more than one day
b. Addition of other systemic agents for lupus (such as antimalarials, methotrexate, rituximab, dapsone)

9.3. Exploratory Efficacy Analysis

The exploratory efficacy analysis are to evaluate the changes from Baseline (Day 1) as compared to Placebo on the following measurements:

- Evaluate the difference on the autoantibody and complement profiles between the two treatment groups
- Evaluate the differences on the gene expression profiles and the serum protein levels between the two treatment groups.
- Compare the mean improvement (from Baseline to Day 85; or Baseline to Day 169 in CLASI damage scores of those randomized to be treated with RSLV-132 and those randomized to receive placebo.

9.3.1. Autoantibody and Complement Profiles

Serum samples will be analyzed by either a local or central laboratory using validated methods. The analysis will provide values for the following autoantibodies and indicate if the result is positive, negative, or equivocal using the validated assay range for the testing laboratory: Ro-52/60, La, Sm, SmRNP, U1 RNP A/68, dsDNA. The summary of actual values of these tests will also be provided. Complement C3 and C4 values will also be summarized.

Summary of observed values: Observed values, change from baseline and a shift from baseline categories at each scheduled visit of autoantibody profile will be summarized. The percentages will be calculated based on the actual number of subjects at each visit in each treatment group of the FAS. No statistical testing will be performed.

9.3.2. Gene Expression Profiles

Ribonucleic acid (RNA) will be extracted from whole blood to measure the expression level of genes that are related to inflammatory pathways though to be involved in SLE. Samples will be obtained at selected visits during the study from Baseline to the End of Study visit. The analysis of gene expression profiles will be performed elsewhere and will not be a part of this SAP.

9.3.3. Serum Protein Levels

Serum samples will be obtained at various visits during the study to analyze the level of circulating serum proteins. The protein analysis will measure protein levels related to the inflammatory process. The analysis will be carried out using a multiplexed immunoassay. The analysis of serum protein levels will be performed elsewhere and will not be a part of this SAP.

9.3.4. CLASI Damage Score

CLASI Damage assessment will be performed for each subject at scheduled visits to determine the SLE disease activity for each subject at the visit. The assessment includes each anatomical location. The total score of the Damage subsection (defined as the sum of the scores from each anatomical location) will be used in the summary.

Summary of observed values: Observed values of total Damage score and the change from baseline at each scheduled visits will be summarized. No statistical testing will be performed.

10. SAFETY ANALYSES

The safety assessment of the treatment will be compared between the two groups by adverse events and laboratory results as well as any physical findings that have changed from baseline. The safety analysis will include adverse events, concomitant medications, laboratory data, vital signs and immunogenicity of RSLV-132.

All data will be summarized as observed and no data imputation will be performed.

10.1. Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA version 19.0 or higher) adverse event dictionary. If a subject experiences multiple events that map to a single preferred term, the greatest severity (by grade) and strongest investigator assessment of relationship to study drug will be reported for the applicable summaries.

Treatment-emergent adverse events (TEAE) are defined as events for which the date of onset is on or after the date of first dose of study drug (RSLV-132 or Placebo). Where an adverse event

(AE) collected after the date of first dose with a partially or fully missing start date or time, and it is unclear as to whether the AE is treatment emergent, it will be assumed that it is treatment emergent.

The number and percentage of subjects with adverse events will be summarized by treatment group. The percentages will be calculated based on the number of subjects in each treatment group of the SAS. System organ class (SOC) and preferred term (PT) within each SOC will be presented in descending frequency of RSLV-132 group. Subjects will be counted only once for each SOC and PT.

All adverse events (treatment-emergent and non-treatment-emergent) will be listed.

10.1.1. Overall Adverse Events

The number and percentage of subjects with at least one treatment-emergent adverse event will be summarized for the following:

- Subjects with any treatment-emergent adverse event
- Subjects with severe (Grade 3+) treatment-emergent adverse event
- Subjects with any study drug related treatment-emergent adverse event
- Any treatment-emergent adverse event leading to study drug discontinuation / study termination
- Subjects with any treatment-emergent serious adverse event
- Subjects with any study drug related treatment-emergent serious adverse event
- Subjects with outcome of death

10.1.2. Incidence of Adverse Events

Subjects with at least one treatment-emergent adverse event will be summarized by SOC, PT, and by treatment group. The incidence rate (IR) of the event per 100 patient years for each SOC and PT as well as the overall patient years of each treatment group will be calculated. IR of the event per 100 patient years will be calculated as (Total # of Events/Patient Year)*100]. Patient year will be calculated as the (Total study drug exposure / 365.25). Total study drug exposure will be defined as the sum of [(Last visit date – First dose date) + 1].

Treatment-emergent adverse event summary by PT with descending order of frequency in the RSLV-132 group will also be presented by treatment group.

10.1.3. Relationship of Adverse Event to Study Drug

Treatment-emergent adverse events with closest relationship to study drug according to the categories specified in the protocol (Not Related, Possibly Related and Definitely Related) will be summarized for related events by SOC, PT, and treatment group.

A study drug related AE is defined as any AE that is assessed by the investigator with the relationships of "Possibly Related" and "Definitely Related". Study drug non-related AE is defined as any AE that assessed by investigator with the relationships of "Not Related".

Any treatment-emergent AEs that have a missing relationship will be presented in the summary table as "Related" but will be presented in the data listing with a missing relationship.

10.1.4. Severity of Adverse Event

Treatment-emergent adverse events with maximum investigator-reported severity (Grade 1-Mild, Grade 2-Moderate, Grade 3-Severe, Grade 4-Life Threatening and Grade 5-Fatal) will be summarized by SOC, PT, and treatment group.

Any treatment-emergent AEs that have a missing severity will be presented in the summary table with Toxicity Grade 4 but will be presented in the data listing with a missing severity.

10.1.5. Serious Adverse Events

All treatment-emergent serious adverse events (SAEs) will be summarized by SOC, PT, and by treatment group.

A summary of study drug related treatment-emergent SAEs by SOC, PT, and treatment group will also be presented.

10.1.6. Adverse Events Leading to Hospitalization / Study Drug Discontinuation / Study Termination

All treatment-emergent adverse events that lead to either required or prolonged inpatient hospitalization or study drug discontinuation or study termination will be summarized by SOC, PT, and by treatment group.

10.2. Laboratory and Other Safety Assessments

Each assessment will be summarized descriptively by treatment groups on the SAS. For assessments not measured at Baseline (Day 1) pre-dose, Screening Visit value will be used as the baseline. No missing data imputation will be used.

All data will be listed.

10.2.1. Laboratory Blood and Urine Samples

Laboratory hematology, serum chemistry and urinalysis samples will be collected for each subject at scheduled visits for safety evaluations. The laboratory test parameters are listed in the Protocol Appendix B. The samples are analyzed by a central laboratory.

Observed values and the change from Baseline (Day 1) at each visit will be summarized for the continuous values. Number and percentage of subjects in each category will be summarized for the categorical values. In addition, the number and percentage of subjects who have the lab results that are noted to be "Clinically Significant" by the investigator will be summarized. The percentages will be calculated based on the actual number of subjects at each visit in each treatment group of the SAS. Grade 3 or higher lab toxicity (based on Rheumatology CTC Grade System) during the study will also be summarized.

Serum and urine pregnancy tests are for women of childbearing potential only. Serum pregnancy test will be performed at Screening Visit and Day 215 (EOS). The samples are analyzed by a central laboratory. The urine pregnancy test will be done at Baseline (Day 1) only and will be performed at each study site. Serum and urine pregnancy test data will be listed only.

10.2.2. Hepatitis and HIV Tests

Test for Hepatitis B, C and human immunodeficiency virus (HIV) viral load will be performed for each subject at Screening Visit. The results will be listed only.

10.2.3. Vital Signs

Vital signs will be evaluated for each subject at scheduled visits for systolic and diastolic blood pressure (SBP and DBP, mmHg), pulse rate (beats per minute [bpm]), respiratory rate (RR, breaths per minute [bpm]), and oral temperature (Fahrenheit °F).

Observed values and the change from Baseline (Day 1) at each visit will be summarized using descriptive statistics. Temperatures in Celsius (°C) will be reported for the summary. Fahrenheit to Celsius conversion °C = (°F - 32) x 5/9 will be used.

10.2.4. Physical Exam

Physical exam will be performed for each subject at scheduled visits. Number and percentage of subjects in each body site system of Normal/Abnormal (Non-Clinically Significant [NCS] or Clinically Significant [CS] determinate by the investigator) category will be summarized. The

percentages of Normal/Abnormal results will be calculated based on the actual number of subjects at each visit in each treatment group of the SAS.

Abnormality changes from Baseline (Day 1) in terms of NCS or CS at each post-baseline visit will be summarized in the categories of (New, Unchanged, Worsened, or Improved). New is defined as an abnormal result in the post-baseline visit compare to the normal result at baseline. Unchanged is defined as the same abnormal result in both the post-baseline visit and the baseline. Worsened is defined as an abnormal CS result in the post-baseline visit compare to the abnormal NCS result at baseline. Improved is defined as an abnormal NCS result in the post-baseline visit compare to the abnormal CS result at baseline or a normal result in the post-baseline visit compare to the abnormal (NCS or CS) result at baseline.

10.3. Immunogenicity Analyses

Serum will be analyzed for the presence of anti-RSLV 132 antibodies using a validated immunoassay. Each positive serum sample will be evaluated for anti-drug antibodies (ADA) specificity by repeating the immunoassay in the presence of an excess of RSLV-132. Confirmed positive, specific serum samples will be titered by serial dilution and a numerical titer will be assigned. The immunogenicity of RSLV-132 as measured by the presence of RSLV-132 antibodies will be evaluated as part of the safety endpoints.

The serum samples for evaluating ADA will be collected for each subject at scheduled visits. To assess immunogenicity, the number and percent of positive and negative results will be summarized descriptively by treatment groups on the SAS. The percentages will be calculated based on the number of subjects in each treatment group with samples available at each visit.

11. PHARMACOKINETIC ANALYSES

Pharmacokinetic (PK) parameters will be calculated for each subject, whenever possible, based on the serum concentrations of RSLV-132. RSLV-132 drug concentration levels will be summarized if it is available. The analysis of PK parameters will be performed elsewhere and will not be part of this SAP.

12. SAP REVISION

Revision Date	Section	Summary of Revision	Reason for Revision
July 6, 2017	2.3.3	Updated Table 1 Study Procedures.	Protocol Amendment 4.0
	2.3.5	Updated that efforts will be made to perform all EOT and EOS assessments outlined in Protocol Appendix A.	Protocol Amendment 5.0
	6.2	Clarify the summaries.	Per sponsor request.
	6.3	Clarify to summarize the major protocol deviations.	Per sponsor request.
	7.1	Added the overall mean for prednisone or equivalent dose.	Per sponsor request.
	7.2	Clarify to summarize the Medical History Body Systems	Per sponsor request.
	9	Remove text “RSLV-132 plasma levels and RNase activity” from Efficacy Analyses.	They are not part of the efficacy analyses.
	9.2.2	No statistical testing will be performed for the imputed values of BILAG-2004 Index Assessment.	Per sponsor request.
	9.2.6	Specify to summarize at Day 169 only.	Per sponsor request.
	9.2.7	Remove text “Fisher’s exact test will be used for the treatment group comparison” under the summary of observed values.	No treatment group comparison will be made on observed values.
	9.3.1	Adding dsDNA as part of the autoantibody profile.	Protocol Amendment 4.0
		Adding a summary for the actual values.	Per sponsor request.
	10.1.2	Adding patient year calculations for the adverse event summary	Per sponsor request.

	10.2.1	Adding grade 3 or higher toxicity summaries for the safety lab data.	Per sponsor request.
	10.2.4	Replace text “Appendix B” with “Appendix A”.	Correct protocol reference.
		Physical exam results will be listed only.	Per sponsor request.
March 10, 2020	3.2.7	Revise baseline definition to consider screening.	Internal document consistency.
	6.2	Removing “plus 1” in the Total duration of infusion (Hours) calculation.	Clarification.
	9.1, 9.2.1, 9.2.3, 9.2.4 and 9.2.5	Adding repeated measurement analysis in addition to the LOCF imputation.	A less biased method by missing data compare to LOCF.
	9.1, 9.2.4, 9.2.7	Add non-censored summaries.	Per sponsor request.
	9.2.6	Include table of Predinsone Equivalent dosing.	Facilitate grouping of corticosteroids.
	10.2.4	Adding Physical Exam summary by categories of Normal/Abnormal (CS/NCS).	To be compliant with FDA ICH E3 guideline and to be consistent with Resolve RSLV-132-04 study.
	11	PK not in scope of SAP.	

13. APPENDIX I: FACIT-FATIQUE SCALE SAS SCORING

```
*======================================================================== *
* FACIT-Fatigue subscale Version 4 Scoring Program (Unweighted)          *
* SAS codes written for all platforms (DOS, Windows, and UNIX)           *
* (c) Copyright, 1995-1998, Chih-Hung Chang & David Cella                *
* All rights reserved                                                    *
*                                                                        *
* Version 4                                                              *
*                                                                        *
* Permission is granted for use and non-profit distribution of these SAS *
* codes providing that all copyright notices remain intact. The right to *
* distribute any portion of this program for profit or as part of any    *
* commercial product is specifically reserved for the authors of that    *
* portion.                                                               *
*                                                                        *
* SAS Programmer: Jennifer Beaumont                                      *
*======================================================================== *

*======================================================================== *
* Note1: Data may be input via CARDS statement or from an external file  *
* with an INFILE statement                                               *
*======================================================================== *;

DATA fatigue;
 INPUT id_code $ hi7 hi12 an1-an5 an7 an8 an12 an14-an16;
 CARDS;
A 0 0 0 2 2 2 1 1 0 0 1 2 3
B 2 0 4 4 0 4 1 2 2 2 0 9 9
C 0 0 4 4 1 3 4 2 1 1 0 9 9
D 1 0 0 3 3 3 2 3 3 9 1 1 1
E 0 0 4 4 0 4 4 4 3 3 1 2 3
F 3 1 1 1 0 2 1 0 0 1 0 9 9
G 0 2 2 4 4 4 4 4 2 3 0 9 9
H 0 0 4 4 0 4 4 4 3 3 0 9 9
I 0 0 4 4 0 4 4 3 1 1 0 9 9
 ;

DATA SCORING;
 SET fatigue;

 ARRAY ITEM {13} hi7 hi12 an1-an5 an7 an8 an12 an14-an16;

 DO I=1 TO 13;
  IF ITEM(I)=8 OR ITEM(I)=9 THEN ITEM(I)=.;
 END;

*======================================================================== *
* SCORE REVERSALS FOR FACIT-Fatigue subscale.                            *
*======================================================================== *;

   HI7=4-HI7;
   HI12=4-HI12;
   AN1=4-AN1;
   AN2=4-AN2;
   AN3=4-AN3;
   AN4=4-AN4;
   AN8=4-AN8;
   AN12=4-AN12;
   AN14=4-AN14;
   AN15=4-AN15;
   AN16=4-AN16;
```

```
*=========================================================================== *
* NUMBERS OF ITEMS ANSWERED.                                                 *
*=========================================================================== *;

      FAT_N = N(OF HI7 HI12 AN1-AN5 AN7 AN8 AN12 AN14-AN16);

*=========================================================================== *
* PRORATED SUBSCALE SCORE =                                                  *
*  [SUM OF ITEM SCORES]x[N OF ITEMS IN SUBSCALE]/[N OF ITEMS ANSWERED]    *
*                                                                           *
* WHEN THERE ARE MISSING DATA, PRORATING BY SUBSCALE IN THIS WAY IS      *
* ACCEPTABLE AS LONG AS MORE THAN 50% OF THE ITEMS WERE ANSWERED.        *
* THE TOTAL SCORE IS CALCULATED AS THE SUM OF THE PRORATED SUBSCALE      *
* SCORES.                                                                   *
* THE FACT SCALE IS CONSIDERED TO BE AN ACCEPTABLE INDICATOR OF PATIENT   *
* QUALITY OF LIFE AS LONG AS OVERALL ITEM RESPONSE RATE IS GREATER THAN   *
* 80%.                                                                      *
*=========================================================================== *;

*=========================================================================== *
* FATIGUE SUBSCALE SCORE                                                     *
*=========================================================================== *;

IF (FAT_N/13 > .50) THEN
   Fatigue = SUM(OF HI7 HI12 AN1-AN5 AN7 AN8 AN12 AN14-AN16)*13/(FAT_N);

RUN;

PROC MEANS DATA=SCORING;
 VAR Fatigue;
 TITLE 'FACIT-Fatigue subscale UNIVARIATE STATISTICS';
 RUN;
```