Study Title:	A Phase 1b Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of EQ001 in Subjects with Moderate-to-Severe Uncontrolled Asthma
Protocol Number:	EQ001-19-001
Investigational Product(s):	EQ001
Sponsor:	Equillium AUS Pty Ltd
Development Phase:	Phase 1b
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Statistical Analysis Plan

Sponsor Name: Equillium AUS Pty Ltd

Protocol Number: EQ001-19-001

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1 Glossary of Abbreviations

Abbreviation	Description
ACQ	Asthma Control Questionnaire
AE	adverse event
AESI	adverse event of special interest
ALC	absolute lymphocyte count
ALT	alanine aminotransferase
ANC	absolute neutrophil count
AST	aspartate aminotransferase
BUN	blood urea nitrogen
Cl	clearance
C_{max}	maximum serum drug concentration
CTCAE	Common Terminology Criteria for Adverse Events
CTMS	Clinical Trial Management System
DLT	dose-limiting toxicity
DRC	Data Review Committee
ECG	electrocardiogram
eCRF	electronic case report form
eDiary	electronic diary
EOS	End of Study, or End-of-Study (adj)
ET	early termination
FDA	Food and Drug Administration
FeNO	fractional exhaled nitric oxide
FEV1	forced expiratory volume in 1 second
FVC	forced vital capacity
GGT	gamma-glutamyl transferase
HBV	hepatitis B virus
Hct	hematocrit
HCV	hepatitis C virus
Hgb	hemoglobin
HIV	human immunodeficiency virus
HBsAg	hepatitis B virus surface antigen
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IgE	immunoglobulin E
IgG1	immunoglobulin G1
IWRS	Interactive Web Response System
LDH	lactate dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
MTD	maximum tolerated dose
PD	pharmacodynamic(s)
PEFR	peak expiratory flow rate
PfM	Precision for Medicine
PFT	pulmonary function test

Abbreviation	Description
PK	pharmacokinetic(s)
PT	preferred term
Q2W	every 2 weeks
RBC	red blood cell
SAE	serious adverse event
SAP	Statistical Analysis Plan
SC	subcutaneous(ly)
SOC	system organ class
$t_{½}$	half-life
TEAE	treatment-emergent adverse event
T_{eff}	effector T cell
TESAE	treatment-emergent serious adverse event
T_{max}	time to maximum concentration
V_d	volume of distribution
WBC	white blood cell
WOCBP	women of childbearing potential

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 Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of EQ001 in Subjects with Moderate-to-Severe Uncontrolled Asthma" 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 Analyses and Data Review

When the last subject in each cohort completes the [redacted], all available safety, [redacted], [redacted] and clinical activity data from all cohorts will be compiled. Randomization in the next dose cohort will not begin until the Data Review Committee (DRC) review of all available safety data from all subjects support escalation to the next dose level. An independent unblinded team from [redacted] will perform the unblinded analyses as described in Section 3.5 of this SAP (please refer to blinding section) to maintain the blinding of the study.

All the analyses presented in this SAP, will be performed after the database lock when all the data will be considered as unblinded. Analyses for the purpose of the DRC data reviews will be based on a data snapshot at the time of the data review.

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).

3.1.2 Secondary Objectives

The secondary objectives of the study are:

- Characterize the PK of EQ001
- [redacted]
- [redacted]
- Characterize the clinical activity of EQ001

3.2 Brief Description

This is a phase 1b, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, PK, [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 moderate-to-severe uncontrolled asthma.

The study will initially enroll up to 32 subjects in up to 4 successive dose cohorts of 8 adult subjects each (up to 10 subjects may be enrolled to achieve 8 DLT evaluable subjects). Doses of 0.8, 1.6, 2.4, and 3.2 mg/kg EQ001, or an equivalent volume of placebo, will be administered subcutaneously (SC) every 2 weeks (Q2W) for a total of 5 doses. Subjects will be randomized in a 3:1 ratio (active: placebo) within each Cohort to characterize the safety, tolerability, PK, [redacted] clinical activity of ascending SC doses of EQ001 and to determine the maximum tolerated dose (MTD). After determination of the MTD, and at the Sponsor's discretion, the MTD cohort may be repeated to increase the number of subjects receiving the MTD to 12 and subjects in the pooled placebo cohort to 10; therefore, the total number of subjects enrolled in the study may be up to 40.

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 Treatment Assignment & Blinding

An interactive web response system (IWRS) will be used to ensure study drug inventory, accountability, and appropriate cohort allocation and blinded treatment assignment. The site's unblinded pharmacist or designee will have access to the IWRS and all treatment assignments.

After informed consent has been obtained, all screening procedures have been assessed, and study eligibility has been confirmed, subjects will be randomized to receive either EQ001 or placebo on Study Day 1. The unblinded study pharmacist or designee will access the IWRS to randomize the subject into the study, receive the unblinded treatment assignment and dose, record drug accountability, and request resupply. EQ001 will be administered Q2W for 8 weeks (a total of 5 doses) at the following dose levels:

- **Cohort 1:** Randomized 3:1 (EQ001: Placebo)
  - EQ001 0.8 mg/kg
  - Placebo
- **Cohort 2:** Randomized 3:1 (EQ001: Placebo)
  - EQ001 1.6 mg/kg
  - Placebo
- **Cohort 3:** Randomized 3:1 (EQ001: Placebo)
  - EQ001 2.4 mg/kg
  - Placebo
- **Cohort 4:** Randomized 3:1 (EQ001: Placebo)
  - EQ001 3.2 mg/kg
  - Placebo

EQ001 or placebo doses will be administered in the clinic; subjects will be observed for a minimum of 30 minutes after administration.

[redacted]

Investigators, site staff, and subjects will be blinded to treatment assignment. The Sponsor may be unblinded to treatment assignment. The unblinded pharmacist or designee will be instructed not to divulge the treatment administered to any subject with the blinded site personnel, study subject or blinded study monitor and any other blinded CRO/vendor team members.

The blind should be broken only if knowledge of the subject's treatment allocation would facilitate specific emergency treatment. Unblinding procedures are provided in the Pharmacy and IWRS Manuals. The investigator should contact the Sponsor and/or designee prior to unblinding a subject's treatment assignment. In the event of an emergency when unblinding is necessary and the Sponsor and/or designee could not be contacted, the investigator must contact the Sponsor and/or designee as soon as possible after the unblinding. Treatment assignment may be provided to the study sites/subjects after database lock.

[redacted]

Following final database lock all roles may be considered unblinded.

[redacted]

[redacted]

[redacted]

[redacted]

4 Endpoints

4.1 Primary Endpoint

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

4.2 Secondary Endpoints

The secondary endpoints of the study are:

- Pharmacokinetics of EQ001, as assessed [redacted]
- [redacted]
- [redacted]
- Clinical activity of EQ001, as assessed by the following variables:
    - Change from baseline in prebronchodilator FEV1
    - Change from baseline in fractional exhaled nitric oxide (FeNO)
    - Change in peak expiratory flow rate (PEFR)
    - Change from baseline in Asthma Control Questionnaire (ACQ-6) score
    - Time to first exacerbation (any severity)
    - Asthma symptoms, peak expiratory flow rate measurements, use of controller and rescue medication, nighttime awakening due to asthma and asthma-related activity limitations (as recorded on an eDiary)
    - Annualized rate of asthma exacerbations (of any severity)

[redacted]

5 Analysis Populations

5.1 Safety Population

The Safety Population consists of all subjects who receive any study drug. Subjects will be analyzed according to treatment actually received.

5.2 Efficacy Population

The Efficacy Population consists of those subjects in the Safety Population who have at least 1 post-treatment clinical activity assessment.

5.3 Pharmacokinetic (PK) Analysis Population

The pharmacokinetic population consists of those subjects in the safety population who have at least 1 measurable post-EQ001 exposure EQ001 serum concentration.

[redacted]

[redacted]

6 General Aspects for Statistical Analysis

6.1 General Methods

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

Summaries of baseline demographics will be presented for pooled Placebo group from all Cohorts, EQ001 treatment group from each Cohort, pooled EQ001 treatment groups from all Cohorts and Total for all Cohorts. Efficacy will be presented for the pooled Placebo group, EQ001 treatment groups from each Cohort and pooled EQ001 treatment groups. In addition, Safety tables will also include a Total, all subjects pooled, column.

- As the objective of this Phase 1b study is to characterize the safety and tolerability of EQ001, formal statistical hypothesis testing will not be performed. Although exploratory confidence intervals (CIs) may be presented, these data will be used for exploratory conclusions only.
- Statistical analyses will be descriptive in nature. Continuous variables will be summarized using the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized using number of observations (n), frequency and percentages of subjects.
- All relevant subject data will be included in listings. All subjects entered into the database will be included in subject data listings. 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.
- For analysis using nominal visits, data collected at unscheduled visits will be included in the subject listings but will not be included in by-visit summary tables, unless otherwise specified.
- Adverse events will be coded for summarization using the Medical Dictionary for Regulatory Activities (MedDRA® Version 22.0). Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary Global B3 (March 2019 Version).

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

6.2 Key Definitions

- Relative study day: A relative study day is a day of any study assessment relative to the first dose of study drug. The day of the first dose of the study drug will be considered as Day 1 (Visit Day 1 per protocol). Pre-treatment and on-treatment study days are numbered relative to the day of the first dose of study drug. The preceding day of the first dose of the study drug will be considered as Day -1 and next day after the first dose of the study drug will be considered as Day 2 and so on. There will not be a study day of Day 0.

- Baseline Value: Unless indicated otherwise, baseline value of a variable is defined as the last non-missing value on or prior to the first dose of study drug. If there are two values qualifying for the baseline value (e.g., FeNO measurements are taken in duplicate), the average of the two will be considered as the baseline value.

[redacted]

6.4 Pooling of Centers

Data from all the sites will be pooled together for the analyses, and there is no plan to summarize the data by center/site due to the small number of subjects enrolled at each site.

7 Non-Efficacy Data Summaries

7.1 Subject Disposition

Subject disposition data will be summarized using the Safety Population and will include the number and percent of subjects randomized, treated, and replaced. The number and percent of subjects completing treatment and study, and the number and percent of subjects discontinuing treatment and discontinuing the study, by primary reason for discontinuation. Subject enrollment will be summarized by study site. The continuous summary statistics will be presented for the 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 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 and summarized using continuous or categorical descriptive statistics as appropriate:

- Age (years)
- Sex
- Race
- Ethnicity
- Height (cm)
- Baseline Weight (kg)
- BMI (kg/m^2)
- Prior Asthma Exacerbations, n (%)
- Baseline FeNO measurement (ppb)
- Baseline Total Serum IgE (IU/mL)
- Baseline ALC ($10^9/L$)
- Baseline Total Eosinophil Count ($10^9/L$)
- Baseline ACQ-6
- [redacted]

[redacted]

- Baseline Pulmonary Function Test (PFT) results including pre-bronchodilator FEV1 (L/min) absolute, forced vital capacity (FVC) (L), FEV1/FVC (%), and FEV1

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

7.4 Baseline Disease Characteristics

Baseline disease characteristics include time from initial diagnosis of asthma to first dose date and will be presented using continuous summary statistics using the Safety Population. Time from diagnosis of asthma in years will be calculated as (year of first dose – year of diagnosis) + 1. Year of the date of diagnosis will always be present. A by-subject listing will also be created.

7.5 Medical and Surgical History

Medical and surgical history will be coded using MedDRA version 22.0. The number and percentage of subjects with a medical history event will be summarized descriptively using the Safety Population. The table will be sorted in descending order of MedDRA system organ class (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 March 2019 version). Medications will be summarized by Anatomic Therapeutic Class (ATC) level 2 terms (ATC2) and ATC level 4 (ATC4) terms using the Safety Population. Subjects will be counted only once for each ATC2 or ATC4 term in the event that they have multiple records of the same ATC level in the database. The table will be sorted by the descending order of frequencies of ATC2 terms and within each ATC2 by the descending order of frequencies in ATC4 terms 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 study drug. Prior medications will be summarized in a table and presented in a by-subject listing.

7.6.2 Concomitant Medications

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

Note that a medication can be both prior and concomitant depending on the start and stop date as related to the first dose date of study drug.

8 Efficacy

All efficacy analyses will be performed using the Efficacy Population. Results will be summarized in a table for the pooled Placebo group, EQ001 treatment group from each Cohort and pooled EQ001 treatment groups from all cohorts.

8.1 Secondary Endpoints Analyses

8.1.1 Change from Baseline in Serum IgE Levels

The actual and change from Baseline values of serum IgE levels will be presented using continuous descriptive summary statistics at each post-Baseline visit. Box and whisker plots of change from baseline by nominal post-baseline visit will also be created. A by-subject listing will be created.

8.1.2 Change from Baseline in Total Eosinophil Count

The actual and change from Baseline values of total eosinophil count will be summarized by visit in a table, using continuous descriptive summary statistics. Box and whisker plots of change from baseline by nominal post-baseline visit will also be created. A by-subject listing will also be created.

[redacted]

[redacted]

8.1.4 Change from Baseline in Prebronchodilator Pulmonary Function Test Parameters

Following pulmonary function test parameters recorded during the site visit using Masterscope will be summarized: FEV1 (L), FEV1 % PredictedFVC (L), FEV1/FVC (%),and PEFR (L/min).

The actual and change from Baseline values of the above parameters will be summarized by visit in a table, using continuous descriptive summary statistics. Box and whisker plots of change from baseline by nominal post-baseline visit will also be created for each of the above parameters. A by-subject listing will also be created.

8.1.5 Change from Baseline in FeNO

The level of FeNO will be measured in each subject at every study visit (other than Day 4) using a standardized single-breath FeNO test. Subjects will inhale to total lung capacity through the NIOX MINO® Airway Inflammation Monitor and then exhale for 10 seconds at 50 mL/sec (assisted by visual and auditory cues). The obtained value will be recorded, and the process will be repeated for a total of 2 measurements. For analysis purposes, the mean of the 2 non-missing measurements will be taken. The actual and change from Baseline values of FeNO will be summarized by visit in a table, using continuous descriptive summary statistics (n, mean, standard deviation (SD), median, minimum, and maximum) at Baseline and each post-Baseline visit. Box and whisker plots of change from baseline by nominal post-baseline visit will also be created. A by-subject listing will also be created.

8.1.6 Change from Baseline in Peak Expiratory Flow Rate and FEV1 Recorded on AM3 Device

Home pulmonary function testing to measure peak expiratory flow rate (PEFR) and FEV1 will be performed twice daily, in the morning upon awakening and in the evening before bedtime, using a peak

[redacted]

flow meter. Subjects perform 3 successive peak flow maneuvers at session to record FEV1 and PEFR; highest of the 3 values will be used in the analysis of each variable.

The diurnal variation of PEFR will be the amplitude percentage mean defined as: Diurnal variation in PEFR (%) = 100 x |Evening-Morning|/mean of the Morning and Evening values, where |.| indicates absolute value.

For data summarization purposes, an average value of the variable of interest (FEV1, PEFR, and Diurnal Variation of PEFR) will be calculated by study week (and for morning and evening for FEV1 and PEFR). Study Days 1 to 7 will be designate as Study Week 1, Study Days 8 to 14 will be Study Wek 2, etc. Similarly Study Days -7 to -1 will be assigned Study Week -1, Study Days -14 to -8 will be Study Week -2 etc. For this summary, baseline value will be considered as the average value calculated for Study Week -1. For example, baseline PEFR in the morning will be the average of the morning PEFR values recorded on Study Week -1 (i.e., Study Days -7 to -1).

The actual and change from Baseline values of PEFR and FEV1 assessed in the morning and evening and the calculated diurnal variation of PEFR, will be summarized by Study Week in a table, using continuous descriptive summary statistics. A by-subject listing will also be created.

8.1.7 Change from Baseline in ACQ-6 score

The actual and change from Baseline in the ACQ-6 score will be summarized by visit using continuous descriptive summary statistics (n, mean, standard deviation (SD), median, minimum, and maximum) at Baseline and each post-Baseline visit. Box and whisker plots of change from baseline by nominal post-baseline visit will also be created. A by-subject listing will also be created.

The ACQ-6 score will be derived by taking the mean of the values of the 6 questions, each question is on a 7-point Likert scale (0=totally controlled, 6=severely uncontrolled).

The number and percent of subjects showing an improvement of ≥ 0.5 points (a minimally important difference, MID) from Baseline to each post-Baseline visit (i.e. the post-Baseline score – the Baseline score is ≤ -0.5) will be summarized by visit. Number and percentage of subjects achieving MID in ACQ6 score at any visit will also be summarized.

An ACQ-6 score of ≤0.75 indicates well-controlled asthma, >0.75-<1.5 indicates partially controlled asthma and ≥1.5 indicates uncontrolled asthma. The number and percent of subjects belonging to each of the above categories will also be summarized by visit.

8.1.8 Time to First Asthma Exacerbation (any severity)

Time to first exacerbation in days is defined as time from the first dose date to the first observed exacerbation date and will be calculated as:

Time to first exacerbation (days) = date of first exacerbation – date of first dose + 1

Subjects who do not experience any exacerbation will be censored at the last contact date of the subject.

Time to first exacerbation will be analyzed using Kaplan-Meier methodology (Kaplan & Meier, 1958). If estimable, the median time to first exacerbation, 25th and 75th percentiles with 2-sided 95% confidence intervals (CIs) will presented. Number and percentage of subjects with exacerbation events will also be presented.

8.1.9 Asthma symptoms, use of controller (standard) and rescue medications, nighttime awakening due to asthma and asthma-related activity limitations – Responses to a Questionnaire (as recorded on an eDiary)

Subjects will be recording their responses to 6 morning questions and 9 evening questions daily related to their Asthma. The questions are as follows (MQ=Morning Question, EQ=Evening Question) with a brief description of possible responses:

[redacted]

[redacted]

8.1.10 Annualized Rate of Asthma Exacerbations (of any severity)

The number of asthma exacerbations will be calculated for each subject. A follow-up duration in years for each subject will be calculated as:

Follow-up duration (years) = (last contact date – date of first dose + 1) / 365.25, rounded to 2 decimal places.

The annualized rate of asthma exacerbations i.e. number of asthma exacerbation per subject year will be calculated as total number of asthma exacerbations for all subjects / total follow-up duration in years for all subjects.

Rate of asthma exacerbation will be tabulated, and a by-subject listing of all exacerbations will be created.

In addition, duration of asthma exacerbations in days is calculated as (the end date – the start date)+1. If asthma exacerbation is ongoing, the missing end date will be imputed as last known visit date. If a subject has multiple asthma exacerbations, each event will be counted separately.

The primary criterion for asthma exacerbations will also be summarized by criterion in number and frequency format. All asthma exacerbations will be included in this summary, a subject may have more than one exacerbation event.

[redacted]

10 Safety

All safety analyses will be performed using the Safety Population.

10.1 Extent of Exposure

Treatment exposure will be determined by duration of treatment and extent of exposure to study drug. Measures of extent of exposure includes the screening weight normalized average dose of study drug (mg) 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/Placebo prepared and volume administered at each dosing visit. As described in the Pharmacy Manual, volume prepared at a dosing visit is calculated 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 for each cohort.

Cumulative volume administered will be summarized by continuous summary statistics by treatment group for each cohort.

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 for each cohort.

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. Dose limiting toxicity (DLT) is defined as any study drug related AE of CTCAE severity Grade of 3 or higher. The occurrence of Grade 3 lymphopenia is classified as a DLT only if present with concomitant infection at least possibly related to the underlying lymphopenia; Grade 4 or higher severity lymphopenia is classified as a DLT. 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 22.0 and graded using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 severity grading scale, as annotated below:

- **Grade 1: Mild**; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- **Grade 2: Moderate**; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL). Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
- **Grade 3: Severe or medically significant**, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL. Self-care ADL refers to bathing, dressing and undressing, feeding oneself, using the toilet, taking medications, and not being bedridden.
- **Grade 4: Life-threatening** consequences; urgent intervention indicated.
- **Grade 5: Death** related to the AE.

For the purpose of the summaries AEs with missing relatedness will be considered to be related to study drug.

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 once at the SOC level and once at PT level. For summaries by SOC, PT, and CTCAE severity grade, a subject will be counted once at highest observed severity grade within an SOC and PT. 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.

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 the end of treatment
  - Any TEAE leading to death
  - Any dose limiting toxicity (DLT)
  - [redacted]

[redacted]

- TEAEs by SOC and PT
- TEAEs Related to Study Drug
- TESAEs by SOC and PT

- TEAEs with Severity Grade ≥ 3 by SOC and PT
- TEAEs by SOC, PT and Worst Severity Grade
- TESAEs Related to Study Drug
- TEAEs Leading to End of Treatment by SOC and PT
- TEAEs Leading to Death by SOC and PT
- Dose Limiting Toxicities by SOC and PT

A by-subject listing of AE data will also be created. In general, adverse events occurring within 30 days after last dose of study drug will be included in the AE summaries but 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

[redacted]

Laboratory parameters that can be graded using CTCAE will be graded and the following subject incidence summaries will be produced:

- Worst post-Baseline severity grade
- Shift summary of Baseline grade to worst post-Baseline severity grade

Line plots selected laboratory parameter values will be produced by plotting actual values against the sample collection study day for individual subjects in Pooled Placebo, and each EQ001 Dose Group. [redacted]

A by-subject listing will also be created. In all laboratory data summaries and listings results reported in SI units will be used.

10.5 Pregnancy

Pregnancy testing in women of childbearing potential (WOCBP) 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 57, and at Day 85 visit.

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 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

Respiratory Rate:
- < 8 breaths per minute
- > 20 breaths per minute

A by-subject listing will also be created. Vital signs will be collected pre-dose and 30 minutes after the injection at each dosing visit and will be listed in a by-subject listing.

10.7 Electrocardiogram (ECG)

A standard 12-lead ECG will be performed at Screening, Day 1, Day 8, Day 57 and Day 85. 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 parameters will be summarized by visit presented in a table, using continuous descriptive summary statistics at Baseline and each post-Baseline visit.

The number and percentage of subjects with worst (highest) increase in QTcF from baseline to post-baseline will be summarized for the following categorical increases:

- ≤ 0 ms
- > 0-≤ 30 ms
- > 30- ≤ 60 ms
- > 60 ms

The frequency and percentage of overall interpretation of ECGs will also be summarized by visit.

A by-subject listing will also be created.

10.8 Physical Examination

A complete physical examination will be done at Screening. A targeted physical exam will be done at all other scheduled visits except Day 4. All clinically significant abnormalities will be recorded either as medical history or adverse event based on the occurrence of the abnormality prior to or after the Baseline visit.

Physical examination findings prior to the first dose of study drug administration will be recorded on the medical history eCRF; clinically significant findings after the first study drug dose will be recorded as AEs.

At a minimum, the complete physical examination will include assessments of the skin, head and neck, lungs, cardiovascular (CV) system, abdomen, thyroid, and extremities. A targeted physical examination will include assessment of the lungs and any new subject complaints or changes from baseline.

A by-subject listing will be created for physical examination data.

[redacted]

[redacted]

[redacted]

12 Changes from Analysis Planned in Protocol

There are no changes from the analyses planned in the protocol.

[redacted]

[redacted]

[redacted]