| | |
|---|---|
| **Study Title:** | A Phase 1b, Multiple Ascending-dose Study of EQ001 in Subjects with Systemic Lupus Erythematosus with or without Active Proliferative Lupus Nephritis |
| **Protocol Number:** | EQ001-19-002 |
| **Investigational Product(s):** | EQ001 |
| **Sponsor:** | Equillium, Inc. |
| **Development Phase:** | Phase 1b |
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**CONFIDENTIAL**

[redacted]

# Statistical Analysis Plan

**Sponsor Name:** Equillium Inc.

**Protocol Number:** EQ001-19-002

**Protocol Title:** A Phase 1b, Multiple Ascending-dose Study of EQ001 in Subjects with Systemic Lupus Erythematosus with or without Active Proliferative Lupus Nephritis

[redacted]

**Notice of Confidential and Proprietary Information:**

[redacted]

[redacted]

[redacted]

## Table of Contents

[redacted]

# 1 Glossary of Abbreviations

| Abbreviation | Description |
|---|---|
| ACR | American College of Rheumatology |
| ADA | Anti-Drug Antibody |
| AE | adverse event |
| AESI | adverse event of special interest |
| ALT | alanine aminotransferase |
| ANA | antinuclear antibodies |
| APAC | Asia-Pacific |
| apLN | active proliferative lupus nephritis |
| AST | aspartate aminotransferase |
| ATC | Anatomic Therapeutic Class |
| ATC2 | Anatomic Therapeutic Class level 2 terms |
| BUN | blood urea nitrogen |
| CD6 | cluster of differentiation 6 molecule |
| CI | confidence interval |
| Cl | clearance |
| CKD-EPI | Chronic Kidney Disease Epidemiology Collaboration equation |
| CRO | contract research organization |
| CTCAE | Common Terminology Criteria for Adverse Events |
| CTMS | Clinical Trial Management System |
| CV | cardiovascular |
| DLT | dose-limiting toxicity |
| DRC | Data Review Committee |
| ECG | electrocardiogram |
| eCRF | electronic case report form |
| eGFR | estimated glomerular filtration rate |
| ET | early termination |
| FACIT-F | Functional Assessment of Chronic Illness Therapy – Fatigue |
| FU | Follow up |
| GGT | gamma-glutamyl transferase |
| HbA1c | glycated hemoglobin |
| HbsAg | hepatitis B virus surface antigen |
| HBV | hepatitis B virus |
| Hct | hematocrit |
| HCV | hepatitis C virus |
| Hgb | hemoglobin |
| HIV | human immunodeficiency virus |
| HRQoL | Health-Related Quality of Life |
| ILIgG1 | immunoglobulin G1 |
| IWRS | Interactive Web Response System |
| LDH | lactate dehydrogenase |
| LN | lupus nephritis |
| MCS | Mental component summary |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MMF | Mycophenolate mofetil |
| MMRM | Repeated Measures Mixed Effects Model |
| MPA | Mycophenolic acid |
| MTD | maximum tolerated dose |
| PCS | Physical component summary |
| PD | pharmacodynamic(s) |
| PF | Physical function |
| PfM | Precision for Medicine |

| Abbreviation | Description |
|---|---|
| PGA | Physician Global Assessment |
| PK | pharmacokinetic(s) |
| PT | Preferred Term |
| Q2W | every 2 weeks |
| QoL | quality of life |
| RBC | red blood cell |
| RNA | ribonucleic acid |
| RO | receptor occupancy |
| SAP | Statistical Analysis Plan |
| SC | subcutaneous(ly) |
| SD | standard deviation |
| SE | standard error |
| SF-36 | The Short Form 36 Health Survey |
| SLE | Systemic Lupus Erythematosus |
| SLEDAI-2K | Systemic Lupus Erythematosus Disease Activity Index 2000 |
| SLICC | Systemic Lupus International Collaborating |
| SOC | system organ class |
| TB | tuberculosis |
| TEAE | treatment-emergent adverse event |
| $T_{eff}$ | effector T cell |
| TESAE | treatment-emergent serious adverse event |
| Th | T helper |
| $T_{reg}$ | regulatory T cells |
| UACR | urine albumin creatinine ratio |
| UPCR | urine protein creatinine ratio |
| $V_d$ | volume of distribution |
| WBC | white blood cell |

# 2 Purpose

The purpose of this statistical analysis plan (SAP) is to provide a detailed description of the statistical methods to be implemented during the analysis of Equillium, Inc. study entitled "A Phase 1b, Multiple Ascending-dose Study of EQ001 in Subjects with Systemic Lupus Erythematosus with or without Active Proliferative Lupus Nephritis" and to ensure that the data listings, summary tables and figures which will be produced are complete and appropriate to allow valid conclusions regarding the study objectives. [redacted]

[redacted]

## 2.2 Timing of Data Reviews and Analyses

An independent Data Review Committee (DRC) was established prior to enrolling the first subject into the study and aid with decisions regarding dose escalation, particularly in the Type A part of the study. Roles and responsibilities of the DRC are outlined in a Charter. Primary responsibility of the DRC is to ensure the safety of the subjects participating in the study. Study enrolls two types of subjects; Subjects with Systemic Lupus Erythematosus (SLE) - without Active Proliferative Lupus Nephritis (apLN) (Type A subjects) and - with apLN (Type B subjects).

The DRC is responsible for reviewing data from Type A (for dose escalation) and Type B (as needed) Cohorts throughout the study.

Enrollment into Type A cohorts has been completed. For Type A Cohorts, at the DRC meetings, the DRC reviewed all safety data through Day 29, [redacted] and clinical activity data from the Type A Cohorts. Type A cohort dose escalation was allowed to proceed if no predefined stopping criteria stipulated in the protocol were met. Enrollment into Type A Cohort dose levels proceeded in a sequential manner; once a dose level has been studied in a Type A cohort and the DRC has determined that dose level not to have exceeded the maximum tolerated dose (MTD), a Type B cohort may be enrolled at that dose or at a lower level.

As per Protocol [redacted] up to approximately 20 subjects will be enrolled and dosed in a single Type B Cohort. Subjects in this cohort will receive a total of 13 doses of EQ001 1.6 mg/kg administered SC every 2 weeks over 24 weeks. If a subject discontinues the study within the initial 29 days after dosing, then the subject may be replaced. [redacted]

[redacted]

[redacted]

The final analyses of safety and efficacy data are planned after all subjects complete the study (or terminate early from the study). Final analyses were planned to be done in two stages; when Type A subjects complete the study and when Type B subjects complete the study. After Type A subjects completed the study, a database freeze was performed and an analysis was conducted on data collected for all Type A subjects. Once Type B subjects complete the study and database is locked, a final analysis will be conducted using all data collected in the database through the time of the database lock.

# 3 Study Summary

## 3.1 Objectives

### 3.1.1 Primary Objective

The primary objective of the study is to characterize the safety and tolerability of EQ001 (itolizumab) in subjects with Systemic Lupus Erythematosus (SLE) with or without active proliferative Lupus Nephritis (apLN).

### 3.1.2 Secondary Objectives

The secondary objectives of the study are to:

- Characterize the PK profile of EQ001

[redacted]

- Characterize the clinical activity of EQ001 in Type B Cohort subjects

### 3.1.3 Exploratory Objectives

[redacted]

- Characterize the clinical activity of EQ001 in Type A Cohort subjects

## 3.2 Brief Study Description

This is a phase 1b, multiple ascending-dose study to evaluate the safety, tolerability, [redacted] clinical activity of EQ001, a humanized immunoglobulin G1 (IgG1) monoclonal antibody that selectively targets CD6 on effector T ($T_{eff}$) cells, in subjects with SLE.

Approximately 30 subjects with active or inactive SLE who do not have apLN are anticipated to be studied in dose escalation cohorts of 6 adult subjects each in "Type A Cohorts." Up to approximately 20 subjects with apLN are anticipated to be studied in a Type B Cohort. Additional subjects may be added at the maximum-tolerated dose (MTD) cohort and/or to an additional cohort at an intermediate or lower dose in Type A.

Type A

Type A will utilize a cohort dose escalation design. If < 2 of the 6 evaluable subjects in a Type A dose-escalation cohort experience a dose-limiting toxicity (DLT) during the DLT evaluation period (Days 1-29), then escalation may occur to the next higher dose level. If 2 or more of the 6 initial subjects in a Type A dose-escalation cohort experience DLTs, then no further dose escalation will occur. That dose will then be considered to have exceeded the MTD and the next-lower dose may be declared the MTD. Once a dose has been determined to have exceeded the MTD, the DRC may recommend continuation of the study (with or without modification) and may expand enrollment to evaluate additional subjects at the MTD and/or in an additional cohort at an intermediate or lower dose to better define the MTD.

Type A Cohort enrollment will proceed in a sequential manner to evaluate escalating dose levels of EQ001. The first dose level to be studied, Dose Level 1, will be 0.4 mg/kg and the maximum dose level to be studied will be 3.2 mg/kg. Intermediate dose levels of 0.8, 1.6, and 2.4 mg/kg are planned for Type A Cohorts, but other intermediate doses may be chosen based on emerging [redacted] and safety data. Subjects in Type A Cohorts will receive a total of 2 doses, 2 weeks apart.

The MTD determination will be made based only on Type A Cohorts. Dose escalation is allowed to proceed if no predefined stopping criteria are met and the DRC recommends that it is safe to proceed.

Type B

Up to approximately 20 subjects will be enrolled and dosed in the Type B Cohort. Subjects will receive a total of 13 doses of EQ001 1.6 mg/kg administered subcutaneously every 2 weeks over 24 weeks. [redacted] Subjects who are pulsed and dosed with MMF/MPA during the Screening Period (within 12 weeks prior to starting study treatment) will be allowed into the study.

[redacted]

### 3.3 Subject Selection

Written informed consent for study participation will be obtained before any study-related procedures or assessments are performed. All potential subjects will be screened for potential participation, and those meeting all eligibility criteria will be offered participation in the study.

[redacted]

### 3.5 Cohort Assignment

An interactive web response system (IWRS) will be used to ensure study drug inventory, accountability, and appropriate cohort allocation.

In Type A Cohorts, the first EQ001 dose level to be studied, was 0.4 mg/kg and the maximum dose level to be studied was 3.2 mg/kg. Intermediate dose levels were anticipated to be 0.8, 1.6, and 2.4 mg/kg, but other intermediate doses or doses lower than 0.4 mg/kg could be chosen based on emerging PK, PD, and safety data. Subjects in Type A cohorts received up to 2 doses on Day 1 and Day 15. Planned Type A dose levels were:

- Dose 1: 0.4 mg/kg
- Dose 2: 0.8 mg/kg
- Dose 3: 1.6 mg/kg
- Dose 4: 2.4 mg/kg
- Dose 5: 3.2 mg/kg

The dose level planned for Type B is 1.6 mg/kg. This dose was chosen to be studied in the Type B Cohort since this dose has been determined not to have exceeded the MTD in the Type A Cohorts. Subjects in Type B are to receive up to 13 doses at the assigned dose level every 14 days.

### 3.6 Administration of Study Medication

EQ001 doses will be administered at the study site by a qualified staff member; [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

# 4 Endpoints

## 4.1 Primary Endpoint

The primary endpoint of the study is the safety and tolerability of EQ001, as assessed by treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), clinical laboratory values, vital signs, 12-lead electrocardiogram (ECG), and physical examinations.

## 4.2 Secondary Endpoints

The secondary endpoints of the study are:

- Pharmacokinetics of EQ001, as assessed by EQ001 serum concentrations at specified timepoints

[redacted]

## 4.3 Exploratory Endpoints

[redacted]

- For Type B cohort subjects: Change from baseline in the Short-Form 36 Health Survey (SF-36) and FACIT-F (Additional Concerns domain) total score to FU1 and FU2 and change from

baseline in the Lupus Quality of Life (QoL), patient global assessment, and physician global assessment (PGA) to FU2

# 5 Analysis Populations

## 5.1 Safety Population

The Safety Population consists of all subjects who receive any study drug. All safety data summaries will use this population.

## 5.2 PK Population

The PK Population consists of subjects in the Safety Population who have at least one measurable post-EQ001 exposure serum concentration.

[redacted]

## 5.4 Efficacy Population

The Efficacy Population consists of subjects in the Safety Population who have at least one post-treatment assessment for a marker of clinical activity. Note that for Type B subjects, only post-treatment within 14 weeks of last treatment will be considered for the purpose of defining the Efficacy Population.

# 6 General Considerations

## 6.1 General Methods

Statistical analysis of data from this study will be performed using SAS version 9.4 or higher.

Summaries of baseline characteristics (including demographics), safety, PD parameter receptor occupancy, and efficacy will be presented for each EQ001 dose level within each Type A cohorts and the Type B cohort as applicable. Additionally, data will also be summarized for all Type A subjects combined. A given dose may be studied in more than one cohort of Type A subjects and/or in Type B subjects. Selected safety summaries will also be produced that combine like doses across Type A and B cohorts.

**Groups Presented for Baseline Characteristics, Safety, PD, and Efficacy Data Summaries**

**Type A Cohorts**

- Dose 1
- Dose 2
- Dose 3
- Dose 4
- Dose 5
- All doses combined

**Type B Cohort**

- Dose 1

**Type A + Type B Cohort**

Selected summaries that combine doses across Type A and B cohorts will be produced for the following: Adverse events by systemic organ class (SOC) and preferred terms, adverse events of special interest, serious adverse events, and adverse events resulting in study drug discontinuation. Like doses from Type A and Type B will be pooled, eg., Type A Dose 1.6 mg/kg combined with Type B Dose 1.6 mg/kg.

As the primary objective of this Phase 1b study is to characterize the safety and tolerability of EQ001, no formal statistical hypothesis testing will be performed. Confidence intervals (CIs) for selected clinical activity parameters may be presented for exploratory purposes only.

Most statistical summaries will be descriptive in nature. Unless otherwise indicated, continuous variables will be summarized using the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum and categorical variables will be summarized using number of observations (n), frequency and percentages of subjects.

All dosed subjects will be included in subject data listings unless otherwise noted. If applicable, the relative day (i.e., relative to date of first dose of study treatment) of all complete dates will be presented in subject listings.

Data collected at unscheduled visits will also be included in the subject listings.

Adverse events, medical and surgical histories will be coded for summarization using the Medical Dictionary for Regulatory Activities (MedDRA® Version 23.1). Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary Global B3 (March 2019 Version).

Summary will include data at all scheduled visits and at last post-baseline visit. All by visit summaries will use the electronic case report form (eCRF) collected nominal visit.

For UPCR, urine albumin creatinine ratio (UACR), eGFR, creatinine, urine protein, urine creatinine, urine albumin, and SLEDAI-2K, all nominal visits will be analyzed as collected in the eCRF except for unscheduled and early termination (ET)

[redacted]

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

### 6.4 Pooling of Centers

Data from all the sites will be pooled together for the analyses.

[redacted]

- [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

# 7 Non-Efficacy Data Summaries

## 7.1 Subject Disposition

Subject disposition data will be summarized using the Safety Population. This summary will include the number and percent of subjects in each of the analysis populations (Safety, Efficacy, PK and PD), subjects completing treatment and study, and subjects discontinuing treatment and discontinuing the study by the primary reason for discontinuation. Study completion is defined by completion of the last scheduled study visit (i.e. The FU2 for Type A subjects and the FU4 visit for Type B subjects), even if some earlier visits were missed. Continuous summary statistics will be presented for follow-up duration, where the follow-up duration in weeks will be calculated as:

> Follow-up duration (weeks) = (date of last contact – date of first dose of study drug + 1) / 7, rounded to 1 decimal place.

The number of subjects enrolled and by site, and the number and percent of subjects who failed screening, along with the reasons for screen failure will be presented for all subjects who signed informed consent. By-subject listings will also be created for disposition data.

[redacted]

## 7.3 Demographic and Baseline Characteristics

A summary of demographics and baseline characteristics will be presented using the Safety Population. The following variables will be summarized using continuous or categorical descriptive statistics as appropriate:

- Age (years)
- Sex
- Race
- Ethnicity
- Body Mass Index (kg/m$^2$)
- Baseline renal function (eGFR) (mL/min/Specific Surface Area [SSA]; SSA=1.73 m$^2$)
- Baseline 24-hour UPCR (mg/g) (for Type B only)
- Baseline spot UPCR (mg/g)
- Baseline 24-hour UACR (mg/g) (for Type B only)
- Baseline spot UACR (mg/g)
- Baseline complements (C3 and C4)
- Baseline serologic markers (anti-dsDNA)
- Baseline anti-C1q (for Type A only)
- Prior and current medications used for SLE including biologic therapies for SLE
- History of prior induction treatments (for Type B only)

A by-subject listing will also be created for demographics and baseline characteristics data.

### 7.4 Baseline Disease Characteristics

For Type A subjects, time from initial diagnosis of SLE to first dose date in years will be summarized for the Safety Population.

For Type B subjects, baseline disease characteristics include time from initial diagnosis of SLE to first dose date in years, time from first biopsy-proven diagnosis of lupus nephritis to first dose in months, time from most recent kidney biopsy date to first dose in months, and most recent kidney biopsy findings regarding presence of lupus nephritis for the Safety Population. Lupus nephritis ISN/RPS class(es) category will also be summarized. For top data summarization purposes, ISN/RPS category will be determined by the main classes a subject belongs to. For example, if a subject belongs to ISN/RPS classes III (A) and IV-S(A), category will be designated as III+IV. Simply put, category is determined by ignoring the additional information after the main class (ie the S and G and the (A) or (C). NIH activity index and chronicity index will be summarized using descriptive statistics. NIH activity index is recorded in the database as x/24, only x whole number will be used for summarization. x ranges from 0-24. Chronicity index is recorded as x/12 in the database, only x will be used for summarization, x ranges from 0-12.

Approximate time from diagnosis of SLE to first dose in years will be calculated as (year of first dose – year of diagnosis + 1). Time from first biopsy-proven diagnosis of lupus nephritis to first dose in Type B subjects in months will be calculated as (first dose date – date of biopsy-proven diagnosis) / 30.4375. Time from the most recent kidney biopsy date to first dose in Type B subjects in months will be calculated as (first dose date – date of most recent kidney biopsy) / 30.4375. Months will be rounded to one decimal place.

[redacted]

### 7.5 Medical and Surgical History

Medical and surgical history will be coded using MedDRA version 23.1. The percentage of subjects with a medical history event will be summarized descriptively using the Safety Population. The table will be sorted in descending frequency of MedDRA system organ classes (SOC) and within each SOC by descending frequency of preferred terms (PT) in the Total column (all subjects pooled). A by-subject listing will also be created.

### 7.6 Medications

All medications will be coded using WHO Drug Dictionary (WHODrug Global B3 September 2020 version). Medications will be summarized by Anatomic Therapeutic Class (ATC) level 2 terms (ATC2) and ATC level 4 terms (ATC4) using the Safety Population. Subjects will be counted only once for each ATC2 term in the event that they have multiple records of the same ATC level in the database. The tables will be sorted in the descending order of frequency ATC2 terms and within each ATC2, descending order of frequency of ATC4 in the Total column (all subjects pooled). By-subject listings will also be created.

### 7.6.1 Prior Medications

Prior medications are defined as those medications with a start date prior to the first dose date of any study drug. Prior medications will be summarized in a table and presented in a by-subject listing.

[redacted]

### 7.6.2 Concomitant Medications

Concomitant medications are defined as any medications taken on or after the date of first dose of any study drug, including any medications that were started before the first dose date of any study drug and are ongoing. Concomitant medications will be summarized descriptively and presented in a by-subject listing.

Medications can be both prior and concomitant depending on the start and stop date as related to the first dose date of any study drug.

### 7.6.3 Induction Treatments

Summary of induction treatments is provided for Type B subjects only using the Safety Population. Time from last induction regimen to first dose (months) and time from last best response to first dose (months) will be summarized as continuous variables. Time from last induction treatment start date to first dose is calculated as (first dose date – start date of last induction treatment) / 30.4375, rounded to one decimal place. Time from last best response to first dose is calculated as (first dose date – end date of the last best response) / 30.4375, rounded to one decimal place. Best response and the last induction regimen will be summarized as categorical variables.

Complete response or partial response are considered as best response for the calculation of time from last best response to first dose. Complete Response > Partial Response > No Response > Ongoing > Unknown where '>' symbol indicates 'better than' and 'Ongoing' indicates that the treatment is ongoing.

### 7.6.4 Systemic Steroid Use

All systemic steroid use will be summarized by ATC2 and ATC4 using the Safety Population. Subjects will be counted only once for each ATC2 term in the event that they have multiple records of the same ATC level in the database. The tables will be sorted in the descending order of frequency ATC2 terms and within each ATC2, descending order of frequency of ATC4 in the Total column (all subjects pooled). By-subject listings will also be created.

### 7.6.5 Systemic Lupus Erythematosus Treatments

The most recent use of prior systemic lupus erythematosus treatments will be summarized by drug/drug class as collected in the CRF and by use (never used, discontinued >6 months ago, discontinued <= 6 months ago, ongoing, unknown) using the Safety Population. By-subject listings will also be created.

# 8 Efficacy

Unless otherwise specified, all efficacy endpoints (clinical activity endpoints) will be summarized using the Efficacy Population for the EQ001 treatment group from each Cohort.

Efficacy data will be analyzed based on the scheduled visits. For sensitivity analysis of Type B subjects, data collected more than 56 days after the last treatment date, or after a subject received new immunosuppressive or other treatments for LN, or after subject had an increase in glucocorticoids will be considered as missing. Details will be described in Section 8.1. [redacted]

[redacted]

[redacted]

[redacted]

## 8.1 Secondary Endpoints Analyses

### 8.1.1 Fold Change from Baseline in UPCR to Follow-Up Visit 2 (FU2)

This secondary endpoint of fold change in 24-hour UPCR from baseline pertains to Type B subjects only. Fold change from baseline is defined as UPCR value at visit/Baseline UPCR value. UPCR data are collected from central and local laboratories for Type B subjects. They are generally left-skewed. UPCR will be analyzed using central and local data combined (as defined in Section 6.2).

The fold change from baseline in UPCR from a 24-hour urine collection to FU2 will be descriptively summarized using geometric statistics (geometric mean, geometric CV, 95% confidence interval of geometric mean etc.). The fold change from baseline over time by visit will also be summarized descriptively and geometric mean and 95% confidence limits will be graphically displayed by visit.

As a sensitivity analysis, the 24-hour UPCR values collected more than 56 days after the last treatment date, or after a subject received new immunosuppressive or other treatments for LN, or after subject had an increase in glucocorticoids will not be included and fold changes from baseline will summarized descriptively as mentioned above.

The proportion of subjects with a > 30% and > 50% decline in UPCR from a 24-hour urine collection and those with a UPCR < 500 mg/g at FU2 will be described, along with their 2-sided exact Clopper-Pearson 95% CIs.

Time to earliest response of 24-hour UPCR with response defined as a decrease of > 50% from baseline, a decrease of > 30% from baseline, and a decrease to a level < 500 mg/g for each of these cases will be summarized using the Kaplan-Meier method. The baseline will be the derived 24-hour UPCR value (as defined in Section 6.2). Post-treatment UPCR values from both scheduled and unscheduled visits will be considered. Subjects who have not had a response at the end of participation will be censored on the date of end of participation.

For both Type A and Type B Cohort subjects, the fold change from baseline in spot UPCR will be descriptively summarized using geometric statistics (geometric mean, geometric CV etc.). The proportion of subjects with a > 30% and > 50% decline in spot UPCR and those with a spot UPCR < 500 mg/g by visit will be described, along with their 2-sided exact Clopper-Pearson 95% CIs specifically provided for FU1 for Type A subjects and FU2 for Type B subjects.

In addition, an exploratory analysis of spot UPCR will be performed for Type A cohorts. In this analysis, two-sided p-value to compare values from FU1 and baseline will be obtained by testing LS mean associated with each dose resulting by fitting an ANCOVA model equals to 0. ANCOVA model will be fitted to the log-transformed fold change data with EQ001 dose level as a factor and log-transformed baseline spot UPCR as a covariate for Type A cohorts.

#### 8.1.2 Change from Baseline to FU1 and FU2 in Serologic Markers (C3, C4, and anti-dsDNA)

This endpoint pertains to both Type A and Type B Cohort subjects.

The mean change from baseline in C3, C4, and anti-dsDNA to FU1 (Type A Cohorts [exploratory endpoint]) and FU2 (Type B [secondary endpoint]) will be summarized, along with their 2-sided 95% CI for the change. For data summarization purposes, if a value is recorded as <x or <=x, the value is considered as x/2. If a value is recorded as >x or >=x, the value is considered as x. For Type A, the 2-sided 95% CI will be presented by fitting an ANCOVA model, that is, an ANCOVA model on the changes in C3 and C4, from baseline to FU1 with EQ001 dose as a factor and baseline value as a covariate will be fitted. Baseline adjusted LS mean changes from each group will also be reported.

Serologic markers are collected from central and local laboratories for Type B cohort. Same tests with both central and local version will be combined and analyzed, using descriptive summary statistics by assessment visit. For site 8xx subjects, only local laboratory data (may come from different local laboratories) will be used for analysis; for non-site 8xx subjects, only central laboratory data will be used for analysis.

#### 8.1.3 Change from Baseline in eGFR to FU1 and FU2

This secondary endpoint pertains to Type B cohort subjects only.

The change from baseline in eGFR (baseline value is defined as the mean of Screening and Day 1 values) will be descriptively summarized by visit with central and local versions combined.

The proportion of subjects with a percent decline in eGFR from baseline to FU2 of >=20%, >=30% and >=40% will be summarized along with their 2-sided Clopper–Pearson 95% CIs. In addition, these proportions will also be summarized for all visits.

#### 8.1.4 Change from Baseline in Daily Prednisone Dose and Cumulative Prednisone Dose Through FU1 and Through FU2

This secondary endpoint pertains to Type B subjects only.

Mean daily systemic prednisone equivalent steroid use (mg/day) and change from baseline in Type B subjects will be summarized descriptively by study windows [redacted] A sensitivity analysis of the average daily systemic prednisone equivalent steroid use (mg/day) in Type B subjects excluding any systemic steroid use after 56 days of last treatment will be provided. [redacted]

[redacted]

The proportion of subjects (with the 2-sided 95% Clopper-Pearson CI) with a prednisone daily dose equivalent < 10.0 mg/day, < 7.5 mg/day and < 5.0 mg/day [redacted] will be summarized.

Cumulative prednisone dose is computed as the total dose taken during the analysis period (Day 1 through a certain analysis visit). The cumulative prednisone dose will be summarized descriptively.

8.1.5 Change from Baseline in SLEDAI-2K scores to FU2

SLEDAI-2K is a 24 items questionnaire measuring SLE disease activity within the last 10 days. The total score is calculated as the total of presence of any of the 24 clinical and laboratory variables, weighted by the type of manifestation. The total SLEDAI-2K score ranges between 0 and 105, with higher scores representing higher disease activity. The total score is the sum of the scores assigned to each item manifestation that was present.

The change in SLEDAI-2K scores from baseline (Type A Cohort subjects) and the change from baseline (Type B subjects) will be summarized in both continuous and binary scale (e.g., decrease from baseline of > 4 or ≤ 4 points) by visit. For binary scale changes the 95% CI will be calculated using the Clopper-Pearson method.

A sensitivity analysis of the change in SLEDAI-2K scores from baseline will be provided for Type B subjects. For the sensitivity analysis, values collected >56 days after the last treatment date, or after a subject received new immunosuppressive or other treatments for LN, or after subject had an increase in glucocorticoids are not included.

8.1.6 Proportion of subjects who meet the definition of complete response and partial response in their apLN at FU2

This secondary endpoint pertains to Type B subjects only.

The proportion of subjects achieving a complete and partial renal response as defined in Table 9 based on UPCR derived from a 24-hour urine collection will be summarized along with the 2-sided 95% Clopper–Pearson CI. Time to earliest complete response and time to earliest partial response will be summarized using the Kaplan-Meier method. For both analyses, subjects who have not had a response at the end of participation will be censored on the date of end of participation.

[redacted]

Rescue medications for lupus are defined as new immunosuppressive medications or biologic agents for lupus started prior to the endpoint evaluation. A confirmed decrease in eGFR is defined by a ≥ 20% decrease from baseline at FU2 (or the last available eGFR prior to the FU2 visit if no value is available at FU2) and a ≥ 20% decrease at the immediately preceding central lab eGFR.

The proportion of subjects with a complete and partial renal response will also be reported at FU4 using analogous definitions (i.e. confirmed decrease in eGFR will be based on values at FU4 and the immediately preceding eGFR).

[redacted]

#### 8.1.8 Changes in FACIT-F, Fatigue Scale Score and SF-36 Domain Scores and Two Component Scores from Baseline to FU1 and FU2

SF-36 endpoint pertains to Type B subjects only. The FACIT-F endpoint pertains to Type A and Type B cohort subjects.

FACIT-F

The FACIT-F Additional Concerns Domain (also known as the fatigue subscale, FS) is a 13 item questionnaire measuring patient's fatigue level. Questionnaire has a 5-point Likert scale response format (0=all the time, 1=a little bit, 2=somewhat, 3=quite a bit, and 4=very much). In the eCRF, the score is recorded using a 1 to 5 scale, thus the actual score associated with a response will be derived by subtracting 1 from eCRF recorded values. FACIT-F score is the mean of all answered items scores, multiplied by 13, with all negatively worded item (Items 1-6, and items 9-13) scores reversed by subtracting from 4 prior to summation. FACIT-F score ranges from 0 to 52, with high scores representing less fatigue contributing to better health.

The change scores in FACIT-F, FS scale from baseline to each post-baseline assessment visit will be summarized descriptively by EQ001 dose group when applicable. In addition, number and percentage of subjects with an improvement (i.e., an increase) in FACIT-F, FS score from baseline of ≥3 and >4 points will be summarized at each post-baseline assessment visit with 2-sided 95% Clopper-Pearson CI.

SF-36

The SF-36 is a multi-purpose, health survey with 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically based physical and mental health summary measures. SF-36 questionnaire responses at each visit for each subject will be scored for the eight health domain scale scores (Physical Functioning Scale, Role Physical Scale, Bodily Pain Scale, General Health Scale, Vitality Scale, Social Functioning Scale, Role Emotional Scale, Mental Health Scale) and the two summary component scores [Physical Component Summary Measure (PCS), Mental Component Summary Measure (MCS)] by Optum. Optum will provide both general population norm based scores and original 0-100 scores. Norm based scoring is done so that each scale has the same average of 50 with a standard deviation 10. Norm based scores of the 8 health domain scores and the two component summary scores will be summarized descriptively by visit.

8.1.9 Change from baseline in the Lupus Quality of Life (QoL), patient global assessment, and physician global assessment (PGA) to FU2

This secondary endpoint pertains to Type B subjects only.

The Lupus QoL is a 34 items questionnaire that measures disease-specific health-related quality of life (HRQoL) in adult with SLE. Individual subscales include the following: physical health (8 items), emotional health (6 items), body image (5 items), pain (3 items), planning (3 items), fatigue (4 items), intimate relationships (2 items), and burden to others (3 items). Questionnaire responses to each item has a 5-point Likert response format (0=all the time, 1=most of the time, 2=a good bit of the time, 3=occasionally, and 4=never). The mean raw domain score is transformed to scores ranging from 0 (worst HRQoL) to 100 (best HRQoL) by dividing the raw domain score by 4 and then multiplying by 100. The result represents the transformed score for that domain. The transformed domain scores are obtainable when at least 50% of the items are answered. The mean raw domain score is then calculated by totaling the item response scores of the answered items and dividing by the number of answered items. A non-applicable response is treated as unanswered and the domain score is calculated as indicated above. The questions for each subscale include:

- Physical health: items 1–8;
- Pain: Items 9–11;
- Planning: Items 12–14;
- Intimate relationships: Items 15 and 16;
- Burden to others: Items 17–19;
- Emotional health: Items 20–25;
- Body image: Items 26–30;
- Fatigue: Items 31–34.

[redacted]

The changes in each domain scores in Lupus QoL, patient global assessment and PGA scores from baseline will be summarized in both continuous and binary scale (e.g., at least 1 point improvement vs no improvement or worsened). The 95% Clopper-Pearson confidence intervals will be provided for the percent of subjects with at least 1 point improvement.

[redacted]

[redacted]including neutralizing antibodies (NAB)], will be measured [redacted] PK parameters will be analyzed using the PK population which is defined as subjects in the Safety Population who have at least one measurable post-EQ001 exposure serum concentration. [redacted] ADA (NAB) data will be analyzed by the Safety Population.

### 9.1 PK

EQ001 serum concentrations will be measured for Type A subjects [redacted] PK samples will be collected prior to study drug administration on dosing days. EQ001 serum concentrations will be analyzed using the PK Population and descriptive statistics will be provided by visit by treatment group and in each Type A and Type B cohort separately. A by-subject listing for EQ001 serum concentrations will also be provided.

[redacted]

[redacted]

[redacted]

[redacted]

### 9.3 Anti-drug antibody (ADA)

Serum from available timepoints will be analyzed for detection of anti-drug antibodies (ADA) against EQ001. A NAB assay will be performed on the same samples, if required. ADA sampling may be requested by the

Sponsor at an unscheduled visit to further evaluate safety in individual subjects. ADA and neutralizing ADA results will be presented in a by-subject listing for the Safety Population with Type A and Type B combined.

# 10 Safety

All safety analyses will be performed using the Safety Population.

## 10.1 Extent of Exposure

All subjects start with dose level of 1.6 mg/kg but allowed to change the dose level to 0.8 mg/kg. Dose level administrated at each visit will be summarized. Treatment exposure will be determined by overall duration of treatment and duration at each dose level. In addition, measures of extent of exposure at each dose level include the screening weight normalized average dose of study drug (mg/kg) administered, total dose of study drug (mg/kg) administered, and the number of doses administered per subject.

The duration of exposure in weeks is defined as the (last dose date - first dose date + 1)/7.

eCRFs captures the volume of EQ001 prepared and volume administered at each dosing visit. As described in the Pharmacy Manual, volume prepared at a dosing visit is based on the subject's weight (kg) and the randomized dose level (mg/kg); i.e., volume prepared (mL) = weight x dose level /100. The weight at screening is used to calculate the study drug dose, unless there has been a weight change of 20% or more from the screening weight, then the weight at visit is used.

The screening weight normalized average dose of study drug (mg/kg) administered at a dosing visit = total volume of study drug administered at all dosing visits (mL) x (100 mg/1 mL)/ (the screening weight x number of doses administered).

Duration of exposure and screening weight normalized average dose of study drug administered per dose will be summarized by continuous summary statistics (n, mean, standard deviation (SD), median, minimum, and maximum). The number and percentage of doses administered will be summarized by treatment group in each Type A and Type B cohort separately.

Cumulative volume administered will also be summarized by continuous summary statistics by treatment group in each Type A and Type B cohort separately.

## 10.2 Treatment Compliance

Overall treatment compliance will be calculated based on the cumulative volume of study drug administered (ml) and the cumulative volume of study drug prepared (ml).

Compliance (%) = 100 x (cumulative volume of drug administered / cumulative volume of drug prepared).

Treatment compliance will be summarized by continuous summary statistics (n, mean, standard deviation (SD), median, minimum, and maximum) by treatment group in each Type A and Type B cohort separately.

A by-subject listing of exposure and compliance data will also be created.

## 10.3 Adverse Events

An adverse event is defined as any untoward medical occurrence in a subject. Treatment-emergent AEs (TEAE) are defined as any AE that started after dosing or prior to dosing and that worsens following exposure to the study drug. If the start date of an AE is partially or completely missing, the date will be compared as far as possible with the date of the start of administration of study drug. The AE will be assumed to be treatment-emergent if it cannot be definitively shown that the AE did not occur during the treatment-emergent period (worst case approach; see Section 6.3 for imputation algorithm).

All AEs will be coded using MedDRA version 23.1 and graded using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 severity grading scale. For AEs not covered by CTCAE, the conventional definition of severity will be used as follows:

- **Grade 1 (mild) AE:** Minor; no specific medical intervention; marginal clinical relevance.
- **Grade 2 (moderate) AE:** Minimal intervention; local intervention; noninvasive intervention.
- **Grade 3 (severe) AE:** Significant symptoms requiring hospitalization or invasive intervention.
- **Grade 4 (life-threatening or disabling) AE:** Complicated by acute, life-threatening complications; need for intensive care or emergent invasive procedure.
- **Grade 5:** Fatal AE

For the purpose of the summaries, AEs with missing relatedness will be considered to be related to study drug and AEs with missing severity will be considered Grade 3 (severe).

Analyses of AEs will include TEAEs summarized descriptively by number of subjects with an event (n), and percentage (%), by MedDRA SOC, PT and CTCAE grade.

A subject will be counted no more than once at the SOC level and no more than once at the PT level. For summaries by SOC, PT, and CTCAE severity grade, a subject will be counted once at highest observed severity grade. Summaries by relatedness would be handled similar to the summaries by severity grade. Summaries by SOC and PT will be ordered by overall descending frequency of SOC and then, within a SOC, by overall descending frequency of PT, and by the All Subjects Combined (Type A + Type B) group for the summary tables with Type A and Type B same dose level combined.

Summaries of AEs will include:

- An overall summary providing subject incidence of the following:
  - Any TEAE
  - Any treatment-emergent serious AE (TESAE)
  - Any treatment-related TEAE
  - Any treatment-related TESAE
  - TEAE by maximum severity
  - Any TEAE leading to study drug discontinuation
  - Any TEAE leading to death
  - [redacted]
  - [redacted]

AESIs include injection site-related reactions > Grade 3, lymphopenia > Grade 3 and fever and other injection related (hypersensitivity) reaction > Grade 3, and anaphylaxis.

- TEAEs by SOC and PT
- TEAEs Related to Study Drug by SOC and PT
- TESAEs by SOC and PT
- TESAEs Related to Study Drug by SOC and PT
- TEAEs with Severity Grade ≥ 3 by SOC and PT
- TEAEs by SOC, PT and Maximum Severity Grade
- TEAEs Leading to Study Drug Discontinuation by SOC and PT
- TEAEs of Special Interest by SOC and PT

- TEAEs of Special Interest by SOC, PT and Maximum Severity Grade

A by-subject listing of AE data will also be created. Adverse events occurring within 30 days after last dose of study drug and AEs occurring >30 days after the last dose of study drug through the end of the study will be separately summarized. All AEs will be included in the listings. AEs occurring before start of study treatment will be included in the data listings but will not be included in the summary tables of AEs.

### 10.4 Laboratory Evaluations

The actual and change from Baseline values of clinical laboratory data (hematology, chemistry, and urinalysis) will be summarized by visit presented in a table, using continuous descriptive summary statistics at Baseline and each post-Baseline visit. For Type B, laboratory tests with both local and central versions will be combined and analyzed.

Laboratory parameters that can be graded using CTCAE will be graded. The number and percentage of subjects will be summarized for the following:

- Grade 2 and Grade 3 or higher laboratory abnormalities
- Worst post-Baseline severity grade
- Shift summary of Baseline grade to worst post-Baseline severity grade
- ALT or AST >=3xULN
- ALT or AST >=3x ULN and total bilirubin > 2x ULN

Box plots of selected hematology (hemoglobin, absolute lymphocyte count, absolute neutrophil count, platelets, white blood cell count) and chemistry parameter values (sodium, potassium, eGFR, ALT, AST) will be produced by assessment visit.

Mean +/- standard error (SE) figures will be provided for serum albumin, spot UPCR, 24-hour UPCR, spot UACR, 24-hour UACR, eGFR and Spot UPCR, spot UPCR and 24-hour UPCR, and spot UACR and 24-hour UACR overtime, for Type-B subjects only.

A by-subject listing will also be created for laboratory results in conventional units.

A by-subject laboratory findings prior to induction listing will also be created for prior to induction laboratory results in conventional units.

### 10.5 Pregnancy

Pregnancy testing in women of childbearing potential will be obtained with a urine and serum beta human chorionic gonadotropin test (βHCG). A pregnancy test will be performed during Screening, Day 1, Day 15, Day 29, Day 43 and at Day 57 visit in Type A subjects and during Screening, Day 1, Day 15, Day 29, Day 43, Day 57, Day 71, Day 85, Day 99, Day 113, Day 127, Day 141, Day 155, Day 169, FU2, FU3, and FU4 for Type B subjects.

Pregnancy test results, including the type of pregnancy test performed at visit will be presented in a by-subject listing.

### 10.6 Vital Signs

Vital signs will be collected pre-dose and 30 minutes after the injection at each dosing visit. For Type B subjects, vital signs will be measured on 2 different days at least 3 days apart at Screening. Additionally for Type B subjects, blood pressure will be measured twice at least 3 days apart at Screening. Vital signs will include systolic and diastolic blood pressures (mmHg), pulse rate (beats/min), respiratory rate (breaths/min), temperature (°C or °F) and weight (kg).

Temperature collected in °F will be converted into °C using the following formula:

Temperature (°C) = [Temperature (°F) – 32] x (5/9)

The actual and change from Baseline values of vital signs will be summarized by visit presented in a table, using continuous descriptive summary statistics at Baseline and each post-Baseline visit. In addition, number and percent of subjects with out of range vital signs at any post-baseline visit will also be summarized for the following categories:

**Blood Pressure**:

- SBP > 150 mmHg or DBP > 100 mmHg
- SBP <90 mmHg or DBP <60 mmHg

**Heart Rate**:

- < 50 beats per min
- >120 beats per minute
- ≥ 30 beats per minute increase from baseline
- ≥ 30 beats per minute decrease from baseline

A by-subject listing will also be created.

### 10.7 ECG

A standard 12-lead ECG will be performed at Screening, Day 1, Day 29, FU2/Day 57, and Early Termination for Type A Cohort Subjects and at Screening, Day 1, Day 43, Day 85, Day 141, Day 169, FU4/Day 253, and Early Termination for Type B Subjects. The subjects will be in a seated, semi-recumbent, or supine position in a rested, calm state for at least 10 minutes before ECG assessment is performed. Any clinically significant abnormal ECG findings will be recorded as an AE.

The actual and change from Baseline values of ECG parameter HR and intervals (PR, RR, QRS, QTcF) will be summarized by visit presented in a table, using continuous descriptive summary statistics at Baseline and each post-Baseline visit. ECG overall interpretation will be summarized by visit as a categorical variable (normal, abnormal – not clinically significant, abnormal – clinically significant).

QT interval corrected for heart rate will be calculated using the Fridericia's formula: $QTcF=10xQT/RR^{1/3}$,

where RR represents RR interval measured in milliseconds.

Worst post-baseline increase in QTcF by visit will be summarized for the following:

- <= 0 msec increase from baseline
- >0 - <= 30 msec increase from baseline
- >30 - <= 60 msec increase from baseline
- >60 msec increase from baseline

Outlier ECG intervals will be summarized for the following:

- PR > 200 msec
- HR > 120 or < 40 bpm
- QTcF increased by >30 msec from baseline
- QTcF increased by >60 msec from baseline
- QTcF > 480 msec
- QTcF > 500 msec

A by-subject listing will also be created.

[redacted]

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]