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
NCT Number:	NCT04007198
Document Version Date:	03 February 2021

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Clinical Study Protocol

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 [redacted]
Development Phase:	Phase 1b
Sponsor's Responsible Medical Officer:	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

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2 SYNOPSIS AND SCHEDULE OF EVENTS

2.1 Synopsis

Title of Study Protocol: 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

Name of Sponsor Company:
Equillium AUS Pty Ltd
[redacted]

Name of Finished Product: EQ001 (itolizumab; Bmab 600)

Phase of Development: Phase 1b

Objectives:

Primary Objective

Characterize the safety and tolerability of EQ001 (itolizumab)

Secondary Objectives

1. Characterize the pharmacokinetics (PK) of EQ001
[redacted]
4. Characterize the clinical activity of EQ001

Endpoints:

Primary Endpoints

Safety and tolerability of EQ001, as assessed by treatment-emergent adverse events (TEAEs), treatment emergent serious adverse events (TESAEs), clinical laboratory values, ECGs, vital signs and physical examinations

Secondary Endpoints

1. Pharmacokinetics of EQ001 will be assessed [redacted]
4. Clinical activity of EQ001, as assessed by the following variables:
   a. Change from baseline in prebronchodilator FEV1
   b. Change from baseline in fractional exhaled nitric oxide (FeNO)
   c. Change in peak expiratory flow rate
   d. Change from baseline in Asthma Control Questionnaire (ACQ-6) score
   e. Time to first exacerbation (any severity)

f. 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)
g. Annualized rate of asthma exacerbations (of any severity)

Study Design:

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 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) to characterize the safety, tolerability, PK, PD, and 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.

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.

The study will be conducted in the following 3 defined periods:

1. **Screening Period**: Will begin when the informed consent form (ICF) is signed. During this period, the subject will undergo baseline assessments to determine eligibility for study participation. The subject will complete an electronic diary (eDiary) to record asthma symptoms, AM and PM peak expiratory flow rate measurements, use of controller and rescue medication, nighttime awakening due to asthma and asthma-related activity limitations. The Screening Period duration will be up to 4 weeks; it will end after at least 2 weeks of baseline assessments have been conducted and all studies required to meet eligibility have been completed. If a subject meets all eligibility criteria (including documented compliance with eDiary completion, peak flow monitoring and adherence to their standard-of-care [SoC] meds), they will be enrolled into the study.
2. **Treatment Period**: Will begin on Day 1 with the first study drug dose and have a duration of 8 weeks. During the Treatment Period, 5 doses of study drug will be administered SC, 1 dose each on Study Days 1, 15, 29, 43, and 57. Subjects will return to the study site for follow-up evaluations according to the Schedule of Events (SOE). Following the last dose of study drug, subjects will enter the Safety Follow-up Period.
3. **Safety Follow-up Period**: Will have a 4-week duration and conclude 4 weeks after the final study drug dose with the End-of-Study (EOS) Visit on Day 85.

Successive cohorts that are randomized in a 3:1 ratio (active:placebo) will be enrolled. Subjects will be treated Q2W for 8 weeks and followed for a total of 12 weeks after the initial study drug dose on Day 1. [redacted] Randomization in the next dose cohort will not begin until the Data Review Committee (DRC) review of all available safety data from all subjects supports escalation to the next dose level. The MTD of EQ001 in subjects with moderate-to-severe uncontrolled asthma will be determined based on all available data, including safety, tolerability, PK, PD, and clinical activity data.

[redacted]

If subjects do not complete the required study visits or discontinue from the study for any reason, they will be asked to return to the clinical study site for an Early Termination (ET) Visit, as described in the SOE.

Study Procedures:

While on study, all subjects will take their standard medications for their moderate-to-severe asthma, as prescribed by the study physician. These standard medications will consist of a moderate- or high-dose inhaled corticosteroid (CS) and one or more additional controller medications (eg, inhaled long-acting beta agonist [LABA], or anticholinergic). Leukotriene antagonists (LTAs) may also be used as controller medications. Allergen immunotherapy at a stable dose is permitted, but monoclonal antibody (mAb) therapeutics are prohibited. Doses of all controller medications must be stable for 4 weeks including the duration of the Screening Period.

Study Day 1 (Baseline) assessments will include the following: a targeted physical examination, vital signs, laboratory tests, anti-EQ001 antibody test, AE and ACQ-6 monitoring, recording concomitant medications, [redacted] pulmonary function testing, and measurement of fractional exhaled nitric oxide (FeNO). If appropriate, repeat assessments can be performed within the Screening Period with approval from the Medical Monitor, as needed.

EQ001 or placebo doses will be administered in the clinic; [redacted]

All subjects will undergo the following procedures at every visit except Day 4 (Screening; Study Day 1 [Baseline]; and Study Days 8, 15, 29, 43, 57, and 85): Complete (Screening) or interval (all other study days) medical and surgical histories; complete (Screening) or targeted (all other study days) physical examination; vital signs; hematology and serum chemistry laboratory tests; pulmonary function test; FeNO; AE monitoring (including assessments for injection site-related and hypersensitivity reactions); ACQ-6; and recording of concomitant medications and treatments. EQ001 serum levels will be measured at every visit except Screening. [redacted]

Pregnancy testing for women of childbearing potential (WOCBP) will be assessed at Screening, Study Day 1 (Baseline), and on Study Days 57 and 85. Electrocardiograms will be performed at Screening, Baseline, and on Study Days 8, 57, and 85.

Early Termination or Unscheduled Visit:

Subjects who receive ≥ 1 dose of study drug should be encouraged to complete all study visits. If subjects do not complete all study visits, or terminate early from the study, they will be asked to return to the study site for an Early Termination (ET) Visit within 28 days of the last dose of study drug administration. [redacted] In addition, if at any time up to Study Day 85 (or ET) a subject has an unscheduled study visit, all procedures that were conducted at that visit will be collected in the electronic case report form (eCRF) as an unscheduled visit.

[redacted]

[redacted]

Study drug should be administered so that there are at least 12 days between doses.

Data Review Committee, Dose-Limiting Toxicity, and Stopping Criteria:

The DRC will periodically review all available clinical and laboratory safety data during the study. When the last subject in a cohort completes the Day 29 assessments, the DRC will convene and make recommendations regarding cohort advancement and study continuation, discontinuation, or modification.

Dose-limiting toxicity is defined as any study drug-related adverse event (AE) of National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 ≥ Grade 3 severity (including ≥ Grade 3 injection-related reaction or other clinical finding associated with hypersensitivity related to study drug) and not related to underlying asthma. The occurrence of Grade 3 lymphopenia will be classified as a DLT only if present with concomitant infection at least possibly related to the underlying lymphopenia; Grade 4 or higher severity of lymphopenia will be classified as a DLT. If 2 subjects experience DLTs in a single cohort (in the DLT assessment period; Study Days 1-29), the DRC will convene to review all available, unblinded safety, PK, PD, and clinical activity data. After its evaluation, the DRC may recommend study continuation (with or without modification) or termination of dose escalation. If dose escalation is terminated, the next-lower dose may be declared the MTD. Alternatively, an additional cohort at an intermediate dose may be added to better define the MTD.

Subject Stopping Criteria:

Dosing of EQ001 will be permanently discontinued in a subject if any of the following occurs:

- Any DLT (see definition above)
- Subject's consent withdrawn
- Investigator or Sponsor decides that the subject will not benefit from further investigational product (IP)
- Pregnancy
- Subject is unable to comply with the study requirements
- Sponsor terminates the study
- A regulatory authority mandates a study dosing cessation
- Subject experiences a DLT anytime during the treatment period

Number of Subjects Planned:
Up to 40 subjects with moderate-to-severe uncontrolled asthma are planned to be enrolled in the study.

Inclusion Criteria:

Subjects will be required to meet all of the following inclusion criteria in order to be eligible for study enrollment:

1. Is male or female, age ≥ 18 and ≤ 75 years
2. Has a documented clinical diagnosis of moderate-to-severe uncontrolled asthma requiring moderate- or high-dose inhaled CS (ICS; ≥ 250 mcg of fluticasone propionate twice daily or equipotent ICS daily dosage to a maximum of 2000 mcg/day of fluticasone propionate or equivalent) and one or more additional controller medications (inhaled LABA or anticholinergic or LTA) for ≥ 3 months, with a stable dose ≥1 month prior to the initial Screening Visit

3. Has a prebronchodilator forced expiratory volume in 1 second (FEV1) ≥ 40% and ≤ 90% of predicted value during the Screening Period, despite use of a moderate- or high-dose ICS and one or more additional controller medications (inhaled LABA or anticholinergic or LTA)
4. Has a history of clinically diagnosed asthma, which could include a history of FEV1 reversibility and/or positive bronchial challenge test
5. Has a history of ≥ 1 clinically significant asthma exacerbation (see definition in Section 10.2.2) prior to the initial Screening Visit, despite use of a moderate- or high-dose ICS and one or more additional controller medications at the time the exacerbation(s) occurred

[redacted]

Exclusion Criteria:

Subjects will be ineligible for enrollment in the study if they meet any of the following criteria:

1. Is a current or former smoker with a smoking history of ≥10 pack-years (number of pack-years = number of cigarettes per day/20 × number of years smoked; a *former smoker* is defined as a subject who stopped smoking ≥ 6 months prior to the Screening Visit)
2. Has a body mass index ≥ 36 kg/m^2
3. Has a documented history or radiological evidence of a clinically important lung condition other than asthma (eg, α1-antitrypsin deficiency, bronchiectasis, cystic fibrosis, primary ciliary dyskinesia, pulmonary fibrosis, allergic bronchopulmonary mycosis, or lung cancer)
4. Has a respiratory tract infection (RTI) within 4 weeks before the initial Screening Visit, or during the Screening Period (these subjects may be re-screened following complete resolution of their RTI)
5. Has an asthma exacerbation within 4 weeks before the initial Screening Visit, or during the Screening Period (these subjects may be re-screened following complete resolution of their exacerbation)
6. Has a diagnosis of currently active malignancy; subjects with a medical history of basal cell carcinoma, localized squamous cell carcinoma of the skin, or in situ carcinoma of the uterine cervix are eligible; subjects with a medical history of other malignancies are eligible if the subject is in remission and curative therapy was completed ≥ 2 years prior to the initial Screening Visit
7. Has a history or presence of clinically concerning cardiac arrythmias, atrial fibrillation, New York Heart Association Class III or IV heart failure, or prolonged QT or corrected QT interval > 500 milliseconds (ms) at the Screening Visit
8. Has any disorder (including, but not limited to, cardiovascular [CV], gastrointestinal [GI], hepatic, renal, neurological, musculoskeletal, infectious, endocrine, metabolic, hematological, psychiatric, or major physical impairment) that is not stable in the opinion of the investigator and/or could:
   a. Affect the subject's safety
   b. Influence the findings of the study or data interpretation
   c. Impede the subject's ability to complete the study
9. Has undergone bronchial thermoplasty

10. Has a history of substance abuse (including alcohol) that may, in the investigator's judgment, increase the risk to the subject of participation in the study
11. Has used monoclonal antibody (mAb) therapy for the management of asthma or any other condition within 3 months prior to the initial Screening Visit (these subjects may be re-screened following the 3 month period)
12. Has required an oral corticosteroid burst within 1 month prior to the initial Screening Visit or during the Screening Period (these subjects may be re-screened following the 1 month period); maintenance oral corticosteroids ≤ 10 mg/d prednisone or equivalent is permitted

[redacted]

Investigational Products, Dosage, and Mode of Administration:

The investigational product (IP) is EQ001 (itolizumab [Bmab 600]), a humanized recombinant immunoglobulin G1 (IgG1) monoclonal antibody (mAb) that selectively targets the extracellular scavenger receptor cysteine-rich (Sc) membrane-distal domain 1 of human CD6. [redacted].

The placebo is comprised of the same excipients at the same concentrations as in the active drug. It will be provided as a preservative-free sterile, clear, colorless solution in a single-use vial for SC administration.

Study drug and placebo will be administered by SC injection.

[redacted]

Criteria for Evaluation:

Safety:

Safety will be assessed by physical examinations, vital signs, 12-lead ECGs, laboratory tests [redacted] and AE monitoring. [redacted]

Pharmacokinetics:

Serum for PK sampling will be collected at specified time points, as outlined in the Schedule of Events and will be descriptively summarized by the nominal assessment time point for each dose. [redacted]

[redacted]

Efficacy:

Clinical activity of EQ001 will be assessed in subjects with moderate-to-severe uncontrolled asthma using the change from baseline in prebronchodilator FEV1, FeNO, peak flow rate, ACQ-6 scores, time to first exacerbation (of any severity), rescue medication use, and annualized rates of asthma exacerbations (of any severity).

Statistical Methods:

All safety, [redacted] and efficacy endpoints will be tabulated using descriptive statistics; data from all placebo subjects will be pooled. Data from EQ001-treated subjects will be presented by dose and combined (a total of up to 30 subjects). If data permits, differences between the treatment groups and 95% confidence intervals for the difference will be presented.

*Analysis Populations***:**

The study consists of the following analysis populations:

Safety Population: Consists of all subjects who receive any study drug.

[redacted].

Efficacy Population: Consists of those subjects in the safety population who have at least 1 post-treatment clinical activity assessment.

The primary analyses of safety and efficacy endpoints will be based on the actual administered treatment if the administered treatment differs from the randomized treatment.

[redacted]

*Safety Analyses***:**

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) v 20.1, or the current version for the purposes of summarization. Incidence of treatment-emergent AEs (TEAEs), treatment-emergent serious AEs (TESAEs), TEAEs leading to study drug discontinuation, and TEAEs with an outcome of death will be summarized by MedDRA system organ class (SOC) and preferred term (PT). Adverse events will also be summarized by worst severity grade and causality relationship to study drug. [redacted]

Clinical laboratory data will be descriptively summarized, including observed values at collection time points and change from baseline. All laboratory parameters that can be graded using CTCAE v5.0 will be graded. For selected parameters, the following summaries may be produced:

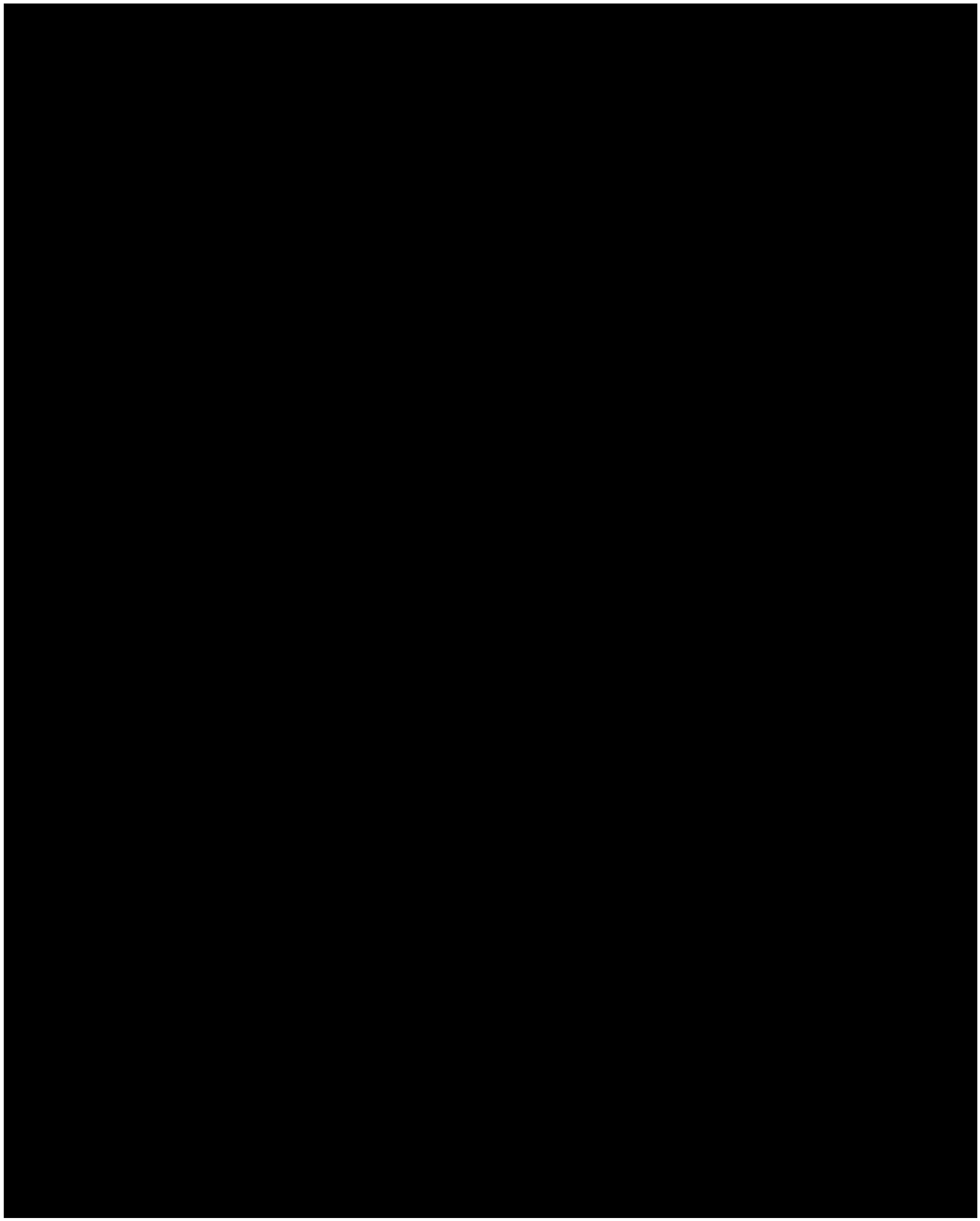
- Worst post-baseline severity grade
- Shift summary of baseline grade to worst post-baseline severity grade

Safety evaluations may also include changes in the subject's physical examination findings, vital signs, and ECG results. The incidence of treatment-emergent anti-EQ001 binding and neutralization antibody will be reported.

PK Analyses:

PK data resulting from SC administration of EQ001 in this study will be compared with those of intravenous (IV) administration in healthy volunteers and subjects with other medical conditions in other clinical studies to the extent possible.

[redacted]



3 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

ACQ	Asthma Control Questionnaire
ADA	anti-drug antibody
ADD	Asthma Daily Diary
AE	adverse event
AESI	adverse event of special interest
ALC	absolute lymphocyte count
ALCAM	activated leukocyte cell adhesion molecule
ALT	alanine aminotransferase
ANC	absolute neutrophil count
AST	aspartate aminotransferase
ATS	American Thoracic Society
BD	bronchodilator
Bmab 600	itolizumab; EQ001
BMI	body mass index
BUN	blood urea nitrogen
CBC	complete blood count
CFR	Code of Federal Regulations
Cl	Clearance
C_{max}	maximum serum drug concentration
CS	corticosteroid
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DBP	diastolic blood pressure
DLT	dose-limiting toxicity
DNA	deoxyribonucleic acid
DRC	Data Review Committee
EAE	experimental autoimmune encephalomyelitis
ECG	electrocardiogram
eCRF	electronic case report form
eDiary	electronic diary
EOS	End of Study, or End-of-Study (*adj*)
ERS	European Respiratory Society
ET	early termination
FDA	Food and Drug Administration
FeNO	fractional exhaled nitric oxide
FEV1	forced expiratory volume in 1 second
FVC	forced vital capacity
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
GI	gastrointestinal(ly)

GINA	Global Initiative for Asthma
HBV	hepatitis B virus
Hct	Hematocrit
HCV	hepatitis C virus
Hgb	Hemoglobin
HIV	human immunodeficiency virus
HBsAg	hepatitis B virus surface antigen
IB	investigator's brochure
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICS	inhaled corticosteroids
IEC	Independent Ethics Committee
IgE	immunoglobulin E
IgG1	immunoglobulin G1
IL-	interleukin-
IM	investigators meeting
INF	Interferon
IP	investigational product
IV	intravenous(ly)
IWRS	Interactive Web Response System
LABA	long-acting beta agonist
LDH	lactate dehydrogenase
LTA	leukotriene antagonist
mAb	monoclonal antibody
MedDRA	*Medical Dictionary for Regulatory Activities*
MTD	maximum tolerated dose
NAB	neutralizing anti-drug antibody
NCI	National Cancer Institute
OVA	Ovalbumin
PBMC	peripheral blood mononuclear cell
PC_{20}	provocative concentration causing a 20% decrease
PD	pharmacodynamic(s)
PEFR	peak expiratory flow rate
PFT	pulmonary function test
Ph.Eur.	*European Pharmacopoeia*
PK	pharmacokinetic(s)
PT	preferred term
Q2W	every 2 weeks
RBC	red blood cell
RNA	ribonucleic acid

RTI	respiratory tract infection
SABA	short-acting beta agonist
SAE	serious adverse event
SAP	Statistical Analysis Plan
SC	subcutaneous(ly)
Sc	scavenger receptor cysteine-rich
SIV	site initiation visit
SOC	system organ class
SoC	standard-of-care
SOE	Schedule of Events
SSDL	site signature and delegation log
SWFI	sterile water for injection
$t_{½}$	half-life
TCR	T-cell receptor
TEAE	treatment-emergent adverse event
T_{eff}	effector T cell
TESAE	treatment-emergent serious adverse event
Th	T helper
T_{max}	time to maximum concentration
TNF	tumor necrosis factor
USP	*United States Pharmacopeia*
US	United States
V_d	volume of distribution
WBC	white blood cell
WOCBP	women of childbearing potential

4 INTRODUCTION

4.1 Background

Asthma is a chronic inflammatory disease of the airways characterized by airway hyperresponsiveness, acute and chronic bronchoconstriction, airway edema, and mucus plugging. The inflammatory component of asthma involves many cell types, including mast cells, eosinophils, T-lymphocytes, neutrophils, and epithelial cells and their biological products. For most asthma patients, a regimen of controller therapy and reliever therapy provides adequate long-term control. However, 10% to 15% of asthma patients have symptomatic disease despite maximum recommended treatment. These patients account for approximately 60% of the total health care costs for patients who have asthma[redacted]

Asthma had long been considered a single disease characterized by airway inflammation and predominantly attributed to Type 2 inflammatory processes. More recent analyses of large cohorts have resulted in the identification of several asthma phenotypes and endotypes, including subgroups of patients for whom disease is driven predominantly by non-Type 2 mechanisms [redacted]

4.2 Itolizumab

Itolizumab (Bmab 600; EQ001) is a humanized recombinant immunoglobulin G1 (IgG1) monoclonal antibody (mAb) that selectively targets the extracellular scavenger receptor cysteine-rich (Sc) membrane-distal domain 1 of human CD6 [redacted] a co-stimulatory membrane glycoprotein associated with T cell modulation and implicated in several autoimmune and inflammatory diseases, including psoriasis, multiple sclerosis, rheumatoid arthritis, and Sjogren's disease [redacted]

EQ001 binds to domain-1 of human CD6 and is believed to sterically hinder the optimal engagement of activated leukocyte cell adhesion molecule (ALCAM) with domain-3, modulating both co-stimulation and trafficking without causing T cell depletion. [redacted]

[redacted]

[redacted]

4.4 Clinical Findings

[redacted]

Three clinical studies of T1h have been performed in India in patients with rheumatoid arthritis and chronic plaque psoriasis. A total of 368 patients have been exposed to T1h to date in clinical studies at doses of 0.1 mg/kg to 1.6 mg/kg. T1h has demonstrated preliminary evidence of efficacy in rheumatoid arthritis and definitive evidence of efficacy in plaque psoriasis, leading to approval of itolizumab in India for the treatment of plaque psoriasis. A conditional approval for itolizumab for the treatment of plaque psoriasis was also granted by Centro de Immunologia Molecular, Cuba on 16 May 2014.

[redacted]

[redacted]

4.5 Rationale for Evaluating EQ001 for the Treatment of Patients with Moderate-to-Severe Uncontrolled Asthma

Patients with severe asthma make up only 10% to 15% of the population of adults with asthma, but account for 60% of the healthcare costs attributable to asthma [redacted] Currently available therapeutics for asthma include corticosteroids, beta agonists, anticholinergics, leukotriene antagonists, cromones, theophylline, and a variety of targeted biologics [redacted]

4.6 Rationale for Selection for Starting Dose of EQ001

[redacted]

[redacted] Clinical experience with itolizumab in patients with psoriasis and rheumatoid arthritis has demonstrated the safety and tolerability of IV doses ranging from 0.1 mg/kg to 1.6 mg/kg, administered chronically as a bimonthly infusion. A Phase 1 study in healthy volunteers with EQ001 administered SC demonstrated safety at single doses as high as 3.2 mg/kg, with a half-life that supports a dosing interval of 2 weeks. The present study is designed to assure adequate trough levels while assessing the potential for accumulation in this short-term study, the first to evaluate multiple SC dosing of EQ001. These clinical data support the proposed clinical study design with a starting SC dose of 0.8 mg/kg itolizumab.

5 STUDY OBJECTIVES

5.1 Primary Objective

Characterize the safety and tolerability of EQ001 (itolizumab)

5.2 Secondary Objectives

1. Characterize the pharmacokinetics (PK) of EQ001
2. [redacted]
3. [redacted]
4. Characterize the clinical activity of EQ001

6 STUDY ENDPOINTS

6.1 Primary Endpoints

Safety and tolerability of EQ001, as assessed by treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), clinical laboratory values, ECGs, vital signs, and physical examinations

6.2 Secondary Endpoints

1. Pharmacokinetics of EQ001 will be assessed by descriptively summarizing the PK [redacted]

4. Clinical activity of EQ001, as assessed by the following variables:

   a. Change from baseline in prebronchodilator FEV1
   b. Change from baseline in fractional exhaled nitric oxide (FeNO)
   c. Change in peak expiratory flow rate
   d. Change from baseline in Asthma Control Questionnaire (ACQ-6) score
   e. Time to first exacerbation (any severity)
   f. 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)
   g. Annualized rate of asthma exacerbations (of any severity)

7 INVESTIGATIONAL PLAN

7.1 Overall Study Design and Plan

This is a phase 1b randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, PK, PD, and clinical activity of EQ001 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 in order 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 SC every 2 weeks (Q2W) for a total of 5 doses. Subjects will be randomized in a 3:1 ratio (active:placebo) to characterize the safety, tolerability, [redacted] and 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 to increase the number of subjects in the pooled placebo cohort to 10; therefore, the study may enroll as many as 40 total subjects.

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.

The study will be conducted in the following 3 defined periods :

1. *Screening Period:* Will begin when the informed consent form (ICF) is signed. During this period, the subject will undergo baseline assessments to determine eligibility for study participation. The subject will complete an electronic diary (eDiary) to record symptoms of asthma, AM and PM peak expiratory flow rates, and use of controller and rescue medications, nighttime awakening due to asthma and asthma-related activity limitations. The Screening Period duration will be up to 4 weeks; it will end after at least 2 weeks of baseline assessments have been conducted and all studies required to meet eligibility have been completed. If a subject provides written informed consent and meets all eligibility criteria (including documented compliance with eDiary completion, peak flow monitoring and adherence to their standard-of-care [SoC] medications), they will be enrolled into the study.
2. *Treatment Period:* Will begin on Day 1 with the first study drug dose and have a duration of 8 weeks. During the Treatment Period, 5 doses of study drug will be administered SC, 1 dose each on Study Days 1, 15, 29, 43, and 57. Subjects will return to the study site for

follow-up evaluations according to the Schedule of Events (SOE, Section 2.2). Following the last dose of study drug, subjects will enter the Safety Follow-up Period.

3. *Safety Follow-up Period:* Will have a 4-week duration and conclude 4 weeks after the final study drug dose with the End-of-Study (EOS) Visit on Study Day 85.

Successive cohorts that are randomized in a 3:1 ratio (active:placebo) will be enrolled. Subjects will be treated Q2W for 8 weeks and followed for a total of 12 weeks after the initial study drug dose on Day 1. [redacted] The MTD of EQ001 in subjects with moderate-to-severe uncontrolled asthma will be determined based on all available data, including safety, tolerability, PK, PD, and clinical activity data.

[redacted]

If subjects do not complete the required study visits or discontinue from the study for any reason, they will be asked to return to their clinical study site for an Early Termination (ET) Visit, as described in the SOE (Section 2.2).

Dose-limiting toxicity is defined in Section 7.2.1. If 2 subjects experience dose-limiting toxicities (DLTs) in a single cohort in the DLT assessment period, the DRC will convene to review all available, unblinded safety, [redacted] clinical activity data. After its evaluation, the DRC may recommend continuation of the study (with or without modification) or termination of dose escalation. If dose escalation is terminated, the next-lower dose may be declared the MTD. Alternatively, an additional cohort at an intermediate dose may be added to better define the MTD.

The study will enroll subjects with an initial clinical diagnosis of moderate-to-severe uncontrolled asthma.

7.2 Data Review Committee, Dose-Limiting Toxicity, and Stopping Criteria

The DRC, comprised of the independent statistician, DRC coordinator, Equillium representatives and 3 independent asthma clinicians, will provide periodic review of the safety data generated by the clinical study. The DRC will be unblinded. A Sponsor representative will also serve as a non-voting member of the DRC to facilitate Sponsor internal planning. Minutes of all DRC meetings will be archived for inclusion in the Trial Master File.

The DRC Chair will be informed by the Sponsor of the potential need for ad hoc meetings and will coordinate such meetings. A formal DRC Charter will be prepared.

The DRC will review all available clinical and laboratory safety data at defined intervals during the study. It will make recommendations regarding cohort advancement and continuation, discontinuation, or modification of the study.

Additional subjects may be enrolled in a cohort if considered necessary by the DRC to further characterize drug safety, tolerability, or efficacy. Also, the DRC may recommend modification of the doses to be evaluated, to not initiate specific dose cohorts, to initiate additional dose cohorts, or to terminate the study if it is deemed necessary. Appropriate regulatory approvals will be obtained prior to initiation of any recommended changes by the DRC, as required.

7.2.1 Dose-Limiting Toxicities

[redacted]

If 2 subjects experience DLTs in the DLT assessment period in a single cohort, the DRC will convene to review all available, unblinded safety, [redacted] and clinical activity data. After its evaluation, the DRC may recommend continuation of the study (with or without modification) or termination of dose escalation. If dose escalation is terminated, the next-lower dose may be declared the MTD. Alternatively, an additional cohort at an intermediate dose may be added to better define the MTD.

[redacted]

[redacted]

7.3 Rationale for Study Design

This study has a double-blinded, placebo-controlled design. Patients and investigators will remain blinded for the duration of the study. Site staff will remain blinded, with the exception of the unblinded pharmacist. The Sponsor will be unblinded, including the Sponsor representatives to the DRC. Subjects will be randomized in a 3:1 ratio (active:placebo) to characterize the safety, tolerability, [redacted] and clinical activity of ascending SC doses of EQ001 and determine the MTD.

After the MTD determination and at the Sponsor's discretion, the MTD cohort may be repeated to increase to 12 the number of subjects receiving the MTD and increase to 10 the number of subjects in the pooled placebo cohort.

7.4 Study Duration

Each subject who completes the study will undergo up to 4 weeks for Screening, 8 weeks of treatment and 4 weeks of follow-up, for a total of up to 16 weeks on study.

8 STUDY POPULATION

8.1 Study Population

Each cohort will enroll unique subjects who may not be treated in more than 1 cohort. Subjects will have moderate-to-severe uncontrolled asthma.

[redacted]

8.3 Inclusion Criteria

Potential subjects will be required to meet all of these inclusion criteria in order to be eligible for study enrollment:

1. Is male or female, age ≥18 and ≤ 75 years
2. Has a documented clinical diagnosis of moderate-to-severe uncontrolled asthma requiring moderate- or high-dose inhaled CS (ICS; ≥ 250 mcg of fluticasone propionate twice daily, or equipotent ICS daily dosage, to a maximum of 2000 mcg/day of fluticasone propionate or equivalent) and one or more additional controller medications (inhaled long-acting beta agonist [LABA] or anticholinergic or LTA) for ≥ 3 months, with a stable dose ≥ 1 month prior to the initial Screening Visit
3. Has a prebronchodilator forced expiratory volume in 1 second (FEV1) ≥ 40% and ≤ 90% of predicted value during the Screening Period, despite use of a moderate- or high-dose ICS and one or more additional controller medications (inhaled LABA or anticholinergic or LTA)
4. Has a history of clinically diagnosed asthma, which could include a history of FEV1 reversibility and/or positive bronchial challenge test
5. Has a history of ≥ 1 clinically significant asthma exacerbation prior to the initial Screening Visit, despite use of a moderate- or high-dose ICS and one or more additional controller medications at the time the exacerbation(s) occurred

[redacted]

[redacted]

8.4 Exclusion Criteria

Potential subjects will be ineligible for enrollment in the study if they meet any of the following criteria:

1. Is a current or former smoker with a smoking history of ≥10 pack-years (number of pack-years = number of cigarettes per day/20 × number of years smoked; a *former smoker* is defined as a subject who stopped smoking ≥ 6 months prior to the Screening Visit)
2. Has a body mass index (BMI) > 36 kg/m^2
3. Has a documented history or radiological evidence of a clinically important lung condition other than asthma (eg, α1-antitrypsin deficiency, bronchiectasis, cystic fibrosis, primary ciliary dyskinesia, pulmonary fibrosis, allergic bronchopulmonary mycosis, or lung cancer)
4. Has a respiratory tract infection (RTI) within 4 weeks before the initial Screening Visit, or during the Screening Period (these subjects may be re-screened following complete resolution of their RTI)
5. Has an asthma exacerbation within 4 weeks before the initial Screening Visit, or during the Screening Period (these subjects may be re-screened following complete resolution of their exacerbation)
6. Has a diagnosis of currently active malignancy; subjects with a medical history of basal cell carcinoma, localized squamous cell carcinoma of the skin, or in situ carcinoma of the uterine cervix are eligible; subjects with a medical history of other malignancies are eligible if the subject is in remission and curative therapy was completed ≥ 2 years prior to the initial Screening Visit
7. Has a history or presence of clinically concerning cardiac arrythmias, atrial fibrillation, New York Heart Association Class III or IV heart failure, or prolonged QT or corrected QT interval > 500 milliseconds (ms) at the Screening Visit
8. Has any disorder (including, but not limited to, cardiovascular [CV], gastrointestinal [GI], hepatic, renal, neurological, musculoskeletal, infectious, endocrine, metabolic, hematological, psychiatric, or major physical impairment) that is not stable in the opinion of the investigator and/or could:
   a. Affect the subject's safety
   b. Influence the findings of the study or data interpretation

c. Impede the subject's ability to complete the study

9. Has undergone bronchial thermoplasty
10. Has a history of substance abuse (including alcohol) that may, in the investigator's judgment, increase the risk to the subject of participation in the study
11. Has used monoclonal antibody (mAb) therapy for the management of asthma or any other condition within 3 months prior to the initial Screening Visit (these subjects may be re-screened following the 3 month period)
12. Has required an oral corticosteroid burst within 1 month prior to the initial Screening Visit or during the Screening Period (these subjects may be re-screened following the 1 month period); maintenance oral corticosteroids ≤ 10 mg/d prednisone or equivalent is permitted

[redacted]

9 STUDY TREATMENTS

[redacted]

9.2 Study Drug: EQ001

All subjects will be randomized in a blinded fashion to receive either EQ001 or matching placebo using a 3:1 (active:placebo) allocation ratio. [redacted]

The study drugs are:

- EQ001, containing the active ingredient itolizumab (Bmab 600), is a humanized recombinant IgG1 mAb that selectively targets the extracellular Sc membrane-distal domain 1 of human CD6 [redacted]
- Placebo is a sterile, clear, colorless, preservative-free solution with the same formulation (without EQ001) as EQ001 [redacted]

[redacted]

[redacted] [redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	

[redacted]

[redacted]

9.3 Treatments Administered

All subjects will take their standard medications for their moderate-to-severe asthma as prescribed by the study physician, consisting of a moderate- or high-dose inhaled corticosteroid (CS) and one or more additional controller medications (eg, inhaled LABA or anticholinergic). Leukotriene antagonists (LTAs) may also be used as controller medications. Allergen immunotherapy at a stable dose is permitted; however, use of monoclonal antibody (mAb) therapeutics is prohibited. Doses of all controller medications must be stable for 4 weeks including the duration of the Screening Period. EQ001 will be administered Q2W for 8 weeks (a total of 5 doses) at the following dose levels:

- Cohort 1: 0.8 mg/kg
- Cohort 2: 1.6 mg/kg
- Cohort 3: 2.4 mg/kg
- Cohort 4: 3.2 mg/kg

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

[redacted]

[redacted]

9.3.1 Study Drug Dosage Preparation and Administration

[redacted]

[redacted]

[redacted]

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

9.4 Prior and Concomitant Medications

Prior and concomitant medications and treatments will be collected from Screening and throughout the study.

9.4.1 Permitted Therapies

All subjects will take standard medications for their moderate-to-severe asthma, consisting of a moderate- or high-dose inhaled CS and one or more additional controller medications (eg, inhaled LABA or anticholinergic). Leukotriene antagonists may also be used as controller medications. Allergen immunotherapy at a stable dose is permitted.

9.4.2 Prohibited Therapies

Treatment with mAb therapeutics other than EQ001 is prohibited.

If a determination is made to treat a subject with any prohibited therapies or medications during the study, the Medical Monitor should be informed. Subjects will be asked to remain in the study and complete all study visits through Study Day 85, but no additional study drug will be administered.

Caffeine and other xanthines (coffee, tea, etc.) should be avoided beginning the night prior to each study visit.

Donation of blood products or sperm is not permitted while on study treatment and for 3 months after the last dose of study drug.

9.5 Treatment Compliance

The study drug will be administered in a blinded fashion at the clinic/facility by a qualified staff member. The time of the SC injection at each administration will be recorded.

9.6 Packaging and Labeling

[redacted]

Placebo is provided in a single-use vial for SC injection.

[redacted]

9.7 Enrollment or Randomization and Blinding

It is the investigator's responsibility to ensure that subjects are eligible to participate in the study prior to enrollment and continue to remain eligible throughout the study. An 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.

The study will be randomized, double blinded, and placebo controlled. Subjects will be randomized in a 3:1 ratio (active:placebo).

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 blinded treatment assignment and dose, record drug accountability, and request resupply.

Investigators, site staff, and subjects will be blinded to treatment assignment. The Sponsor will 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 Manual. The investigator must 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 should 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.

9.8 Storage and Accountability

[redacted]

The Sponsor or designee will supply the study drug. The site will maintain the following records: receipt of shipments, dispensation to subjects, and return of partially used, or unused study drug. Upon completion or early termination of the study, all unused and partially used IP must be returned to the Sponsor (or designated agent), unless the Sponsor authorizes the study site to destroy the IP.

If the Sponsor authorizes the study site to destroy IP, the investigator is responsible to ensure that arrangements are made for proper disposal. Written authorization should be issued by the Sponsor or designee; procedures for proper disposal should be established according to applicable regulations and guidelines; appropriate records of the disposal should be documented and forwarded to the Sponsor or designee.

If the study site is unable to destroy the IP, the unblinded study monitor will facilitate the return of unused and/or partially used IP, if required prior to database lock. After database lock, the study monitor will close out the site and may complete any returns as needed.

10 STUDY PROCEDURES

The following assessments will be conducted during Screening and at the time points specified in the SOE (Section 2.2) and protocol Section 12. Additional procedures deemed necessary as part of standard of care may be performed at the investigator's discretion. All missed visits and any performed procedures that are not protocol-specified activities must be documented in the subject's medical record and the appropriate eCRF.

10.1 Screening and Informed Consent

Each subject must sign and date the ICF before participating in any study-specific activities, including washout periods to screen for the study.

After the ICF is signed, the subject enters the Screening Period. Each subject will be assigned a unique subject identification number by IWRS at Screening.

The subject number, assigned at the time of Screening, will be used to identify the subject during the study and must be used on all study documentation related to that subject. The subject identification number will remain constant throughout the entire study and must not be changed after initial assignment. Each study site will maintain a list identifying all subjects by subject identification number and subject initials.

After completing the Screening Period, the subject will be evaluated by the investigator to confirm eligibility. A subject is considered enrolled when the investigator decides that all of the eligibility criteria are met. The investigator will document this decision and date in the subject's medical record. Screen failure subjects will be entered into the eCRF. Investigators will maintain a Screening log of all potential study subjects that includes limited information about each candidate, including dates of Screening and procedures, and the outcome of Screening process (eg, enrolled into the study, reason for ineligibility, or withdrawal of consent).

At Baseline and before any study drug is administered, potential subjects will be reviewed by the site to reconfirm their eligibility. If appropriate, repeat assessments can be performed within the Screening Period with approval from the Medical Monitor, as needed.

10.2 Demographics and Medical/Surgical History

10.2.1 Demographics

Demographic data will be collected, including each subject's sex, age, race, and ethnicity.

10.2.2 Medical and Surgical Histories

The investigator or designee will collect the subject's medical and surgical histories, including information on the subject's concurrent medical conditions. All findings will be recorded on the medical history eCRF.

A *complete medical history* at the Screening Visit will include, but will not be limited to, the following information:

- Date of diagnosis of asthma
- Current medications
- Past medications
- History of hospitalization and intubations for asthma
- History of allergies
- History of asthma exacerbations

The subject's interval history of asthma exacerbations is to be obtained at every scheduled study visit (except Day 4); *clinically significant asthma exacerbation* is defined as a > 20% decrease in AM or PM peak flow measurements sustained for 2 days, a doubling of the inhaled corticosteroid dose, initiation of an oral corticosteroid burst for asthma or an emergency department visit/hospitalization for asthma.

A *complete surgical history* at the Screening Visit will include, but not be limited to, any history of upper or lower airway surgeries, such as sinus or laryngeal surgery. An *interval surgical history* is to be obtained at every scheduled study visit (except Day 4 and any unscheduled visits).

10.3 Physical Examination

The investigator or designee will conduct a complete physical examination at Screening and a targeted physical examination at selected time points thereafter.

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* should 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.

10.4 Vital Signs

The following vital sign measurements will be performed: systolic (SBP) and diastolic blood pressure (DBP), pulse, respiration rate, and temperature. On dosing days, vital signs will be taken pre-dose. Vital signs (except for temperature) will also be periodically monitored for a minimum of 30 minutes following the SC administration of study drug. The subject must be seated or in a semi-recumbent position in a rested, calm state for at least 3 minutes before vital signs are collected. The position selected for a subject should be the same throughout the study and documented on the vital signs eCRF.

Height will be measured without shoes at Screening.

Weight without shoes will be obtained at Screening. On dosing days, weight will be obtained before dosing. The weight at Screening will be used to calculate all study drug doses, unless there has been a weight change of ≥ 20% from Screening.

10.5 Asthma Clinical Status Assessment

The investigator and/or designee will conduct an asthma clinical status assessment at specific time points, as specified in the SOE. These clinical status assessments will include:

- Pulmonary function test
- FeNO level measurement
- PRO assessment, ACQ-6

A history of *clinically significant asthma exacerbations* (defined as a > 20% decrease in AM or PM peak flow measurements sustained for 2 days, a doubling of the inhaled corticosteroid dose, initiation of an oral corticosteroid burst for asthma or an emergency department visit/hospitalization for asthma) will be obtained at each scheduled study visit (other than Day 4) and any unscheduled visits. Diary entries that meet the criteria for a clinically significant exacerbation should also be recorded in the eCRF.

10.6 Pulmonary Function Assessment

Spirometry will be performed at every visit by the investigator or qualified designee according to ATS/European Respiratory Society (ERS) guidelines [redacted] Spirometry testing should be started each day between 6 AM and 12 PM; every effort should be made to conduct spirometry testing at the same time at every study visit. Spirometry should be performed before study drug or placebo administration. Subjects should refrain from strenuous exercise for a minimum of 30 minutes prior to spirometry testing and must not use short-acting bronchodilator medication within 6 hours, and long-acting bronchodilator medications within 12-24 hours (as determined by

the regular dosing interval for the specific long-acting bronchodilator medication), prior to spirometry testing. If the subject takes these medications within the prohibited timeframe, spirometry testing should be rescheduled.

The subject should rest for at least 15 minutes prior to the test. The subject should be sitting during spirometry testing; however, if the subject is unable to sit, then standing is acceptable. Spirometry testing should be completed in the same manner (ie, sitting or standing) at every study visit. Multiple forced expiratory efforts (at least 3, but no more than 8) will be performed for each spirometry session, and the 2 best efforts that meet ATS/ERS acceptability and reproducibility criteria will be recorded. The best efforts will be based on the highest FEV1. The maximum FEV1 of the 2 best efforts will be used for the analysis. Both the absolute measurement (for FEV1 and forced vital capacity [FVC]) and the percentage of predicted normal value will be recorded using appropriate reference values. The highest FVC will also be reported, regardless of the effort in which it occurred (even if the effort did not result in the highest FEV1). Nose clips may be used for spirometry; however, if nose clips are used, they should be used consistently for all spirometry.

Post-bronchodilation (BD) spirometry testing, when performed, will be assessed after the subject has induced maximal BD using a short-acting beta agonist (SABA), such as albuterol (90 µg metered dose) or salbutamol (100 µg metered dose) or equivalent, with a spacer device for a maximum of 8 total puffs [redacted] according to ATS/ERS guidelines (Miller 2005), a dose of 400 µg salbutamol/albuterol or lower is recommended for the reversibility test. The same number of puffs (ie, 4, 6, or 8 puffs) and post-BD maneuvers should be used each time post-BD spirometry testing is performed.

10.7 FeNO Assessment

The level of FeNO will be measured in each subject at every study visit (other than Day 4) using a standardized single-breath FeNO (American Thoracic Society; ATS, 2005) test. FeNO testing must be completed before spirometry is performed. In addition, subjects should not eat or drink within ≤ 1 hour prior to FeNO measurement.

The subject should be sitting during FeNO testing; however, if the subject is unable to sit, then standing is acceptable. FeNO testing should be completed in the same manner (ie, sitting or standing) at every study visit using the same equipment. Subjects are to inhale to total lung capacity through the NIOX VERO® Airway Inflammation Monitor, then exhale for 10 seconds at 50 mL/sec (assisted by visual and auditory cues). The obtained value will be recorded and the process repeated, for a total of 2 measurements. The 2 measurements will be printed to serve as a source document.

10.8 Home Peak Flow Testing

Home peak flow testing for peak expiratory flow rate (PEFR) will be performed twice daily, in the morning upon awakening and in the evening before bedtime, using a peak flow meter. PEFR will be recorded during the Screening, Treatment, and Safety Follow-up Periods in the eDiary. PEFR measurements should be taken at least 6 hours after the last dose of SABA rescue medication. Subjects should perform 3 successive peak flow maneuvers while the subject is sitting or standing, but the subject should be in the same position at every testing. The highest of the 3 values should be captured for each time point. At each study visit, the investigator or authorized delegate will check the subject's compliance with the peak flow measurements and confirm that the subject is using the peak flow meter correctly.

10.9 Measurement of Patient-reported Outcomes

10.9.1 Asthma Daily Diary

The subject's Asthma Daily Diary (eDiary) will be provided at Screening and includes the following daily assessments: asthma symptoms; peak expiratory flow rate measurements; use of controller and rescue medication; nighttime awakening due to asthma; and asthma-related activity limitations. The eDiary will be completed each morning and evening. Triggers will alert subjects to signs of worsening of asthma, and they will be instructed to contact their investigator.

10.9.2 Asthma Control Questionnaire-6

The ACQ-6 is a patient-reported questionnaire that assesses asthma symptoms (ie, nighttime waking, symptoms on waking, activity limitation, shortness of breath, and/or wheezing) and daily rescue bronchodilator use during the past week [redacted] Questions are equally weighted and scored from 0 (totally controlled) to 6 (severely uncontrolled). The mean ACQ-6 score is the mean of the responses. Mean scores of ≤ 0.75 indicate well-controlled asthma, scores between 0.75 and ≤ 1.5 indicate partly controlled asthma, and a score > 1.5 indicates uncontrolled asthma [redacted] individual changes of at least 0.5 are considered clinically meaningful. The subject's ACQ-6 score will be assessed at every study visit prior to pulmonary function and FeNO assessments.

10.10 12-Lead Electrocardiography

The subject must be in a seated, semi-recumbent, or supine position in a rested, calm state for at least 10 minutes before ECG assessment is performed. Each 12-lead ECG should be performed prior to blood draws, dosing (if applicable), or other invasive procedures.

A single ECG will be recorded using the equipment provided by the Sponsor designee. The investigator or designated study site physician will review, sign, and date all ECGs.

Any clinically significant abnormal ECG findings will be recorded as an AE.

10.11 Clinical Laboratory Tests

10.11.1 Safety Laboratory Tests

Blood samples will be collected according to the SOE (Section 2.2), protocol Section 12, and below. All safety laboratory tests will be performed at the central laboratory. Samples will be collected pre-dose on study dosing days. Repeat laboratory testing will not be required if a test was already performed within the specified time window for collection. Samples may be analyzed for the tests outlined in this protocol and for any additional tests necessary to ensure each subject's safety. These may include, but are not limited to, investigation of unexpected results. Subjects will be in a seated, semi-recumbent, or supine position during blood collection.

During the Treatment Period, ALC must be monitored by the investigator within 7 days prior to dosing (Section 9.3.2).

[redacted]

10.11.2 Central Laboratory Tests

Validated assays will be used for analysis of serum samples for determination of EQ001 and treatment-emergent anti-EQ001 antibodies (anti-drug antibody [ADA]) concentrations. Collection procedures are described in the study Laboratory Manual.

10.11.2.1 Pharmacokinetics

Serum will be assayed for EQ001 concentrations using a validated assay. The PK samples will be collected at time points specified in the SOE; the PK samples should be obtained after the ECG is recorded.

10.11.2.2 Anti-Drug Antibody and Neutralizing ADA

Serum samples will be obtained for detection of ADA against EQ001 at the time points specified in the SOE, and, if required, a neutralizing ADA (NAB) assay will be performed on the same samples. Samples will be taken on Study Days 1, 29, and 57 (pre-dose), and on Study Day 85 or ET.

[redacted]

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11 ADVERSE EVENTS

An *adverse event* (AE) is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease or any worsening of a pre-existing condition temporally associated with the use of a study drug, whether or not related to study drug. The AEs that occur after the first dose of EQ001 or during the study treatment and safety follow-up periods will be documented on the AE eCRF. The investigator will assess AE severity and the causality relationship of the AE to study drug. The investigator will treat the subject as medically required to ensure the subject's safety.

Laboratory values that are outside the laboratory reference range should be reported as AEs only if the investigator considered those AEs to be clinically significant.

From the time of signing the ICF through the first study drug administration, all SAEs and nonserious AEs related to protocol-mandated procedures will be recorded on the SAE/AE eCRF. All other untoward medical occurrences observed during Screening, including exacerbation or changes in the medical and surgical history, will be captured on the medical and surgical history eCRF. Details on recording and reporting AEs are provided below. All AEs will be captured through Study Day 85 or the ET Visit.

Investigators should use their clinical judgment to determine whether a subject is to be withdrawn due to an AE. In the event the subject requests to withdraw from study-related treatment or the study due to an AE, the subject should be asked to return for all remaining study visits through Study Day 85. In the event a subject is withdrawn from study, an ET Visit should be completed.

All subjects experiencing AEs, including clinically significant abnormal laboratory values, whether or not associated with use of the study drug, must be monitored until the condition (1) returns to normal, (2) returns to the subject's baseline, (3) the investigator determines the AE has reached a stable outcome and is no longer clinically significant, or (4) the subject is considered lost to follow-up.

11.1 Severity

All AEs, both serious and nonserious, will be assessed for severity using the NCI CTCAE v 5.0. The CTCAE scale includes unique clinical descriptions of AEs categorized by anatomy and/or pathophysiology. Reference the following website:

https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf

The CTCAE scale displays Grades 1 through 5 with unique clinical descriptions of severity for each AE (including abnormal laboratory values), based on this general guideline provided in the 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.

11.2 Causality Assessment

The investigator or qualified subinvestigator is responsible for assessing and assigning the causality relationship of the event to study drug using clinical judgment and the following categories of relatedness:

- Related: There is at least some possibility that the AE could be related to study drug administration.
- Not related: There is a high degree of certainty that the AE is NOT related to study drug administration.

The investigator or qualified subinvestigator is also responsible for assessing and assigning the causality relationship of the event to study-related procedures (eg, invasive procedures, such as venipuncture) using clinical judgment and the following categories of relatedness:

- Related: There is at least some possibility that the AE could be related to study drug administration.
- Not related: There is a high degree of certainty that the AE is NOT related to study drug administration.

In making a causality assessment of an AE, it should be considered as to whether or not the AE is expected to occur due to the underlying disease, based on the investigator's clinical experience in managing moderate-to-severe uncontrolled asthma (Section 10.5).

11.3 Clinical Laboratory Adverse Events

The investigator is responsible for reviewing the results of all laboratory tests as they become available and determining whether an abnormal value in an individual subject is a clinically significant change from the subject's baseline value(s). The investigator may repeat the laboratory

test or request additional tests to verify the results of the original laboratory tests. In general, abnormal laboratory findings without clinical significance (based on the investigator's judgment) are not to be recorded as AEs. However, laboratory value changes that require treatment or adjustment in current therapy are to be considered AEs. When applicable, clinical sequelae (not the laboratory abnormality) are to be recorded as the AE.

11.4 Serious Adverse Events

A *serious adverse event* (SAE) is defined as any AE occurring at any dose that results in any of the following outcomes:

- Death
- Life-threatening AE (Note: A life-threatening AE is one that, in the view of the investigator places the subject at immediate risk of death from the reaction as it occurred)
- Hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity
- A congenital anomaly/birth defect.

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include blood dyscrasias or convulsions that do not result in subject hospitalization, or the development of drug dependency or drug abuse.

An *unexpected AE* is defined as any adverse event for which the specificity or severity is not consistent with the AE profile in the current EQ001 Investigator's Brochure.

All SAEs, regardless of cause(s) or causal relationship to study drug, must be reported within 24 hours to the study Sponsor and/or designee.

11.5 Reporting Adverse Events

11.5.1 Reporting Procedures for Nonserious Adverse Events

The investigator is responsible for ensuring that all AEs observed by the investigator or designee or reported by the subject are reported using the AE eCRF.

The investigator will assign the following AE attributes:

- AE diagnosis or syndrome(s), if known (if not known, signs or symptoms)
- Dates of onset and resolution (if resolved)

- Severity
- Causality relationship to study drug or study-related procedures
- Action taken
- Outcome

Follow-up of nonserious AEs will continue through the last day on the study and/or until a definitive outcome (eg, resolved, resolved with sequelae, lost to follow-up) is achieved.

When a subject is withdrawn from the study because of a nonserious AE, the Sponsor and/or designee must be notified by email or phone within 48 hours.

11.5.2 Reporting Procedures for Serious Adverse Events

The investigator is responsible for ensuring that all SAEs observed by the investigator or reported by the subject are promptly assessed and reported to the Sponsor and/or designee. The investigator must assess the causality relationship of the SAE to study drug or any study-related procedure.

The procedures for reporting SAEs are as follows:

- Record the SAE on the AE eCRF and complete the Serious Adverse Event Report form.
- Within 24 hours of the investigator's knowledge of the event, enter via the eCRF the SAE Report form to the attention of the Sponsor and/or designee. Additional contact numbers and AE/SAE reporting instructions will be provided in the Study Manual.
- For fatal or life-threatening events, also email and/or fax redacted copies of hospital case reports, autopsy reports, and other documents, when requested and applicable. Transmission of such documents should occur with personal subject details de-identified, without losing the traceability of a document to the subject identifiers. Transmission of the initial report of the event should not be delayed in order to include these additional documents.
- The Sponsor or/or designee may request additional information from the investigator to ensure the timely completion of accurate safety reports.

The investigator must take all necessary therapeutic measures for resolution of the SAE. Any medications or therapies necessary for treatment of the SAE must be recorded in the event description section of the SAE form and the concomitant medication eCRF.

Follow-up of SAEs will continue through the last day on the study and/or until a definitive outcome (eg, resolved, resolved with sequelae, lost to follow-up, fatal) is achieved.

While pregnancy is not considered an AE, all cases of fetal drug exposure via a maternal parent as study subject or pregnancy of a partner of a male study subject will be reported immediately to

the Sponsor or its designee. Information related to the pregnancy must be documented on a Pregnancy Confirmation and Outcome Form, provided by the Sponsor or its designee, and the pregnancy should be followed until a definitive outcome has been determined.

The Sponsor or its designee will report SAEs as required to regulatory authorities and investigators in compliance with all reporting requirements, according to local regulations and International Council for Harmonisation (ICH) Good Clinical Practice (GCP).

The investigator will notify the appropriate Independent Ethics Committee (IEC) of SAEs occurring at the study site and other AE reports received from the Sponsor, in accordance with local requirements. The investigator or designee at each study site is responsible for submitting safety reports (initial and follow-up) and other safety information (eg, in the revised EQ001 Investigator's Brochure) to the IEC and/or other applicable regulatory authorities for retaining a copy in the study files.

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13 PLANNED STATISTICAL METHODS

A detailed description of data analysis and statistical methods to be used will be outlined separately in the SAP.

13.1 General Considerations

Data will be summarized using descriptive statistics (n, mean, median, standard deviation, minimum, maximum) for continuous variables and frequencies and percentages for discrete variables. All data summaries will be displayed by cohort and by treatment group (EQ001 or placebo). A total column for treated cohorts separated by treatment group will also be included. Baseline values of variables are considered the last available non-missing value prior to receiving any study drug. By-subject listings of the data will also be provided. All data summaries and listings will be produced using the SAS® software, version 9.3 or higher.

[redacted]

13.3 Analysis Populations

13.3.1 Safety Population

The *safety population* consists of all subjects who receive any study drug.

13.3.2 Pharmacokinetic Analysis Population

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

[redacted]

13.3.4 Efficacy Population

The *efficacy population* consists of those subjects in the safety population who have at least 1 post-treatment clinical activity assessment.

13.4 Subject Disposition

Subject disposition data will be summarized and will include the number and percent of enrolled subjects; number and percent of subjects initiating and completing treatment; and number and percent of subjects discontinuing treatment and discontinuing the study, further broken down by the reasons for discontinuation. Subject enrollment will also be summarized by study site. A summary of major protocol deviations will be tabulated for each cohort and cohorts combined by treatment group.

13.5 Demographics and Baseline Characteristics

Demographics and other baseline characteristics will be summarized for the subjects in the safety population. Demographic data will include age, gender, race, and ethnicity. Baseline characteristics data will include (but not be limited to) total serum IgE, FeNO, ACQ-6, and PFT (FEV1 absolute, FVC, FEV1/FVC ratio, and FEV1 %) with bronchodilator reversibility. Medical history data will include (but not be limited to) time from diagnosis of asthma to Screening, prior and current medications used for asthma control, history of biologic therapy use for asthma control, hospitalizations, and intubations.

[redacted]

13.7 Safety Analyses

All safety data summaries will use the safety population.

The number and percent of subjects experiencing any DLTs will be presented by cohort. A listing of DLTs will also be provided.

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, v 20.1, or the current version) and will be graded by the investigator using the CTCAE v 5.0 or the current version. Subject incidence of TEAEs, treatment-emergent serious AEs (TESAEs), TEAEs leading to treatment discontinuation and TEAEs with an outcome of death will be summarized by SOC and preferred term (PT). Adverse events will also be further summarized by

worst severity grade and relationship to study drug. [redacted]

Clinical laboratory data will be summarized descriptively, these summaries will include observed values at collection time points and their changes from baseline. All laboratory parameters that can be graded using the CTCAE will be graded. For selected parameters, following summaries may be produced:

- Worst post-baseline severity grade
- Shift summary of baseline grade to worst post-baseline severity grade.

Safety evaluations may also include changes in the subject's physical examination findings, vital signs, and 12-lead ECG findings.

[redacted]

13.9 Efficacy Analyses

All efficacy analyses will use the Efficacy population. Following efficacy data summaries will be produced by cohort.

Change from baseline in FeNO, serum total IgE, PFT (FEV1) and ACQ-6 will be assessed at specific data collection time points, as described in the SOE (Section 2.2). Number and percent of subjects showing an improvement of ≥ 0.5 points (a minimally important difference) in ACQ-6 score will also be tabulated. Percent changes will be assessed over time in AM and PM peak flow measures and changes in diurnal variation of peak flow. Use of concomitant medications will also be assessed, specifically the number and percent of subjects with a need for rescue medications prior to each assessment time point will be tabulated. If data permit, the time to first exacerbation (of any severity) will be summarized and plotted using the Kaplan-Meier method, and further, annualized rates of asthma exacerbations (of any severity) will be calculated by study drug dose to inform future study designs. All efficacy data will be provided in a data listing.

14 ADMINISTRATIVE CONSIDERATIONS

14.1 Investigator Responsibilities

The investigator is responsible for complying with all regulatory requirements relating to performing clinical research with an IP. The investigator is responsible for ensuring that the investigation is conducted according to the signed investigator Agreement (FDA Form 1572, or equivalent), the approved protocol, and applicable regulations for protecting the rights, safety, and welfare of study subject under the investigator's care. The investigator is additionally responsible for the control of IP and for providing accurate and verifiable data to the Sponsor.

The investigator must obtain the written informed consent of each subject before participation in the study. The investigator must assure initial and continuing review of the study by an IEC that complies with applicable national and local regulations.

The investigator will ensure adequate documentation of the training of research study personnel for conduct of the study, including qualifications, experience, and study role.

The investigator will be given a copy of the most current version of the EQ001 IB and appropriate study process manuals and plans. The investigator is obligated to become familiar with these documents prior to initiation of the study.

Other investigator responsibilities relative to the IEC include, but are not limited to, the following:

- Submit to the IEC for review any advertisements that will be used to recruit subjects, as applicable
- Submit all protocol amendments, revisions of the Investigator’s Brochure, or revisions of the Informed Consent to the IEC for review
- If Sponsor notifies the investigator about SAEs reported in other studies associated with this IP, report that information to the IEC if required per local regulations
- Provide the IEC with any other information it requests before or during the conduct of the study
- Report to the IEC all adverse drug reactions that are serious, unexpected, and related to IP as per local regulations
- Maintain a file of study-related information
- Update the IEC on a minimum of a yearly basis as per local regulations

14.2 Independent Ethics Committee Approval

Before initiation of the study at a study site, the protocol, including the final version of the ICF, the subject information sheet (if applicable), and any other applicable/relevant study documentation will be submitted to the appropriate IEC. In addition, the IEC must approve all advertising used to recruit subjects for the study prior to use. Written approval of the study documentation must be obtained and sent to the Sponsor or its designee before the study drug can be released to the investigator.

The investigator is responsible for informing the IEC of any amendments to the protocol, ICF, written information provided to subjects, and/or other procedures in accordance with local requirements. The protocol must be re-approved by the IEC upon receipt of amendments, in accordance with applicable law. The investigator must send a copy of the approval letter from the IEC to the Sponsor or its designee.

The investigator will report promptly to the IEC and the Sponsor any new information that may adversely affect the health or safety of past or current subjects or the conduct of the study, including deviations from the protocol or reports of any reportable SAEs, during and for one (1) year after study completion.

The investigator should submit written reports of clinical study status to their IEC annually or more frequently if required. A final study notification will also be forwarded to the IEC after the study is completed or in the event of premature termination of the study in accordance with the applicable regulations. After completion of the study, the investigator will provide the IEC with a report of the outcome of the study. Copies of all contacts with the IEC should be maintained in the study file. Copies of clinical study status reports (including termination) should be provided to the Sponsor.

14.3 Ethical Conduct of Study

The investigator(s) and all parties involved in this study should conduct the study in adherence to the ethical principles based on the Declaration of Helsinki, GCP, ICH Guidelines, and the applicable national and local laws and regulatory requirements (referred to herein as “applicable law”).

Investigators and all sub-investigators will comply with 21 Code of Federal Regulations (CFR), Part 54, 1998 and similar conflicts of interest laws requiring documentation of financial interests or arrangements with the Sponsor, or proprietary interests in the drug under study and any other local regulatory requirements as applicable. Any required documentation must be provided prior to the investigator’s (and any subinvestigator’s) participation in the study. The investigator and

subinvestigator(s) will notify the Sponsor or its designee of any change in reportable interests during the study and for 1 year following completion of the study. Study completion is defined as the date when the last subject completes all protocol-defined activities.

14.4 Subject Information and Consent

Prior to conducting any study-related procedures, the investigator must obtain written informed consent from each subject, in accordance with applicable law. Consent will be documented on a written ICF. The ICF must be approved both by the Sponsor and by the reviewing IEC prior to presenting it to a subject. Each ICF must comply with the ICH GCP Guidelines and applicable regulatory requirements.

Investigators may discuss study availability and the possibility for entry with a potential subject without first obtaining consent. However, informed consent must be obtained and documented prior to initiation of any procedures that are performed solely for the purpose of determining eligibility for research, including withdrawal from current medication(s). The informed consent process should take place under conditions where the subject has adequate time to consider the risks and benefits associated with his/her participation in the study. The investigator or qualified designee must explain to each subject the aims, methods, reasonably anticipated benefits, and potential hazards of the study.

Once appropriate essential information has been provided and fully explained in layman's language to the subject by the investigator (or a qualified designee), the approved ICF will be signed and dated by both the subject and the person obtaining consent (investigator or designee), as well as by any other parties required by the IEC. The subject will receive a copy of the signed ICF; the original will be retained in the study files. The investigator must document the consent interview and place the record in the study files. The investigator shall also maintain a log of all subjects who sign the ICF and indicate if the subject was enrolled into the study or reason for non-enrollment.

14.5 Confidentiality

The investigator must assure that subjects' anonymity will be strictly maintained and that their identities are protected from unauthorized parties. Only subject initials, age, another unique identifier (as allowed by local law) and an identification code will be recorded on any form or biological sample submitted to the Sponsor, IEC, or laboratory. Laboratory specimens must be labeled in such a way as to protect subject identity while allowing the results to be recorded to the proper subject. Refer to specific laboratory instructions (or in accordance with local regulations). NOTE: The investigator must keep a Screening log showing codes, names, and addresses for all

subjects screened and for all subjects enrolled in the study. Subject data will be processed in accordance with all applicable regulations. (Some studies may require double-coding of samples).

The investigator agrees that all information received from the Sponsor, including but not limited to the Investigator's Brochure, this protocol, CRF/eCRF, the study drug, and any other study information, remain the sole and exclusive property of the Sponsor during the conduct of the study and thereafter. This information is not to be disclosed to any third party (except employees or agents directly involved in the conduct of the study or as required by law) without prior written consent from the Sponsor. The investigator further agrees to take all reasonable precautions to prevent the disclosure by any employee or agent of the study site to any third party or otherwise into the public domain. In compliance with applicable law and/or ICH GCP Guidelines, the investigator will permit the Sponsor's representatives and, when necessary, representatives of the regulatory authorities, direct access to any medical records relevant to the study for verification of study-related procedures and data. Direct access includes examining, analyzing, verifying, and reproducing any records and reports that are important to the evaluation of the study.

Investigators will obtain authorization from the subject to permit access to study-related records, including personal information.

Authorization is required from each subject (ie, specific permission granted by such individual to a covered entity for the use or disclosure of an individual's protected health information). The investigator and institution must obtain such waiver/authorization in writing from the subject. Valid authorization must meet the implementation specifications under the applicable privacy laws. Authorization may be combined in the ICF (approved by the IEC), or it may be a separate document (approved by the IEC) or provided by the investigator or Sponsor (without IEC approval).

14.6 Study Initiation

Before the study drug can be shipped to the study site and before enrollment can begin, all applicable documentation and approvals as per local regulations must be in place.

The Sponsor or designee will notify the site when they are activated.

14.7 Case Report Forms and Other Study Records

The investigator will comply with the requirements for all assessments and data collection for each subject, as specified in the protocol.

During each subject's visit to the clinic, the investigator or qualified designee will record progress notes in the subject's medical record to document all significant observations. At a minimum, these notes will contain the following:

- Documentation of the informed consent process, including any revised consents.
- The date of the visit and the corresponding visit or day in the study schedule.
- General subject status remarks, including any significant medical findings. The severity, frequency, and duration of any AEs and the investigator's assessment of relationship to study drug must also be recorded.
- Any changes in concomitant medications.
- A general reference to the procedures completed.

In addition, any contact with the subject via telephone or other means that provides significant clinical information will also be documented in the progress notes, as described above.

Data for this study will be captured in electronic eCRFs. Study auditing, data entry, verification and validation, and subsequent analysis will be performed by the Sponsor, or its designees, in accordance with GCPs and established Standard Operating Procedures.

Clinical data (including AEs, concomitant medications, and applicable clinical laboratory data) will be entered into a database. The creation and validation of the database, data entry, validation, and verification will be performed according to 21 CFR and other applicable local regulations. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

14.8 Study Monitoring

The Sponsor or designee will assign monitors who will perform on-site monitoring as frequently as necessary and in accordance with ICH GCP.

Source documents and eCRFs will be reviewed at monitoring visits and any findings will be discussed with the investigational staff. The Sponsor expects that at monitoring visits study documents and staff will be available and a suitable space will be provided for review of the study documents. The monitor will meet with the investigator on a regular basis to provide feedback on the conduct of the study.

14.9 Access to Source Documentation

The study may be subject to audit by the Sponsor, its designee, or by regulatory authorities. If such an audit occurs, the investigator must agree to allow access to required subject records. The

investigator should notify the Sponsor promptly of regulatory authority audits that are scheduled and must forward copies of any findings or audit reports to the Sponsor promptly.

By signing this protocol, the investigator grants permission to personnel from the Sponsor, its representatives, and appropriate regulatory authorities for on-site monitoring and review of all appropriate study documentation, as well as on-site review of the procedures employed in data collection, where clinically appropriate.

14.10 Study or Study Site Termination

The Sponsor may suspend or stop the study at all centers or at specific study centers due to (but not limited to) the discovery of an unexpected, serious, or unacceptable risk to the subjects enrolled in the study, a decision on the part of the Sponsor to suspend or discontinue development of the product, failure of the investigator to enroll subjects into the study at an acceptable rate, failure of the investigator to comply with regulatory authority or ICH Guidelines, or submission of knowingly false information.

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14.13 Quality Assurance

Authorized representatives of the Sponsor, a regulatory authority, or IEC may visit the study site to perform audits or inspections, including source data verification. The purpose of any such audit or inspection is to systematically and independently examine all study-related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol, ICH GCP Guidelines, and any other applicable regulatory requirements.

The investigator should contact the Sponsor immediately if contacted by a regulatory agency about an inspection.

It is important that the investigator and relevant personnel are available during the possible audits or inspections and that sufficient time is devoted to the process.

14.14 Retention of Data

When the study is completed, the investigator must retain the essential documents for as long as needed (up to 25 years) to comply with regulatory guidelines and Sponsor requirements. The investigator will notify the Sponsor prior to moving or destroying any of the study documents. It is the responsibility of the Sponsor to inform the investigator/institution as to when these documents no longer need to be retained. The investigator should take measures to prevent any accidental or premature destruction of these documents.

14.15 Study Report and Publications

A clinical study report (CSR) will be prepared and submitted to the appropriate regulatory agency or agencies. The Sponsor will ensure that the report meets the standards set out in the ICH Guideline for Structure and Content of Clinical Study Reports (ICH E3). Note that an abbreviated report may be prepared in certain cases.

Investigators in this study may communicate, orally present, or publish in scientific journals or other scholarly media only after written consent has been obtained from the Sponsor.

The investigator will submit to the Sponsor any proposed publication or presentation along with the respective scientific journal or presentation forum at least 60 days before submission of the publication or presentation.

No such communication, presentation, or publication will include the Sponsor's confidential information (see Section 14.5).

The investigator will comply with the Sponsor's request to delete references to its confidential information (other than the study results) in any paper or presentation and agrees to withhold publication or presentation for an additional 60 days in order to obtain patent protection if deemed necessary.

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