Statistical Analysis Plan

Sponsor: Resolve Therapeutics, Inc.

Protocol Number: 132-04

Protocol Version / Date: 2.0 / July 18th, 2018

Protocol Title: A Phase 2, Double-Blind, Placebo-Controlled Study of RSLV-132 in Subjects with Primary Sjogren's Syndrome

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1. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

ADA	Anti-drug antibodies
AE	Adverse event
ATC	Anatomical Therapeutic Chemical Classification
bpm	Beats per minute
°C	Celsius
CRF	Case report form
CRO	Contract Research Organization
CSR	Clinical study report
DBP	Diastolic blood pressure
eCRF	Electronic case report form
ESR	erythrocyte sedimentation rate
ESSDAI	EULAR Sjogren's syndrome disease activity index
ESSPRI	EULAR Sjogren's syndrome patient reported index
FACIT	Functional Assessment of Chronic Illness Therapy
FAS	Full analysis set
HIV	Human immunodeficiency virus
ITT	Intent-to-Treat analysis set
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
PGA	Physician's global assessment
PK	Pharmacokinetic
pSS	primary Sjogren's syndrome

PT	Preferred term
RNA	Ribonucleic acid
RR	Respiratory rate
SAP	Statistical analysis plan
SAS	Safety analysis set
SBP	Systolic blood pressure
SD	Standard deviation
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 132-04: A Phase 2, Double-Blind, Placebo-Controlled Study of RSLV-132 in Subjects with Primary Sjogren's Syndrome. The analyses described in this document will be performed for the final clinical study report (CSR) after the database lock and unblinding. 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 9.4 or higher.

2.1. Study Objectives

The present study will examine the role of circulating RNA complexed with autoantibodies and immune complexes and its role in activation of inflammatory pathways in patients with primary Sjogren's syndrome. The study will be conducted in a subset of Sjogren's patients who have elevated levels of SSA/Ro autoantibodies and a pattern of elevated interferon-stimulated gene expression in blood cells. Given the well-established inflammatory properties of RNA, RSLV-132 will be administered to digest the RNA which is circulating bound to autoantibodies and thereby attenuate chronic activation of multiple inflammatory pathways. A number of biochemical and clinical parameters will be analyzed to determine the potential therapeutic utility of nuclease therapy in Sjogren's syndrome.

2.2. Endpoints

2.2.1. Primary Study Endpoint

The primary endpoint of the study is to assess the following biochemical parameters in the active versus control groups comparing Baseline (Day 1) with Day 99:

- changes in blood cell gene expression or serum protein levels indicative of reduced inflammation.

2.2.2. Secondary Study Endpoint

The secondary endpoints of the study are to assess the following parameters in the active versus control groups comparing Baseline (Day 1) with Day 99:

- safety and tolerability;
- Ro 52/60 autoantibody levels (ICON);
- total immunoglobulins (ICON);
- erythrocyte sedimentation rate (ESR);

- complement levels (C3 & C4) (ICON)
- minor salivary gland histopathology (not summarized)
- minor salivary gland interferon-stimulated gene expression (not summarized)
- disease activity (ESSDAI or PGA, Schirmer's test, stimulated and unstimulated salivary flow) (assessment worksheets provided in study regulatory binder);
- patient-reported outcomes as measured by the following: ESSPRI, FACIT, Profile of fatigue, EQ-5D-L, Fatigue VAS, and Neuropsychological analysis scales (not summarized) (assessment worksheets provided in study regulatory binder);
- Additional exploratory evaluations may be considered as driven by the evolving understanding of the mechanism of action, technical feasibility, and any other clinical or immunological information that may become available during the course of the clinical study.

2.3. Study Design

2.3.1. Study Population

This is a multi-center, double-blind, placebo-controlled study to evaluate the impact of 8 intravenous infusions of RSLV-132 in 28 patients enrolled at approximately 2-3 clinical centers in the United Kingdom with primary Sjogren's syndrome (pSS). The study population will be 18 to 85 years male or female with pSS, elevated levels of anti Ro-52 or anti Ro-60 antibodies, positive interferon signature and minimum weight of 45 kg.

2.3.2. Treatment Groups and Dosing

Following Baseline evaluations on Day 1 subjects will receive their first intravenous infusion of RSLV-132. Subjects will return to the research unit for additional visits as described in Table 1. The subjects will be randomized 3:1 (active: placebo) to receive 8 intravenous administrations of 10 mg/kg of study drug or placebo on days: 1, 8, 15, 29, 43, 57, 71, and 85.

2.3.3. Study Visits and Assessments

Potential subjects will be screened to assess their eligibility to enter the study within 60 days prior to study entry (i.e., prior to Baseline visit). Following Baseline evaluations on Day 1, subjects will receive their first infusion of RSLV-132 or placebo. Subjects will return to the research unit for follow-up visits. A total of 9 post-baseline visits will occur; once weekly for two weeks, then every two weeks for 14 weeks, plus one further visit 8 weeks after the last study drug administration. There will then be two additional telephone contacts made to subjects at weeks 13 and 18 after the last dose, to monitor any potential late-emerging adverse

events. See Table 1 and the schedule of events for the specific procedures and collection time points.

Table 1. Study Procedures

Study Procedures	**Screen (-60 to -1)**	**Baseline Day 1**	**Day 8**	**Day 15**	**Day 29**	**Day 43**	**Day 57**	**Day 71**	**Day 85**	**Day 99/ ET**	**Day 141**	**Day 176 Tel. FU**	**Day 211 Tel. FU EOS**
Acceptable visit window (days)[f]			± 2	± 2	± 2	± 2	± 2	± 2	± 2	± 2	± 5	+ 10	+ 10
Informed consent	X												
Inclusion/exclusion	X	X											
Demographics/weight/height	X												
Hepatitis, HIV tests	X												
FSH (female subjects only) [g]	X												
Whole blood for interferon signature	X												
Physical exam	X	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]		
Pregnancy test	X[b]	X[c]	X[c]	X[c]	X[c]	X[c]	X[c]	X[c]	X[c]		X[b]		
Medical/medication history	X	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]		
Vital signs	X	X	X	X	X	X	X	X	X	X	X		
Chem-20, CBC, UA	X	X			X		X		X	X			
AE assessment		X	X	X	X	X	X	X	X	X	X	X	X
ESSDAI, PGA, salivary flow, Schirmer's test		X			X		X		X	X			
Patient reported outcomes		X			X		X		X	X			
Minor salivary gland biopsy (consented subjects)		X								X			
Serum for study drug concentration and RNase activity		X			X		X		X	X	X		
Serum for protein analysis		X			X		X		X	X			
Whole blood for gene expression		X			X		X		X	X			

Whole blood for ESR (performed by local) laboratory)		X			X		X		X	X			
Whole blood for DNA analysis		X											
Plasma for RNA analysis (selected subjects)		X								X			
Serum for anti-Ro-52 and anti-Ro-60 autoantibodies	X	X			X		X		X	X			
Serum for total immunoglobulins, C3 and C4		X			X		X		X	X			
Serum for anti-RSLV-132 antibodies		X			X						X		
Study Drug administration		X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]	X[e]				

Abbreviations: ET = Early Termination, EOS = End of Study

[a] directed physical exam.
[b] serum pregnancy test
[c] urine pregnancy test
[d] interim medication/medical history only.
[e] intravenous infusion of RSLV-132 (10 mg/kg) or placebo according to infusion rate in the Study Drug Reference Manual.
[f] minimum interval between administrations of RSLV-132 during the 2 week dosing period is 10 calendar days.
[g] to be collected when confirmation of menopause is required in female subjects
[h] assessments to be performed for any subjects that terminate early
[i] biopsies may be performed up to 14 days prior to the baseline visit and at or within 7 days prior to or after Day 99

2.3.4. Concomitant Medications

Subjects entering the study who had no changes to their medications used to treat pSS in the previous 30 days prior to the Baseline visit shall remain on the background medications at the same doses until Day 141 of the study. The use of pilocarpine or cevimeline during the trial is allowed, however subjects shall not use these medications within 12 hours prior to clinical disease activity measurements on days 1, 29, 57, 85, and 99 or use eye drops within 6 hours prior to clinical disease activity measurements on days 1, 29, 57, 85, and 99.

No changes in Sjogren's medications shall be permitted during the study with the exception of eye drops and analgesics. Medications prohibited prior to the study are listed in the exclusion criteria section of the protocol. The following medications are prohibited during the trial: hydroxychloroquine cyclophosphamide, belimumab, abatacept, TNF inhibitors, rituximab, and oral corticosteroids >10 mg/day.

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. A subject should be discontinued from study drug treatment for any of the following reasons: AE which is either intolerable or poses safety concerns, pregnancy or disease worsening. The Investigator may also remove a subject from investigational treatment if, in the Investigator's opinion, it is not in the best interests 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 protocol specified procedures for remaining study visit time points or at a minimum perform early termination assessments specified in 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 3:1 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 such time that all discrepancies in the clinical database are resolved (i.e., at the time of the database lock). The date/initials and reason for the investigator and/or clinical staff removing the study blind will be documented.

2.3.7. Sample Size and Power

The sample size of approximately 28 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 2-3 clinical centers in the United Kingdom. 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. If a measurement of a variable is not made on a given subject prior to the first dose of study drug, then that subject will be considered not to have a baseline value for that variable. 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 0.9999 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 10 weeks (in total 8 administrations) to subjects with pSS. These analyses will use the SAS population.

Total duration of study drug dosing (days), total duration of infusion (Hours), total volume infused (mL) and total duration of study drug exposure will be summarized by treatment group. 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. The percentages will be calculated based on the number of subjects in each treatment group.

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 duration of infusion 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 ~~plus 1~~.

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]) from screening visit and baseline characteristics from baseline Day 1 visit (complement levels (C3 & C4), ESR, ESSDAI, Schirmer's Test, stimulated and unstimulated salivary flow, VAS, ESSPRI, FACIT, Profile of fatigue, EQ-5D-L) 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.

Age at Screening Visit will be calculated as (the informed consent date-birth date)/365.25.

7.2. Medical History

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

A subject with multiple occurrence of the same body system category will be counted only once. Medical history body system categories 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 changes in disease activity using blood cell gene expression, serum protein level, ESSDAI, PGA, stimulated and unstimulated salivary flow, and Schirmer's test.

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.

If the data are collected at the Screening Visit and are not collected at the Baseline (Day 1), the Screening values will be used as the baseline.

All data will be listed.

9.1. Analysis of Primary Efficacy Endpoints

The primary endpoint is to assess changes in blood cell gene expression and serum protein level as surrogate endpoints in the active versus control groups comparing Baseline with Day 99 among FAS population.

9.1.1. Blood Cell Gene Expression

Blood will be collected into PAX gene RNA collection tubes, RNA will be extracted and analyzed by Resolve Therapeutics (Seattle, WA) to measure the expression level of genes that are related to inflammatory pathways thought to be involved in primary Sjogren's syndrome and to analyze the presence of various micro RNAs. The analysis of gene expression profiles will not be a part of this SAP.

9.1.2. Serum Protein Level

Serum samples will be obtained at various visits during the study and the level of circulating serum cytokines and other proteins that are thought to be related to the inflammation and autoimmunity process shall be measured by MyriadBRM (Austin, TX). The analysis of serum protein level will not be a part of this SAP.

9.2. Analysis of Secondary Efficacy Endpoints

The following measurements will be used to assess efficacy:ESSDAI, PGA, stimulated and unstimulated salivary flow, and Schirmer's test. Patient reported outcomes such as ESSPRI, FACIT, Profile of

fatigue, EQ-5D-L, and Fatigue VAS are also summarized as a part of secondary measures.

9.2.1. ESSDAI

European League Against Rheumatism (EULAR) Sjögren's syndrome disease activity index (ESSDAI) will be performed for each subject at Baseline (Day1), Day 29, Day 57, Day 85 and Day 99 to determine the pSS disease activity for each subject at the visit. The total score will be summarized. The improvements from Baseline (Day 1) to Day 99 in ESSDAI total scores will be evaluated as part of the efficacy endpoints. Lower score represents less disease activity.

Summary of observed values: Observed values and the change from baseline, including percent change from baseline at each scheduled visit will be summarized. No statistical testing will be performed.

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

9.2.2. PGA

Physicians Global Assessment (PGA) will be performed for each subject at Baseline (Day1), Day 29, Day 57, Day 85 and Day 99 to determine the pSS 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 99 in PGA scores will be evaluated as part of the efficacy endpoints.

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

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 for descriptive purposes. LOCF will be used to impute missing values on the FAS.

9.2.3. Salivary Flow

Stimulated and unstimulated salivary flow will be measured by each subject at Baseline (Day1), Day 29, Day 57, Day 85 and Day 99 for each subject at the visit. The changes from Baseline (Day 1) to Day 99 in two total weights (grams) of stimulated and unstimulated salivary flow will be evaluated as part of the efficacy endpoints.

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

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

9.2.4. Schirmer's test

Schirmer's test will be performed by each subject at Baseline (Day1), Day 29, Day 57, Day 85 and Day 99 for each subject at the visit. The changes from Baseline (Day 1) to Day 99 in the wetting measurement (mm) of left and right eyes will be evaluated as part of the efficacy endpoints.

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

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

9.2.5. Patient Reported Outcomes (EULAR Sjogren's syndrome patient reported index (ESSPRI), Functional Assessment of Chronic Illness Therapy (FACIT), Profile of fatigue, EQ-5D-5L, Fatigue Visual Analog Scale (VAS))

Patient reported outcomes will be performed by each subject at Baseline (Day1), Day 29, Day 57, Day 85 and Day 99 for each subject at the visit.

Summary of observed values: Observed values and the change from baseline at each scheduled visit will be summarized. No statistical testing will be performed. Specifically, ESSPRI will also include summaries of percent change from baseline at each scheduled visit.

Regarding FACIT, the composite scores at each time point will be summarized.

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.

Sponsor will clean all the data and lock the database once the last subject completes the day 99 visit. Once all the subjects have completed day 211 sponsor will clean any pending data queries, and plan to compile the complete safety data set.

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

10.1. Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA version 20.0 or higher) adverse event dictionary. If a subject experiences multiple events that map to a single preferred term, the greatest severity 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 adverse event will be summarized for the following:

- Subjects with any treatment-emergent adverse event
- Subjects with severe 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.

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 (Mild, Moderate, Severe, Life Threatening and 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 the worst severity 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 number and percentage of subjects who have Grade 3 or higher lab toxicity (based on Rheumatology CTC Grade System) during the study will also be summarized. The percentages will be calculated based on the number of subjects in each treatment group of the SAS.

Serum and urine pregnancy tests are for women of childbearing potential only. Serum pregnancy test will be performed at Screening Visit and Day 141 (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. 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, bpm), and oral temperature (Celsius °C).

Observed values and the change from Baseline (Day 1) at each visit will be summarized using descriptive statistics.

10.2.3. Physical Exam

Physical exam will be performed according to the Study Procedures indicated in the Protocol Appendix B.

The number and percentage of subjects with clinically significant abnormality in each body system will be summarized for each visit. The percentages will be calculated based on the actual number of subjects at each visit in each treatment group of the SAS.

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.

12. REFERENCES

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;
```

Signature Page

Reviewed and Accepted by:

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Anna Leonen, Director, Clinical Data Operations Axio Research, LLC	Date

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