BIOLOGIC:	ALT-803
STUDY NUMBER(S):	CA-ALT-803-03-17
PROTOCOL(S) TITLE:	QUILT-1.004: A single center, open-label, pharmacokinetic study of subcutaneous ALT-803
IND NUMBER:	118280
SPONSOR:	Altor BioScience
ORIGINAL PROTOCOL DATE:	09 November 2017
VERSION NUMBER:	1.0
VERSION DATE:	09 November 2017

CLINICAL PROTOCOL APPROVAL FORM

Protocol Title: QUILT-1.004: A single center, open-label, pharmacokinetic study of subcutaneous ALT-803

Study No: CA-ALT-803-03-17
Original Protocol Date: 09 Nov 2017
Protocol Version No: 1.0
Protocol Version Date: 09 Nov 2017

This study protocol was subject to critical review and has been approved by the appropriate protocol review committee of the sponsor. The information contained in this protocol is consistent with:

- The current risk-benefit evaluation of the investigational product.
- The moral, ethical and scientific principles governing clinical research as set out in the Declaration of Helsinki, and principles of GCP as described in 21 CFR parts 50, 54, 56 and 312 and according to applicable local requirements.

The Investigator will be supplied with details of any significant or new findings, including adverse events, relating to treatment with the investigational product.

Name and Title	Signature	Date
Clinical Development: Amy Rock, PhD Vice-President, Clinical Development & Regulatory Affairs		17 NOV 2017
Medical Lead: Hing Wong, PhD CEO		17 NOV 2017
Regulatory Affairs: Monica Jones Director, Regulatory Affairs & Quality Assurance		17 NOV 2017

CA-ALT-803-03-17

QUILT-1.004: A SINGLE CENTER, OPEN-LABEL, PHARMACOKINETIC STUDY OF SUBCUTANEOUS ALT-803

CONFIDENTIALITY AND INVESTIGATOR STATEMENT

The information contained in this protocol and all other information relevant to ALT-803 are the confidential and proprietary information of Altor BioScience Corporation (Altor BioScience), and except as may be required by federal, state or local laws or regulation, may not be disclosed to others without prior written permission of Altor BioScience.

I have read the protocol, including all appendices, and I agree that it contains all of the necessary information for me and my staff to conduct this study as described. I will conduct this study as outlined herein, in accordance with the regulations stated in the Federal Code of Regulations for Good Clinical Practices and International Conference on Harmonization guidelines, and will make a reasonable effort to complete the study within the time designated.

I will provide all study personnel under my supervision copies of the protocol and any amendments, and access to all information provided by Altor BioScience or specified designees. I will discuss the material with them to ensure that they are fully informed about ALT-803 and the study.

Principal Investigator Name (printed) Signature:

Stuart T Harris MD

Date: 13 Nov 2017

STUDY SYNOPSIS

Title: A single center, open-label, pharmacokinetic study of subcutaneous ALT-803

[redacted]

Study Population: The study population consists of healthy male and female volunteers, aged 18 - 65 years.

Number of Subjects: 16

Objectives: *Primary:* To determine the PK profile after single dose subQ injection(s) of 10 µg/kg and 20 µg/kg ALT-803 at concentrations of 1.0 mg/mL or 2.0 mg/mL.

Secondary: To assess safety after single dose subQ injection(s) of 10 µg/kg and 20 µg/kg ALT-803 at concentrations of 1.0 mg/mL or 2.0 mg/mL.

Study Design: This is a single center, open-label, pharmacokinetic study of ALT-803 administered as a subQ injection to healthy volunteers.

Subjects meeting the entry criteria will be randomized in a 1:1 ratio (n = 8; Groups A and B) to one of two ALT-803 drug concentrations. Subjects randomized to Group A will receive 1.0 mg/mL ALT-803 and subjects in Group B will receive 2.0 mg/mL ALT-803. Groups A and B will receive a single 10 µg/kg subQ dose of ALT-803. After a Rest Period, groups A and B will receive a single 20 µg/kg subQ dose of ALT-803.

Blood samples to determine serum levels of ALT-803 will be collected prior to dosing, and at 1, 4, 24, 48, 72, 96, 120, 144, 168 and 192 hours after dosing. Vital signs (heart rate, blood pressure, respiration, temperature) will be monitored.

Safety will be assessed for all subjects and will include monitoring of vital signs, and incidence and severity of adverse events. Blood samples will be collected for hematology and chemistry, immune cell levels and activity, immune cell phenotype subsets, cytokine levels, and immunogenicity testing, which include assays for anti-ALT-803 antibodies.

Subjects will be followed for 6 days after study period 2, and will have an End of Study visit on Day 15 which will include safety labs.

Primary Endpoint:

Serum concentration will be used to calculate the following PK parameters:

- half-life ($t_{½}$)
- apparent (extravascular) volume of distribution (V_z/F)
- apparent (extravascular) clearance (CL/F)
- maximum observed concentration (C_{max})
- time of the observed maximum concentration (T_{max})
- area under the plasma concentration curve from time 0 through the last measurable concentration (AUC_{0-t})
- area under the plasma concentration curve from time 0 extrapolated to infinite time (AUC_{0-inf})

Secondary Endpoint:

1. Safety, as assessed by the incidence and severity of adverse events.

Measures of Interest:

1. Blood samples will be collected for immune cell levels and activity, immune cell phenotype subsets, cytokine levels and immunogenicity testing, which include assays for anti-ALT-803 antibodies.
2. General health as assessed by the RAND General Health Questionnaire (SF-36).

STUDY SCHEMATIC

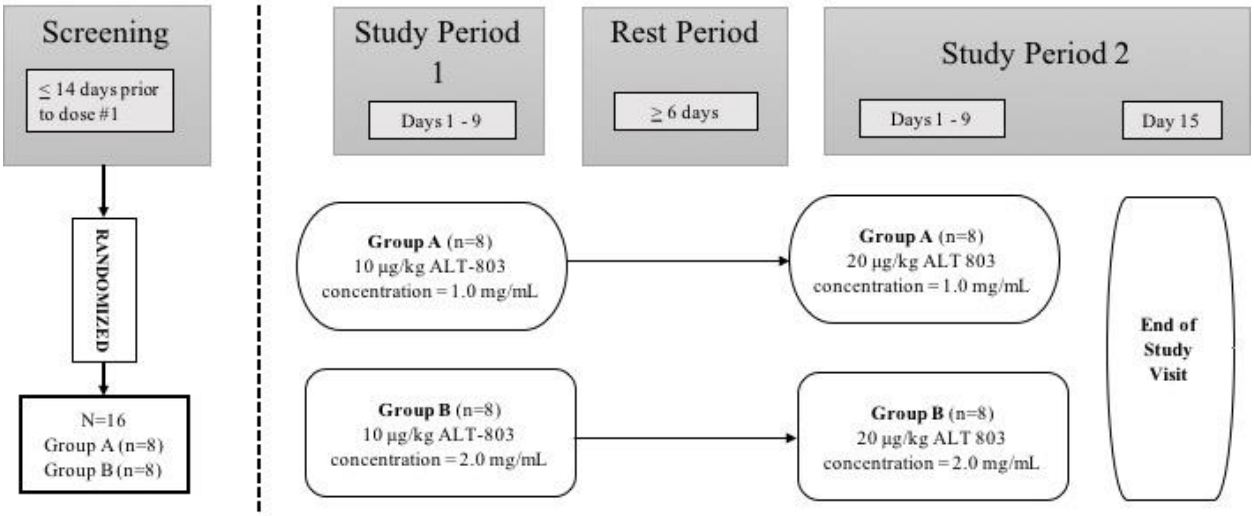


TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AE	Adverse Event
$AUC_{0\text{-}inf}$	Area under the plasma concentration curve from time 0 extrapolated to infinite time
$AUC_{0\text{-}t}$	Area under the plasma concentration curve from time 0 through the last measurable concentration
C_{max}	Maximum observed concentration
CL	Clearance
CL/F	Apparent (extravascular) clearance
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GHQ	General Health Questionnaire
HIPAA	Health Insurance Portability and Accountability Act
IEC	Independent Ethics Committee
IL	Interleukin
IRB	Institutional Review Board
IV	Intravenous
MedDRA	Medical Dictionary for Regulatory Activities
Omics	Genomic, Transcriptomic and Proteomic analysis
PBMC	Peripheral Blood Mononuclear Cell
PK	Pharmacokinetics
RAND	Research and Development
RPMI	Roswell Park Memorial Institute
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
subQ	Subcutaneous
SUSAR	Suspected Unexpected Serious Adverse Reaction
T_{max}	time of the observed maximum concentration
$t_{½}$	Half-life
V_z/F	Apparent (extravascular) volume of distribution

1 INTRODUCTION AND RATIONALE

[redacted]

[redacted]

1.6 Dosing Regimen

All 16 subjects will be randomly assigned in a 1:1 ratio (n=8), to one of two ALT-803 drug concentrations. Subjects randomized to Group A will receive ALT-803 at a concentration of 1.0 mg/mL, and subjects randomized to Group B will receive ALT-803 at a concentration of 2 mg/mL.

- On Day 1 of study period 1 (study days 1 – 9), ALT-803 will be administered as a single subQ dose of 10 µg/kg. A 6-day minimum rest period will follow, starting the day after the last PK sample collection visit for Period 1.

- On Day 1 of study period 2 (study days 1-9), ALT-803 will be administered as a single subQ dose of 20 µg/kg.

2 STUDY OBJECTIVES

2.1 Primary

The primary objective of this study is to determine the PK profile after single dose subQ injection(s) of 10 µg/kg and 20 µg/kg ALT-803 at concentrations of 1.0 mg/mL or 2.0 mg/mL.

2.2 Secondary

The secondary objective of this study is to assess safety after single dose subQ injection(s) of 10 µg/kg and 20 µg/kg ALT-803 at concentrations of 1.0 mg/mL or 2.0 mg/mL.

3 STUDY ENDPOINTS

3.1 Primary

Serum concentration will be used to calculate the following PK parameters:

- half-life ($t_{½}$)
- apparent (extravascular) volume of distribution (V_z/F)
- apparent (extravascular) clearance (CL/F)
- maximum observed concentration (C_{max})
- time of the observed maximum concentration (T_{max})
- area under the plasma concentration curve from time 0 through the last measurable concentration (AUC_{0-t})
- area under the plasma concentration curve from time 0 extrapolated to infinite time (AUC_{0-inf})

3.2 Secondary

The secondary endpoint of the study is to assess safety as measured by the incidence and severity of adverse events.

3.3 Measures of Interest

Blood samples will be collected for immune cell levels and activity, immune cell phenotype subsets, cytokine levels and immunogenicity testing, which include assays for anti-ALT-803 antibodies.

General health will be assessed by the RAND General Health Questionnaire (SF-36).

4 STUDY PLAN

4.1 Study Design

This is a single center, open-label, pharmacokinetic study of ALT-803 administered as a subQ injection to healthy volunteers. Subjects meeting the entry criteria will be randomized in a 1:1 ratio (Groups A or B) to one of two ALT-803 drug concentrations. Subjects randomized to Group A (n=8) will receive ALT-803 at a concentration of 1.0 mg/mL and subjects randomized to Group B (n=8) will receive ALT-803 at a concentration of 2.0 mg/mL. Subjects will receive a single 10 µg/kg subQ dose of ALT-803 on Day 1 of study period 1. After a rest period, subjects will receive a single 20 µg/kg subQ dose of ALT-803 on Day 1 of study period 2. Blood samples to determine serum levels of ALT-803 will be collected prior to dosing, and at 1, 4, 24, 48, 72, 96, 120, 144, 168 and 192 hours after dosing. Vital signs (heart rate, blood pressure, respiration, temperature) will be monitored.

Safety will be assessed for all subjects, and will include monitoring of vital signs and incidence and severity of adverse events. Blood samples will be collected for hematology and chemistry, immune cell levels and activity, immune cell phenotype subsets, cytokine levels and immunogenicity testing, which include assays for anti-ALT-803 antibodies.

After the completion of study period 2, subjects will be followed for an additional 6 days and will have an End of Study visit on Day 15 which will include safety labs, immune cells, and cytokines.

Concomitant medications and adverse events will be collected throughout the study.

4.1.1 Screening and baseline (Day -14 through Time 0)

Time 0 is defined as the start of the first study treatment administration. Baseline is defined as Study Day 1 prior to the first dose of study treatment (Time 0). The Screening Period is the 14-day period prior to Baseline.

The Principal Investigator or designee will obtain the signed Informed Consent and HIPAA authorization from each subject prior to performing screening tests and procedures. All results obtained from the screening tests and procedures must be reviewed by a study Investigator to determine the subject's eligibility to participate in the study.

Subjects that are enrolled to the study but do not receive any study treatment will be replaced.

4.1.2 Study Period 1, Day 1 – Day 9

Study period 1 is defined as the 9 days following Time 0, Day 1.

In study period 1, subjects will be administered a single subQ injection of ALT-803. Blood sampling for PK, immune cells, cytokines and safety labs will commence on Day 1, and will continue daily throughout the nine-day study period.

4.1.3 Rest Period (≥6 days)

No study visits will occur during the rest period (please see Section 4.3). Monitoring for adverse events and use of concomitant medications will continue throughout this period.

4.1.4 Study Period 2, Day 1 – Day 9

Study period 2 is defined as the 9 days following the Rest period.

In study period 2, subjects will be administered a single subQ injection of ALT-803. For study period 2, blood sampling for PK, immune cells, cytokines and safety labs will commence on Day 1, and will continue daily throughout the nine-day study period.

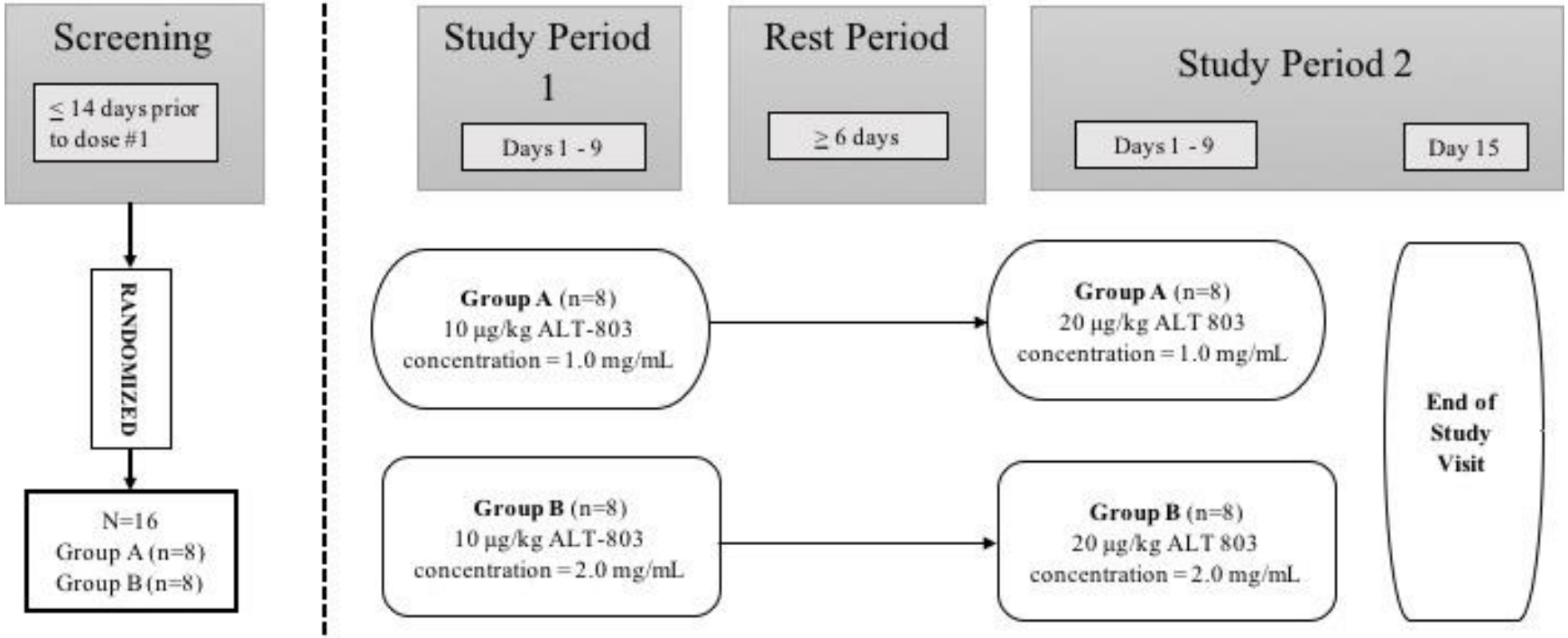
4.1.5 Follow-up: Study Period 2, Day 10 – Day 15

The follow-up period is defined as the 6-day period following the completion of study period 2.

Monitoring for adverse events and use of concomitant medications will continue throughout this period. Subjects will be asked to return to the clinical research site on Day 15 for an End of Study visit.

The study schematic is presented in Section 4.2. The schedule of assessments is presented in Section 4.3.

4.2 Study Schematic



4.3 Schedule of Assessments

Tests & Procedures	**Screen**[1]	**BL**[2]	**Study Period 1**									**Rest Period**	**Study Period 2**										
Study Day		1	1	2	3	4	5	6	7	8	9	≥ 6d	1 (pre-dose)	1	2	3	4	5	6	7	8	9	End of Study, D15
Medical History & Demographics	X																						
Complete Physical Exam	X																						
Routine Physical Exam		X											X										X
HIV, Hepititis B/C	X																						
Serum/Urine Pregnancy Test[3]	X	X											X										X
Urine Drug Test[4]	X	X											X										
Alcohol Breath Test[5]	X	X											X										
Vital Signs, Height and Weight[6,7]	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
CBC with differential	X	X		X	X	X	X	X	X	X	X		X		X	X	X	X	X	X	X	X	X
Blood Chemistry (CMP)	X	X		X	X	X	X	X	X	X	X		X		X	X	X	X	X	X	X	X	X
Blood Sampling for Immune Cells		X		X	X	X	X	X	X	X	X		X		X	X	X	X	X	X	X	X	X
Blood Sampling Cytokines		X		X	X	X	X	X	X	X	X		X		X	X	X	X	X	X	X	X	X
Blood Sampling for Immunogenicity Testing		X											X										X
Blood Sampling for ALT-803 Pharmacokinetics[8]		X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	
General Health Questionnaire		X																					X
Drug Administration																							
ALT-803			X											X									
Safety Monitoring																							
Injection Site Reaction (ISR) Diary[9]		As applicable																					
Digital Photography of Injection Site and ISR [10]		X	As applicable										X	As applicable									
Adverse Events Monitoring		Continual																					
Concomitant Meds		Continual																					

[1]Screening evaluations performed ≤14 days prior to dose #1 unless otherwise specified.

[2]Baseline (BL) evaluations will be performed on Treatment Day 1 (pre-dose).

[3]For women with childbearing potential only. Screening test should be serum. Baseline test may be urine.

[5]A positive read (≥ 0.010% BAC) is an exclusion criteria during screening or will result in subject not being dosed while on study.

[6]Vital signs will be assessed prior to dosing with ALT-803 and 1 hour post-dose. On all other days, vital signs will be collected prior to sample collection.

[7]Height should only be measured at screening. Weight will be measured prior to ALT-803 dose, for study periods 1 and 2.

[8]Blood sampling for PK will be collected prior to ALT-803 dose, 1 and 4 hours post dose and at 24, 48, 72, 96, 120, 144, 168 a nd 192 hours after dosing for study periods 1 and 2.

[9]Injection site reaction diaries should be completed through Day 6 or resolution of symptoms, whichever is longer.

[10] A digital photograph of the Injection site will be taken prior to subQ injection of ALT-803. Photograph ISR's daily in 2 views through Day 6 or resolution, whichever is longer.

5 POPULATION

5.1 Number of Subjects

A total of 16 evaluable subjects will be enrolled.

5.2 Inclusion Criteria

Subjects must meet ALL of the following criteria for inclusion in the study:

1. Signed Written Informed Consent

    a. Subjects must have signed and dated an IRB/IEC approved written informed consent form in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any protocol related procedures that are not part of subject care.

    b. Subjects must be willing and able to comply with the scheduled visits, study drug dosing schedule, procedures, laboratory tests, and other requirements of the study.

2. Study Population

    a. Body mass index (BMI) must be within the range of 18 to 28 kg/m^2. Subjects must weigh between 50 and 100 kg (inclusive).

    b. Subjects must be in good health as determined by past medical history, complete physical examination, vital signs and laboratory tests at screening.

3. Age and Reproductive Status

    a. Men and women, 18 - 65 years of age.

    b. Female participants of childbearing potential must adhere to using a medically accepted method of birth control up to 28 days prior to screening and agree to continue its use during the study or be surgically sterilized (e.g., hysterectomy or tubal ligation) WOCBP must agree to use effective contraception during the study and for at least 1 month following the last dose of the study drug.

    c. WOCBP must have a negative serum pregnancy test < 14 days prior to first dose of the study drug. Non-childbearing is defined as greater than one year postmenopausal or surgically sterilized.

    d. Male subjects must be willing to use barrier contraception (i.e. condoms and spermicide) from the day of dosing until at least 1 month following the last dose of study drug.

5.3 Exclusion Criteria

Subjects with ANY of the following criteria are excluded from participation in the study:

1. Medical History and Concurrent Diseases

    a. A past medical history of clinically significant 12 lead EKG abnormalities

    b. Subjects with a history of interstitial lung disease and/or pneumonitis.

    c. HIV-positive.

    d. Significant illness within 2 weeks prior to dosing.

    e. Positive hepatitis C serology or active hepatitis B infection.

    f. Known autoimmune disease requiring active treatment. Subjects with a condition requiring systemic treatment with either corticosteroids (>10 mg daily prednisone equivalent) or other immunosuppressive medications within 4 weeks or 5 half-lives of registration are excluded.

    g. Psychiatric illness/social situations that would limit compliance with study requirements.

    h. Previous malignancies, unless basal or squamous cell carcinoma of the skin or cervical carcinoma in situ with a complete remission achieved at least 5 years prior to study entry and no additional therapy is required or anticipated to be required during the study period.

    i. Loss of ≥ 475 mL blood volume or blood donation transfusion of any blood product within 3 months prior to screening.

    j. Other illness or laboratory abnormality that in the opinion of the Investigator should exclude the subject from participating in this study.

2. Prohibited Treatments and/or Restricted Therapies

    a. Use of any prescription drugs within 4 weeks (hormonal methods of contraception are allowed) or less than 5 half-lives prior to dosing, or over-the-counter (OTC) medication (vitamins, herbal supplements, dietary supplements) within 2 weeks or less than 5 half-lives prior to dosing.

    b. Exposure to any investigational drug or placebo within 3 months of first dose of study drug.

    c. Previous treatment or clinical trial participation with monoclonal antibody therapy.

    d. History of drug or alcohol abuse within 12 months prior to dosing, or those who have a positive urine drug test or breath alcohol test at Screening or Baseline.

e. Transfusion of blood or any blood product within 3 months prior to screening.

f. History of using nicotine-containing products or smoking more than 5 cigarettes weekly for at least three months prior to the study through the final evaluation.

3. Allergies and Adverse Drug Reaction

a. History of severe hypersensitivity reactions to other monoclonal antibodies.

b. Known history of clinically significant drug allergy at Screening or Baseline

4. Sex and Reproductive Status

a. Women who are pregnant or nursing.

6 STUDY CONDUCT

6.1 Subject Screening and Enrollment ID

Screening and Enrolled Subject ID's

Once a potential subject is confirmed to meet the inclusion criteria, assign a screening ID using the following format: letter 'S', 4-digit study ID (0317), 3-digit site ID (assigned by Altor), dash, and single-digit number starting from '1'. For example, the first subject screened by site 067 will be S0317067-1.

For each enrolled patient, complete the **Screening and Enrollment Log** (Section 16.8) after the patient is screened. Send the form to Altor BioScience when requested.

Once screening is complete and the subject is enrolled, assign the subject study ID using the following format: 4-digit study ID (0317), dash, 3-digit site ID (assigned by Altor), dash, and 3-digit number starting from '001'. For example, the first subject enrolled by site 067 will be 0317-067-001.

For each enrolled patient, complete the **Notification of Enrollment & Dosing Form** (Section 16.9) after the patient is enrolled and the first dose is administered. Send the form to Altor BioScience.

6.2 General Instructions

The total duration of subject participation, from Study Day 1 until the "End of Study" visit, is 29 days.

6.3 Study Procedures by Time Point

6.3.1 Screening and Baseline

Time 0 is defined at the start of the first dose of ALT-803. Baseline is defined as Study Day 1 prior to the administration of the first dose of ALT-803 (Time 0). The Screening Period is the 14-day period prior to Baseline.

6.3.1.1 Screening: Within 14 days prior to first ALT-803 dose

The following procedures and assessments must be performed within the 14 days prior to first dose of ALT-803:

- Medical History and Demographics
- Complete Physical Exam
- Serum Pregnancy Test
- Urine Drug Test
- Alcohol Breath Test
- HIV, Hepatitis B and C serologies
- Vital Signs

- Height and Weight
- CBC with Differential
- Blood Chemistry (CMP)

6.3.1.2 Baseline: Study Day 1, Study Period 1

The following procedures and assessments must be performed during the baseline period (prior to ALT-803 dose):

- Routine Physical Exam
- Urine Pregnancy Test
- Urine Drug Test
- Alcohol Breath Test
- Vital Signs
- Weight
- CBC with Differential
- Blood Chemistry (CMP)
- Blood Sampling for Immune Cells
- Blood Sampling for Cytokines
- Blood Sampling for Immunogenicity
- Blood Sampling for PK prior to ALT-803 dose (should be drawn immediately prior to ALT-803 dose)
- General Health Questionnaire
- Digital photography of injection site

6.3.2 Study Period 1

The following procedures and assessments must be performed during study period 1:

Study Day 1:

- ALT-803 subQ Injection
- Vital Signs (one-hour post ALT-803 dose)
- Blood Sampling for PK (one hour and four hours post-dose ALT-803)
- Injection site reaction diary
- Digital photography of injection site (prior to discharge)
- Adverse Event Monitoring
- Concomitant Medications

Study Day 2-9:

- Vital Signs (prior to blood sample collection)
- CBC with Differential
- Blood Chemistry (CMP)
- Blood Sampling for Immune Cells

- Blood Sampling for Cytokines
- Blood Sampling for PK
- Injection site reaction diary (Day 2-6 & as applicable post-Day 6)
- Digital photography of ISR (Day 2-6 & as applicable post-Day 6)
- Concomitant Medications
- Adverse Events

6.3.3 Study Period 2

The following procedures and assessments must be performed during study period 2:

Study Day 1:

Prior to ALT-803 dose:

- Routing Physical Exam
- Urine Pregnancy Test
- Urine Drug Test
- Alcohol Breath Test
- Vital Signs
- Weight
- CBC with differential
- Blood Chemistry (CMP)
- Blood Sampling for Immune Cells
- Blood Sampling for Cytokines
- Blood Sampling for Immunogenicity
- Blood Sampling for PK (immediately prior to ALT-803 dose)
- Digital photography of injection site
- Adverse Event Monitoring (rest period – Day 1, Study Period 2)
- Concomitant Medications (rest period – Day 1, Study Period 2)

- ALT-803 subQ Injection

Post ALT-803 dose:

- Vital Signs (one-hour post ALT-803 dose)
- Blood Sampling for PK (one hour and four hours post-dose ALT-803)
- Injection site reaction diary
- Digital photography of injection site (prior to discharge)
- Adverse Events Monitoring
- Concomitant Medications

Study Day 2-9:

- Vital Signs (prior to blood sample collection)
- CBC with Differential
- Blood Chemistry (CMP)

- Blood Sampling for Immune Cells
- Blood Sampling for Cytokines
- Blood Sampling for PK
- Injection site reaction diary (Day 2-6 & as applicable post-Day 6)
- Digital photography of injection site (Day 2-6 & as applicable post-Day 6)
- Concomitant Medications
- Adverse Events

6.3.4 End of Study Visit

The following procedures and assessments must be performed at the follow-up visit:

Study Day 15:

- Routine Physical Exam
- Serum Pregnancy Test
- Vital Signs
- CBC with Differential
- Blood Chemistry (CMP)
- Blood Sampling for Immune Cells
- Blood Sampling for Cytokines
- Blood Sampling for Immunogenicity
- General Health Questionnaire
- Injection site reaction diary (as applicable post-Day 9)
- Digital photography of ISR (as applicable post-Day 9)
- Concomitant Medications
- Adverse Events

6.4 Premature Discontinuation and Subject Replacement

Any subject who meets the following criteria will be replaced:

- Subjects who are enrolled but do not receive ALT-803
- Subjects who withdraw consent
- Subjects who have a positive alcohol or drug test after enrollment
- Subjects who miss more than one PK collection timepoint during study period 1 or study period 2 will be replaced.

Subjects who are replaced will be followed for up to 14 days, following their last dose of ALT-803 for adverse events monitoring only.

7 DESCRIPTION OF STUDY PROCEDURES

7.1 Clinical Assessments and Procedures

7.1.1 Medical History

A complete medical history (e.g. review of all body systems, summary of all illnesses, surgeries, allergies, drug sensitivities, menstrual history for women, and methods of contraception) will be performed at screening. Medical history will also include history of drug, nicotine and alcohol consumption.

7.1.2 Physical Examination

A complete physical exam [head, eyes, ears, nose, throat, skin, heart, lungs, abdomen, extremities, and neurological (e.g. level of consciousness, pupils, motor and sensory responses, and reflexes)] will be performed at screening and a routine physical exam will be performed on all study visits per schedule of assessments.

7.1.3 Vital Signs, Body Weight & Height

Vital signs (heart rate, blood pressure, respiratory rate, body temperature) will be collected at screening and at study visits per Schedule of Assessments (Section 4.3). Vital signs will be performed prior to, and one-hour post-ALT-803 subQ injection. On PK sample collection days, vital signs are to be collected prior to blood draw. Height (in cm) will be measured at screening and body weight (in kg) will be noted before each ALT-803 subQ injection.

7.1.4 General Health Questionnaire

The General Health Questionnaire (GHQ), RAND 36-item Short Form Survey 1.0 (SF-36) will be completed by the subject at baseline on Day 1, study period 1, and at the Follow-up visit, please refer to (Section 16.2). The subject must complete the GHQ at the PK Unit (research site) during the scheduled visit.

7.1.5 Injection Site Reaction Subject Diary and Digital Photographic Documentation

The ALT-803 Injection Site Reaction Diary (Section 16.1) will be given to subjects on the day that the ALT-803 subQ injection is administered (Day 1 of Study Period 1 and 2). The diary is to be completed by the subject daily for six days or until the resolution of symptoms, whichever is longer. The subject will return the completed diaries to the study coordinator.

Since injection site reactions are an adverse event, close clinical follow up is a requirement. Prior to subQ injection of ALT-803, a photograph should be taken of the injection area (i.e. right abdomen). The PI should photograph the injection site daily for six days or until the resolution of symptoms, whichever is longer (Schedule of Assessments, Section 4.3), a camera with a minimum of 10 megapixels should be used, and 2 views of the lesion (one identifying the region of the body and one close-up) should be taken. An adhesive label with the study I.D., PID, patient initials, date, time and the corresponding number of the photo (i.e. image 1 or image 2) should be placed next to the injection site (on the skin) for both views (please see photographic example below).

(Mocci 2013)

7.2 Test Collection and Processing

The following tests will be processed/performed at the study site's (or local) laboratory:

- Hematology: CBC (Complete Blood Count) with Differential
- Blood Chemistry: CMP (Complete Metabolic Panel)
- Serum/Urine Pregnancy Test
- Alcohol Breath Test
- HIV Test
- Hepatitis B Test
- Hepatitis C Test

Blood/Urine Sample Collection and Processing

- Follow standard blood/urine collection procedures according to site guidelines.
- Use the sample collection tubes/containers specified by site guidelines for the following routine tests: Serum and urine pregnancy (if applicable), CBC with differential, and CMP.
- Follow the Sponsor guidelines for PBMC isolation for immune cells (Section 7.3) and serum for PK, cytokines, and immunogenicity (Section 7.4).
- Collect samples at the designated time points according to the Schedule of Assessments (Section 4.3). Screening tests are performed <14 days prior to the start of therapy unless otherwise specified.
- The Study Coordinator or designee will review the test results as soon as possible.
- The specimens should be saved until the Study Coordinator has reviewed the test results.

- The Study Coordinator will transcribe the test results into the corresponding subject case report forms (CRFs) and will record Adverse Events in the Adverse Event Log CRF for any clinically significant laboratory abnormalities.

7.3 Immune Cells (PBMCs)

These assays will be performed at Altor BioScience for the purpose of monitoring immune cell levels and activity, and immune cell phenotype subsets. The test/collection schedule is specified in the Schedule of Assessments (Section 4.3).

If available, these samples may be retained and used for additional biomarker research studies.

Immune Cells Collection and Processing

Materials/equipment:

- Histopaque-1077; Sigma-Aldrich; Cat#10771-100ML
- HBSS (1X); Gibco; Cat#14175-095
- 1X BD FACS Lysing Solution:
  - → 10X BD FACS Lysing Solution; BD; Cat#349202 (10mL)
  - → Purified H2O
- Roswell Park Memorial Institute Wash Media (RPMI + 10%FBS):
  - → RPMI; Gibco; Cat#22400-089
  - → Fetal Bovine Serum (FBS); Hyclone; Cat#SH30071.03
- RPMI Freezing Media (RPMI Wash Media + 10%DMSO):
  - → RPMI Wash Media (above)
  - → Dimethyl Sulfoxide (DMSO); Sigma; Cat#D-8418
- 15mL Conical Tubes; Corning; Cat#430790
- Thermo Scientific Sorvall ST-16R swinging bucket Centrifuge, refrigerated. (Or equivalent centrifuge)
- 0.5 or 1.7mL Eppendorf Tubes
- Trypan Blue; Sigma-Aldrich; Cat#T8154
- Microscope
- Hausser Scientific Bright-Line Counting Chamber; Fisher Scientific; Cat#02-671-51B (or equivalent Hemocytometer w./ 0.1mm Neubauer ruling) (ViCell may also be used if available)
- 2mL sterile Cryovials w./ silicone seal; Phenix Research; Cat#C-402-4 (or equivalent 2mL freezer tube)
- Pipets, various.

Immune cells isolation procedure:

Follow the standard blood collection procedures according to site guidelines. Collect at least 4 mL of blood per collection tube. Altor BioScience will provide the blood collection tubes (and corresponding labels) described in the table below. Contact Altor BioScience for re-supply.

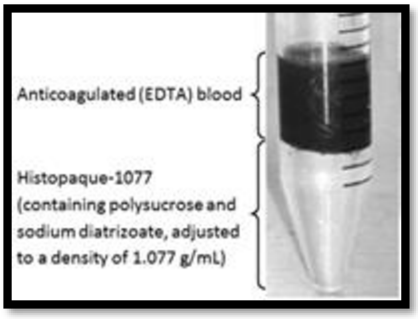
Test(s)	Tube Type & Size (Per Time Point)	Sample Processing Required	Pick-up
Immune Cells	Two 6 mL purple top tube	Yes	Foam container, Dry ice

1. Place the appropriate label (Immune Cells) provided by the Sponsor on the collection tube. Space is provided on each label to specify the following information:
   - Immune Cells: Subject ID No., subject initials, date & time of draw, visit (*Day #)* and time point (*pre-dose, N/A*).

   The format required for each recorded **Date** is mm/dd/yyyy and **Time** hh:mm;0-23:0-59.
2. Collect blood from the subject at the designated time points according to the Schedule of Assessments (Section 4.3). The purple top tubes must be gently inverted 8-10 times immediately after collection.
3. Transport the collection tubes to the study laboratory (or designated processing area) for immediate processing.

Prior to beginning the isolation, ensure that the work area has been sterilized and proper aseptic technique will be used.

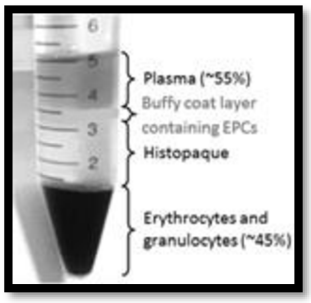
4. Bring all reagents to room temperature.
5. Add 4mL of Histopaque-1077 to a 15mL conical tube.
6. In a separate tube, dilute subject whole blood with equal volume of HBSS and carefully layer the diluted blood over top of the Histopaque-1077 being careful to minimize mixing of blood with Histopaque, (image below).



(Tan 2013)

7. Centrifuge at 400G for 30min at room temperature. Acceleration/deceleration should be set as follows: ACC=9, DEC=7.

8. After centrifugation, carefully remove the top plasma layer and discard (see image below).
9. Carefully collect the opaque interface ("buffy coat") into a clean 15mL tube already containing 4mL of HBSS.



(Tan 2013)

10. Centrifuge at 300G for 5 min at room temperature.
11. Pour off HBSS saving the cell pellet at the bottom.
12. Add 2mL of BD Lysing Solution to the pellet and resuspend. Allow to sit for 3-5 min to lyse remaining red blood cells.
13. Add 2mL of RPMI Wash Media to neutralize the lysing solution.
14. Centrifuge at 300G for 5 min at 4°C.
15. Pour off RPMI and resuspend the pellet in a fresh 4mL RPMI Wash Media. In a clean 0.5 or 1.7mL Eppendorf tube, pipet a small volume of resuspended cells. Dilute cells with equal volume Trypan Blue and add approx. 20µL to a hemocytometer* and count the cells at 10X Magnification (0.25NA). (See below for cell count calculation).

    *Vycell may be used if available

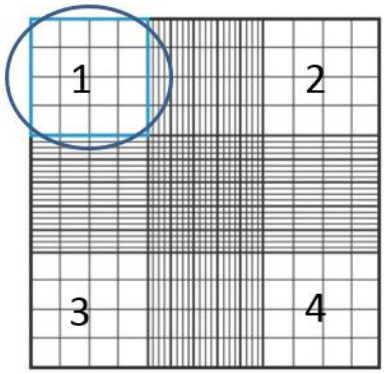
16. While counting, centrifuge the cell tube once more at 300G for 5 min at 4°C.
17. Pour off RPMI being careful to save the cell pellet. Resuspend the pellet in 2mL of RPMI Freezing Media.
18. Transfer 1mL each of resuspended cells in freezing media into two 2mL freezer tubes (*four tubes total will be yielded from blood collected for procedure).
19. Label each tube with subject ID, timepoint, date of isolation, study ID and cell count.
20. Store the freezer tubes at -80°C inside a storage box (provided by Altor BioScience) designated for the study.
21. Label the storage box with the following information: Sponsor name (Altor BioScience), protocol no. (CA-ALT-803-03-17) and box no. Box no. is a sequential number starting with "1".
22. Record the specimen collection information in the Immune Cell Specimen Storage Log (Section 16.4) for every sample processed and stored in a -80°C freezer. Use one immune cell storage log for each subject.

Counting Immune cells

23. Prior to counting, ensure the hemocytometer* and coverslip are both clean and dry. A 70% reagent alcohol solution or equivalent can be used.

    *Vi-cell may be used if available

24. Pipet approx. 10-15µL of isolated immune cells diluted 1:2 in Trypan Blue into the loading area of the counting chamber.
25. With the chamber underneath the objective, focus the microscope and adjust the light as necessary.
26. The counting area in the Neubauer Ruling should look like this:



27. Within the confines of the 16 squares circled above (corner #1), count all **live** immune cells. (Live cells will appear round and opaque and dead cells will be stained blue).
28. Count the 4 corners of the Neubauer Ruling (64 small squares) and total the live immune cells.
29. Example Calculation:
    - (200 cells/ 4 corners) x 2 (dilution) x 10^4 = (1.00 x 10^6 cells/mL)
    - (1x 10^6 cells/mL) x 4mL (initial volume) = 4.0 x 10^6 cells
    - (4.0 x 10^6 cells) / 2mL (final volume in freezing media) = 2.0 x 10^6 cells/mL

**Repeat all steps for the second purple top tube.*

7.4 PK, Cytokines and Immunogenicity

7.4.1 PK

Altor Bioscience will use validated ELISA methods for PK analysis. These tests will be performed at Altor BioScience. The pharmacokinetic profile of ALT-803 will be assessed using blood collected at the following time points:

Study Periods 1 & 2:

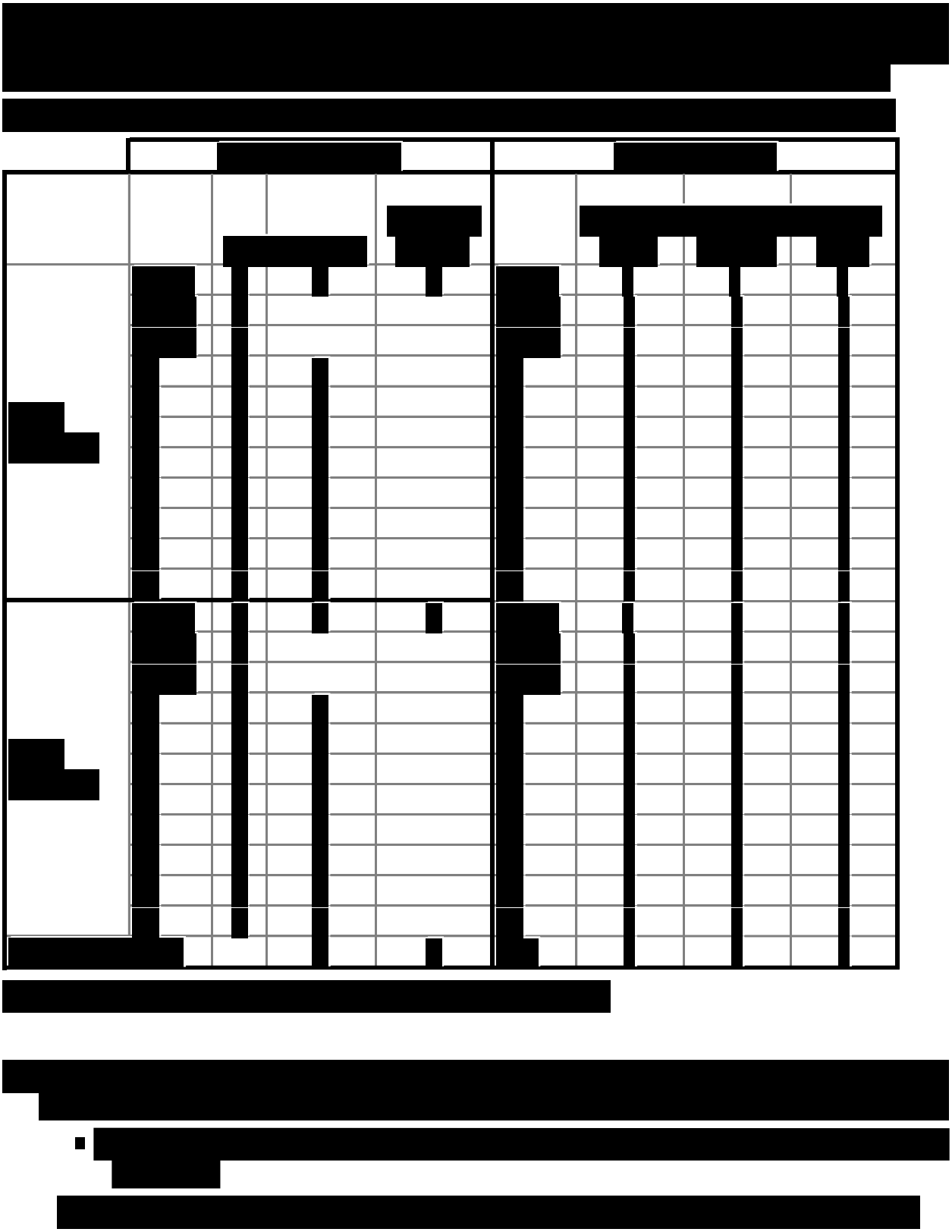
Day 1	Immediate Pre-dose (time 0)	± 5 minutes
Day 1	1 hour post-dose	± 5 minutes
Day 1	4 hour post-dose	± 15 minutes
Day 2	24-hour post-dose	± 60 minutes
Day 3	48-hour post-dose	± 60 minutes
Day 4	72-hour post-dose	± 60 minutes
Day 5	96-hour post-dose	± 60 minutes
Day 6	120-hour post-dose	± 120 minutes
Day 7	144-hour post-dose	± 120 minutes
Day 8	168-hour post-dose	± 120 minutes
Day 9	192-hour post-dose	± 120 minutes

[redacted]

[redacted]

[redacted]

[redacted]



[redacted]

7.6 Adverse event assessment

Subjects who have an on-going study drug-related adverse event or serious adverse event upon study completion or at discontinuation of the study will be contacted by the Investigator or his/her designee every week until the event is resolved or determined to be irreversible. Adverse event information will be collected for all subjects per Section 9.

7.6.1 ALT-803 Injection Site Reaction

Based on current experience, localized, transient skin rashes thought to be indicative of an immune response to ALT-803, are common with subQ administration. Adverse event monitoring will include an Injection Site Reaction Subject Diary (Section 16.1) to collect incidence and severity of potential injection site reactions and related symptoms.

7.7 Concomitant Medications

Concomitant medications [prescription drugs and over-the counter (OTC) medications (vitamins, herbal supplements, analgesics)] are not permitted while on study. At screening, use of any prescription drugs within 4 weeks (hormonal methods of contraception are allowed) or less than 5 half-lives prior to dosing, or OTC medications within 2 weeks or less than 5 half-lives prior to dosing are not permitted (for further details, please see Section 5.3, Exclusion Criteria, Prohibited Treatments and/or Restricted Therapies, page 23).

7.8 Protocol Deviations

In general, a protocol deviation is an inadvertent excursion to, or non-compliance with, the institutional review board (IRB) approved protocol. The Investigator is responsible for ensuring the study is conducted in accordance with the procedures described in this protocol and should not implement any changes to the protocol unless it is required to eliminate an immediate hazard to the subject. If a deviation occurs and affects the safety of a subject, Altor BioScience must be notified immediately. Please refer to Section 13, Quality Control and Quality Assurance, for detailed guidance on documentation of and severity of protocol deviations.

8 STUDY DRUG MANAGEMENT

8.1 ALT-803

8.1.1 Formulation

ALT-803 is a soluble complex consisting of two protein subunits of a human IL-15 variant associated with high affinity to a dimeric human IL-15 alpha receptor sushi domain / human IgG1 Fc fusion protein (Xu 2013).

8.1.2 Storage

ALT-803 must be maintained at a temperature between 2°C and 8°C.

8.1.3 Packaging and Delivery

ALT-803 is provided in a 2 mL vial containing 1.2 mL of ALT-803 at a concentration of 1 mg/mL or a 2 mL vial containing 0.6 mL of ALT-803 at a concentration of 2 mg/mL. Vials are packaged in cartons and are delivered to the research site.

8.1.4 Disposal/Destruction

No special considerations are necessary when disposing of used vials, dispose/destroy according to standard site guidelines. Maintain disposal/destruction records for inspection by Altor or Altor representative to review at a later time.

At the end of the study or at another pre-determined time, Altor will request the return of all remaining unused IP vials. At that time, Altor will provide specific packaging instructions and packing materials.

To record the return of IP vials, complete the following fields on the Study Medication Inventory Tracking **(SMIT)** form (Section 16.10): Date Returned, Returned By, and Returned To (e.g. Altor).

Be sure to use the next available row on the form.

8.2 Dose and Administration

Dose calculation will be based on subject's assigned dose level and actual body weight collected prior to ALT-803 dose for each study period. The calculated amount of ALT-803 will be drawn into a syringe for subQ injection. Stability studies have been conducted on IP diluted in 0.9% saline. The results of the studies show that the potency of ALT-803 is maintained within the specifications when diluted in 0.9% saline to a concentration of 25 µg/mL and stored in a syringe for ≤ 24 hour at 4°C.

The assigned concentration for study period 1 and 2 for all subjects enrolled in Group A is 1.0 mg/mL and 2.0 mg/mL for all subjects enrolled in Group B. Doses will be drawn directly into the syringe for injection. If the total subQ dose is greater than 1.5 mL, the dose will be divided into 2-3 subQ injections as needed. Injection sites should be rotated for study period 2, per institutional

guidelines and each injection site (preferably the abdomen) separated by at least 1 inch. The description of the injection site (i.e. left abdomen, left arm, right thigh, etc.), as well as any side effects such as redness, swelling or itching at the injection site should be recorded for each dose, in the Injection Site Reaction Diary (Section 16.1). No special considerations are necessary when handling (other than handling with gloves) the vialed product.

[redacted]

8.3.1 Altor Delivery Procedures

Altor will deliver the IP vials at 2-8°C in a reusable Greenbox with a TempTale® temperature monitor. The package will be hand delivered by an Altor Bioscience representative.

Altor will complete and include the following with each delivery:

a) **Study Medication Inventory/Tracking (SMIT) Form**. The following fields in the first row will be completed by Altor: The Total No. of Vials, Lot No., Concentration (Conc.), Date Delivered and Prepared by By. An example of the blank form is included in (Section 16.12).

b) **Study Medication Shipping Notice/Receipt (SMSNR) Form**. The sender section will be completed by Altor. An example of the blank form is included in (Section 16.11).

c) **Study Medication Shipping Requisition (SMSR) Form**. This is a blank order form for IP vial re-supply. An example of the blank form is included in (Section 16.12).

d) The first delivery will include the Certificate of Analysis for ALT-803.

8.3.2 Site IP Receipt Procedures

1. Immediately open the package upon arrival and turn off the TempTale® by pressing the Stop Button (red button) for about 3 seconds until the "Stop sign" icon appears in the upper right corner of the display window.
    a. Notate the date/time the TempTale® was turned off on the Recipient and Return Section of the **SMSNR Form** (Section 16.11).
    b. Note: If an alarm symbol is displayed in the display window, call Altor immediately (954-443-8600 ext. 838 or 879). A plan of action will be determined by Altor at that time.

2. Remove the vials from the payload box, inspect each vial as you complete the questions on the Recipient and Return Section of the **SMSNR Form** (Section 16.11) and place the vials in a temperature controlled/monitored refrigerator at 2-8°C.

3. The vials must remain quarantined and cannot be used until further notice from Altor. Notification will occur after Altor reviews the temperature report and receives the shipper back from your site.

4. Email the **SMSNR Form** (Section 16.13) to Altor BioScience. Keep a copy of the **SMSNR form** in the pharmacy binder.

5. Enter the Date Received and initial the "Received By" fields in the first row on the **SMIT Form** (Section 16.12). Keep this form in the pharmacy binder for Altor or Altor representative to review at a later time.

8.3.3 Site Shipper Return Procedures

1. Place all shipping materials including the TempTale® monitor, payload box and panels back into the Green Box. Close the Green Box, taping is not necessary.

2. Seal the outermost cardboard box with tape.

3. Schedule local pick-up with representative from Altor BioScience.

8.3.4 Altor IP Vial Approval

Once the shipper is received, Altor will review the temperature report and complete the bottom 'for Altor Use Only' section of the **SMSNR** Form (Section 16.13). The form will be emailed to the site. Print and keep the signed form in the pharmacy binder.

8.3.5 IP Dispensing, Accountability and Resupply

1. To record IP dispensing, the SMIT form (Section 16.12) is optional provided that the site has an equivalent accountability log (e.g. NIH-2564) or electronic record.

2. Using the SMIT form (Section 16.12): When dispensing a vial or vials for the preparation of study treatment, record the No. of Vials Used, Date Dispensed, pharmacist initials in the "Dispensed By" column, the Subject Study ID No. and the Dose.

8.3.6 IP Study Treatment Preparation

Refer to the ALT-803 Study Treatment Preparation Worksheet (Section 16.13).

8.3.7 Temperature Excursions

If storage conditions for investigational product have been compromised resulting in a temperature excursion (from the acceptable range), or if there is any suspicion that the investigational product has not been properly stored the following actions must be taken:

1. Notify Altor representative immediately via telephone and email
2. Complete the Temperature Excursion Report Form (Section 16.14) and return via scanned email to Altor BioScience as soon possible, within 24 hours of the noted excursion.
3. Quarantine the investigational product under the correct storage conditions until further notice from Altor.
4. Altor will send back the Temperature Excursion Report Form (Section 16.14) with the Temperature Excursion Assessment section (bottom) completed confirming if the investigational product is acceptable or not acceptable for clinical use.
5. If the investigational product is not acceptable for clinical use, Altor will provide a replacement and will provide further instructions for the quarantined vials.
6. Keep a copy of the Temperature Excursion Report Form (Section 16.14) in the pharmacy binder.

8.4 Prohibited Concomitant Therapy

No investigational, commercial or OTC medications other than ALT-803 may be administered during the duration of the study with the exception of those listed in (Section 8.6, Post-ALT-803 Therapy Guidelines).

Topical steroid cream is permitted.

8.5 Compliance

The protocol, specifically the Schedule of Assessments, requires complete adherence to safeguard subject wellbeing and ensure data integrity. Noncompliance, may result in a deviation or subject replacement (please see Section 6.4, Premature Discontinuation and Subject Replacement).

[redacted]

9 ADVERSE EVENTS

9.1 Monitoring, Recording and Reporting of Adverse Events

An adverse event (AE) is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the subject's health, including laboratory test values (Section 9.3), regardless of etiology. Any worsening (i.e., any clinically significant adverse change in the frequency or intensity of a pre-existing condition) should be considered an AE. A diagnosis or syndrome should be recorded on the AE page of the case report form (CRF) rather than the individual signs or symptoms of the diagnosis or syndrome.

If death occurs, this must be reported as an SAE to the Sponsor or their designated safety group within 24 hours of learning of this event.

An overdose, accidental or intentional, whether or not it is associated with an AE, or abuse, withdrawal, sensitivity or toxicity to an investigational product should be reported as an AE. If an overdose is associated with an AE, the overdose and AE should be reported as separate terms. In the event of overdose or exaggerated response, the subject should be monitored as appropriate and should receive supportive measures as necessary. There are no known specific antidotes for ALT-803 overdose. Actual treatments should depend on the severity of the clinical situation and the judgment and experience of the treating Investigator.

All AEs will be documented and reported by the Investigator from the time the subject is administered the first dose of ALT-803 to 14 days after the last dose of study drug or until the last study visit, whichever is longer. AEs and SAEs will be recorded on the AE page of the CRF and in the subject's source documents. When an AE/SAE occurs, the Investigator is expected to review all documentation (e.g., hospital progress notes, consultations, laboratory and diagnostics reports) related to the event. The Investigator must determine the relationship between the administration of the study drug and the occurrence of an AE/SAE as "not suspected" or "suspected". The Investigator is responsible for informing the IRB/IEC of SAEs and providing them with all relevant initial and follow-up information about the event as applicable. The Investigator must keep copies of all SAE information on file, including correspondence with Altor BioScience or Nant Safety and the IRB/IEC of record.

Please report all SAEs within 24 hours of the Investigator's awareness of the event by email (SAE@altorbioscience.com), using the provided **Serious Adverse Event Report Form** and **SAE Fax Cover Sheet** (Section 16.3). Please attach available copies of redacted/de-identified relevant source documents. Upon review of the SAE Report Form, Altor BioScience or its safety group, Nant Safety (an identical copy of the email sent to Altor will be automatically generated and sent to Nant Safety), may request the site to provide additional de-identified source documents describing the event.

IT IS MANDATORY THAT THE PRINCIPAL INVESTIGATOR (PI) OR SUB-INVESTIGATOR SIGN ALL SAE REPORTS AND ASSIGN RELATIONSHIP TO ALT-803, AND THAT HE/SHE IS LISTED ON THE FDA 1572.

The Investigator is responsible for informing the IRB/IEC of SAEs and providing them with all relevant initial and follow-up information about the event as applicable. The Investigator must keep copies of all SAE information on file, including correspondence with Altor BioScience or Nant Safety and the IRB/IEC of record.

If there are any questions regarding SAE reporting, please send all inquiries to SAE@altorbioscience.com (an identical copy of email sent to Altor will be automatically generated and sent to Nant Safety).

9.2 Evaluation of Adverse Events

Assignment of a grade of adverse events based on intensity of symptoms, degree of limitation of daily activities, or level of abnormality of objective clinical signs or laboratory parameters using Terminology Criteria for Adverse Events V4.03 (CTCAE).

9.2.1 Seriousness

An SAE is any AE that fulfils one or more of the following:

- Results in death.
- Is life-threatening (i.e., in the opinion of the Investigator, the subject is at immediate risk of death from the AE as it occurred).
- Requires in-subject hospitalization or prolongation of existing hospitalization (hospitalization is defined as an in-subject admission, regardless of length of stay).
- Results in persistent or significant disability or incapacity (a substantial disruption of the subject's ability to conduct normal life functions).
- Results in a congenital abnormality or birth defect.
- Is an important medical event that may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed above. Important medical events are defined as those occurrences that may not be immediately life-threatening or result in death, hospitalization, or disability, but may jeopardize the subject or require medical or surgical intervention to prevent one of the other outcomes listed above. Medical and scientific judgment should be exercised in deciding whether such an AE should be considered serious.

If an AE is considered serious, both the AE page/screen of the CRF and the SAE Report Form must be completed.

For each SAE, the Investigator will provide information on severity, start and stop dates, relationship to the study drug, action taken regarding the study drug, and outcome.

9.2.2 Severity/Intensity

The severity/intensity of AEs and SAEs will be graded based upon the subject's symptoms according to the NCI CTCAE Version 4.03.

http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf

AEs that are not defined in the NCI CTCAE Version 4.03 should be evaluated for severity/intensity according to the following scale:

- Grade 1 = Mild: transient or mild discomfort, no limitation in activity; no medical intervention/therapy required.
- Grade 2 = Moderate: mild to moderate limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required.
- Grade 3 = Severe: marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalization possible.
- Grade 4 = Life threatening: extreme limitation in activity, significant assistance required; significant medical intervention/therapy required, hospitalization or hospice care probable.
- Grade 5 = Death: the event results in death.

It is important to distinguish between serious and severe AEs. Severity is a measure of intensity whereas seriousness is defined by the criteria under Section 9.2.1. An AE of severe intensity may not be considered serious. Seriousness, not severity, serves as a guide for defining regulatory obligations.

9.2.3 Relationship to the Study Drug

The Investigator must determine the relationship between the administration of the study drug and the occurrence of an AE/SAE as "not suspected" or "suspected," as defined below:

- Not suspected: The temporal relationship of the AE or SAE to the study drug administration makes a causal relationship unlikely or remote, or other medications, therapeutic interventions, or underlying conditions provide a sufficient explanation for the observed event.
- Suspected: The temporal relationship of the AE or SAE to the study drug administration makes a causal relationship possible, and other medications, therapeutic interventions, or underlying conditions do not provide a sufficient explanation for the observed event.

If an event is assessed as suspected of being related to a comparator, ancillary, or additional study drug that has not been manufactured or provided by Altor BioScience, please provide the name of the manufacturer when reporting the event.

9.2.4 Duration

For all AEs and SAEs, the Investigator will provide a record of the start and stop dates of the event. Please see study specific CRF data entry completion guidelines and SAE report completion guidelines for instructions for capturing the start and stop dates of AEs and SAEs.

9.2.5 Action Taken

The Investigator will report the action taken with the study drug as a result of any AE or SAE, as applicable (e.g., discontinuation of the study drug) and report if concomitant and/or additional treatments were given for the event.

9.2.6 Outcome

The Investigator will report the outcome of the event for both AEs and SAEs. Non-serious AEs will be followed for 14 days after the subject's last dose of the study drug. AEs will be followed until resolution or stabilization. All SAEs that have not resolved upon discontinuation of the subject's participation in the study must be followed until recovered, recovered with sequelae, not recovered (death due to other cause), death (due to the SAE), lost to follow up, or otherwise explained.

9.3 Abnormal Laboratory Values

An abnormal laboratory value is considered to be an AE if the abnormality:

- Results in discontinuation from the study;
- Requires treatment, modification/interruption of the study drug dose, or any other therapeutic intervention; or
- Is judged to be of significant clinical importance.

Regardless of the severity grade, only laboratory abnormalities that fulfill a seriousness criterion need to be documented as an SAE.

If a laboratory abnormality is one component of a diagnosis or syndrome, then only the diagnosis or syndrome should be recorded on the AE page/screen of the CRF. If the abnormality was not a part of a diagnosis or syndrome, then the laboratory abnormality should be recorded as the AE.

9.4 SAE Report Form Completion Guidelines

Please do not leave report fields blank. If the information requested is unknown, please indicate so by placing UNK in that field.

1. Provide reporter's name (person completing the form).
2. Provide date of report using date format (DD/MMM/YYYY).
3. Provide Investigator's name.
4. Provide site name.

5. Provide site address.

6. Provide site country.

7. Provide site telephone number of site staff/Investigator who can be reached to answer questions. Please do not provide a general office number (receptionist).

8. Provide site email address of site staff/Investigator who can be reached via email to answer questions.

9. Indicate if this is an initial or follow up SAE report. If follow up, indicate follow-up number in sequential order (example: follow-up #1, follow-up #2, etc.)

10. Provide date the site became aware of the event using date format (DD/MMM/YYYY).

11. Provide subject initials (N/A for EU or other territories that prohibit).

12. Provide subject study ID (10-digit ID).

13. Provide subject gender.

14. Provide subject date of birth (N/A for EU or other territories that prohibit) using date format (DD/MMM/YYYY).

15. Provide subject weight in kilograms.

16. Provide subject height in centimeters.

17. Check all applicable SAE criteria and provide additional details as indicated.

    - In case of in-subject hospitalization or prolongation of hospitalization:

      - Record date of admission using date format (DD/MMM/YYYY)

      - Record date of discharge using date format (DD/MMM/YYYY)

    - In case of death:

      - Record date of death using date format (DD/MMM/YYYY)

      - Record cause of death

      - Indicate if death certificate was obtained by checking the appropriate box. If yes, attach the redacted certificate.

      - Indicate if the autopsy report was obtained by checking the appropriate box. If yes, attach the redacted report.

18. Provide adverse event term (the reported term must represent the event that met SAE criteria; for example, fever, nausea, vomiting are symptoms of flu, and therefore, hospitalization due to the flu is the SAE event, reported as flu). Only one event can be reported per SAE form. If additional SAEs occurred, they will need to be reported separately on separate SAE forms. Death is considered an outcome and should only be reported as the SAE term if death is the only information available at the time of reporting. On follow up, the SAE term will need to be amended to the event term that resulted in death.

19. Provide SAE start date using date format (DD/MMM/YYYY). Start/onset date should be the date the event became serious/met SAE criteria.

20. Provide the SAE start time using 24-hour clock (if known).

21. Provide stop date using date format (DD/MMM/YYYY). Stop/end date should be the date the event no longer met the recorded SAE criteria.

22. Provide stop time using 24-hour clock (if known).

23. If the SAE is not resolved at the time of the report, check if ongoing.

24. Provide event severity grade using Terminology Criteria for Adverse Events V4.03 (CTCAE).

25. Provide relationship to ALT-803. Please do not leave blank; attribution can be changed on follow up. If not suspected, indicate cause of the event in the SAE report narrative, if applicable [e.g. lack of efficacy, concurrent disorder (specify), concomitant medication (specify), other (specify)].

26. Provide event outcome. In the event of a subject's death and the reported SAE was ongoing at the time of death, please mark the outcome as 'Unresolved' and leave the SAE stop date blank. Please indicate in the SAE report narrative that the reported SAE will remain as 'Unresolved' due to the fact that the SAE was unresolved at the time of death (this will keep Altor BioScience or Nant Safety from having to query for a resolution date.) If the reported SAE is the cause of death, the outcome should be recorded as 'Fatal' and the SAE end date should be recorded as the date of death.

27. Provide site ID (067).

28. Provide subject study ID (10-digit ID) and subject initials.

29. Provide date of first dose of ALT-803 using date format (DD/MMM/YYYY).

30. Provide date of last dose of ALT-803 prior to onset of SAE using date format (DD/MMM/YYYY).

31. Provide dose amount and unit for ALT-803.

32. Indicate # of doses received for ALT-803.

33. Provide lot number for ALT-803.

34. Provide action taken with each study medication for this event including abatement/reappearance/NA.

35. In the narrative, describe event fully. Include baseline medical status including relevant medical history, signs and symptoms, diagnosis, diagnostic test results, clinical course, treatment (all drugs/procedures used as interventions for SAE), outcome, hospital course for hospitalizations, etc. Provide rationale for causality assessment. Document other potential causes of the event. If additional space is needed for narrative please include additional page.

36. Attach relevant de-identified test results and hospital records when submitting the form. If subject was hospitalized, submit discharge summary, if available. If not available at time of initial report, submit discharge summary when it is available.

37. **Complete AE, Medical History, applicable Study Treatment Administration, and Concomitant Medications eCRFs as soon as possible.** Instructions regarding recording of AEs and SAEs in the EDC are available in the eCRF Completion Guidelines.

38. Provide Principal Investigator or Sub-Investigator's printed name, signature and date using date format (DD/MMM/YYYY).

No Changes are to be made on the initial SAE form (this is a legal document). Therefore, any changes or additional information must be documented on a follow-up SAE form.

9.5 Pregnancy

9.5.1 Females of Child-Bearing Potential

Pregnancies and suspected pregnancies (including a positive pregnancy test regardless of age or disease state) of a female subject occurring while the subject is on the study drug, or within 14 days of the subject's last dose of the study drug, are considered immediately reportable events.

The study drug is to be discontinued immediately. The pregnancy, suspected pregnancy, or positive pregnancy test must be reported to Altor BioScience/Nant Safety (an identical copy of email sent to Altor will be automatically generated and sent to Nant Safety) immediately by email (SAE@altorbioscience.com), using the Pregnancy Questionnaire (Section 16.6). The female subject may be referred to an obstetrician-gynecologist (not necessarily one with reproductive toxicity experience) or another appropriate healthcare professional for further evaluation.

The Investigator will follow the female subject until completion of the pregnancy and must notify Altor BioScience Drug Safety immediately about the outcome of the pregnancy (either normal or abnormal outcome) using the Follow-up Pregnancy Questionnaire (Section 16.6).

If the outcome of the pregnancy was abnormal (e.g., spontaneous or therapeutic abortion), the Investigator should report the abnormal outcome as an AE. If the abnormal outcome meets any of the serious criteria, it must be reported as an SAE to Altor BioScience/Nant Safety by email (SAE@altorbioscience.com), within 24 hours of the Investigator's knowledge of the event using the SAE Report Form.

All neonatal deaths that occur within 28 days of birth should be reported, without regard to causality, as SAEs. In addition, any infant death after 28 days that the Investigator suspects is related to the *in utero* exposure to the study drug should also be reported to Altor BioScience/Nant Safety immediately by email (SAE@altorbioscience.com), within 24 hours of the Investigator's knowledge of the event using the SAE Report Form. Male Subjects

If a female partner of a male subject taking the study drug becomes pregnant, the male subject should notify the Investigator as soon as possible, who will provide a copy of the Pregnant Partner Informed Consent Form and a copy of the pregnancy questionnaire to the male study subject to provide to the pregnant partner.

If the pregnant partner consents, she will check the appropriate box on the consent form, sign the consent form, and complete the pregnant partner questionnaire; the male subject will also sign the consent form and provide the pregnant partner with the Investigator's contact information should she have any questions on the consent form or questionnaire. The male subject shall return the signed consent form and completed questionnaire to the study coordinator or Investigator. The pregnant partner will be contacted for information regarding outcome of the pregnancy (e.g., live birth, etc.) and will be contacted up to 6 months following a live birth for information on the health of the child. The reporting and collection of AEs will follow the process described in Section 9.4.1.

If the pregnant partner refuses to consent, the male subject will indicate on the consent form, and will sign that he presented the consent to his pregnant partner. The Investigator will record that a pregnancy occurred and that the pregnant partner refused consent.

9.6 Reporting of Adverse Events

Any AE that meets any criterion for an SAE requires the completion of an SAE Report Form in addition to being recorded on the AE page/screen of the CRF. All SAEs must be reported to Altor BioScience Drug Safety within 24 hours of the Investigator's knowledge of the event by facsimile, email using the SAE Report Form. This instruction pertains to initial SAE reports as well as any follow-up reports.

SAE Reporting information:
Email: SAE@AltorBioScience.com
(an identical copy of email sent to Altor will be automatically generated and sent to Nant Safety)

The Investigator is required to ensure that the data on these forms are accurate and consistent. This requirement applies to all SAEs (regardless of relationship to the study drug) that occur during the study (from the time the subject signs informed consent to 14 days after the last dose of the study drug), and those made known to the Investigator at any time thereafter that are suspected of being related to the study drug.

The SAE report should provide a detailed description of the SAE and include summaries of hospital records and other relevant documents. If a subject died and an autopsy has been performed, copies of the autopsy report and death certificate are to be sent to Altor BioScience Safety as soon as these become available. Any follow-up data will be detailed in a subsequent SAE Report Form and sent to Altor BioScience Drug Safety. Hospital records and other relevant documents must be de-identified and the study identifier must be included.

Where required by local legislation, the Investigator is responsible for informing the IRB or independent ethics committee (IEC) of the SAE and providing them with all relevant initial and follow-up information about the event. The Investigator must keep copies of all SAE information on file including correspondence with Altor BioScience and the IRB/IEC.

9.7 Expedited Reporting of Adverse Events

For events considered related to the study drug by the Investigator, Altor BioScience Drug Safety will determine the expectedness of events suspected of being related to ALT-803 based on the Investigational Brochure.

AEs such as disease progression, death related to disease progression (in the absence of serious study drug-related events), and serious events due to the relapse of the studied indication will not be subject to expedited reporting by the Sponsor to Regulatory Authorities.

Altor BioScience or its authorized representative shall notify (no later than 15 calendar days of receipts per regulations) the Investigator of the following information:

- Any AE suspected of being related to the use of the study drug in this study or in other studies that is both serious and unexpected (i.e., SUSAR).
- Any finding from tests in laboratory animals that suggests a significant risk for human subjects, including reports of mutagenicity, teratogenicity, or carcinogenicity.

Where required by local legislation, the Investigator shall notify his/her IRB/IEC promptly of these new serious and unexpected AE(s) or significant risks to subjects.

10 STATISTICS

10.1 General Procedures

Descriptive statistical methods will be used to summarize the data from this study. Unless otherwise stated, the term descriptive statistics refers to the number of subjects, mean, median, standard deviation, minimum, and maximum for continuous data, and frequencies and percentages for categorical data. No statistical testing will be performed.

10.2 Sample Size

A total of 16 patients will be enrolled (8 patients in Group A and 8 patients in Group B)

10.3 Populations for Analysis

The safety population will include subjects who receive at least one dose of ALT-803.

The evaluable population (for pharmacokinetics) will include all subjects who have received both doses of ALT-803 and have no more than one missing PK sample during each study period.

10.4 Statistical Methods

10.4.1 Demographic and Baseline Characteristics

Demographic data and baseline characteristics including age, gender, race/ethnicity, screening height and weight, and limited medical history will be summarized.

10.4.2 Study Drug Exposure

Exposure to ALT-803 will be summarized.

10.4.3 Analysis of Safety

Safety will be evaluated by vital signs, clinical laboratory tests, the subject diary and adverse events. Subjects will be monitored and queried throughout the entire duration of the study for Adverse Events (AEs). All adverse events will be graded by using the NCI Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.03) and will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Adverse events will be summarized by system organ class, preferred term, and greatest severity. Separate summaries for adverse events related to study drug, serious adverse events, adverse events leading to discontinuation, and adverse events with an outcome of death will be produced. Separate summaries for vital signs and clinical laboratory tests will also be generated.

10.5 Interim Analysis

No interim analysis is currently planned for this study.

11 ETHICS AND RESPONSIBILITIES

11.1 Good Clinical Practice

The procedures set out in this study protocol pertaining to the conduct, evaluation, and documentation of this study are designed to ensure that the Sponsor, its authorized representative(s), and Investigator(s) abide by Good Clinical Practice (GCP), as described in the International Conference on Harmonization (ICH) Guideline E6 and in accordance with the general ethical principles outlined in the Declaration of Helsinki. The study will receive approval from an IRB/IEC prior to commencement. The Investigator will conduct all aspects of this study in accordance with applicable national, state, and local laws of the pertinent regulatory authorities.

11.2 Investigator Responsibilities

Investigator responsibilities are set out in the ICH Guideline for Good Clinical Practice and in the local regulations. Sponsor staff or an authorized representative will evaluate and approve all Investigators who in turn will select their staff.

The Investigator should ensure that all persons assisting with the study are adequately informed about the protocol, amendments, study treatments, as well as study-related duties and functions. The Investigator should maintain a list of Sub-Investigators and other appropriately qualified persons to whom he or she has delegated significant study-related duties.

The Investigator is responsible for keeping a record of all subjects who sign an informed consent document and are screened for entry into the study. Subjects who fail screening must have the reason(s) recorded in the subject's source documents.

The Investigator, or a designated member of the Investigator's staff, must be available during monitoring visits to review data, resolve queries and allow direct access to subject records (e.g., medical records, office charts, hospital charts, and study-related charts) for source data verification. The Investigator must ensure timely and accurate completion of CRFs and queries.

11.3 Subject Information and Informed Consent

The Investigator must obtain written informed consent from the subject or a legal representative prior to performing any study-related procedures. Each Investigator has both ethical and legal responsibility to ensure that the subjects being considered for inclusion in this study are provided a full explanation of the protocol and the roles and responsibilities of the subject for participation in the study.

Documentation that written informed consent was obtained prior to the study subject's entry into the study and of the informed consent process should be recorded in the study subject's source documents, including the date. The original informed consent document signed and dated by the study subject and by the person consenting the study subject prior to the study subject's entry into the study must be maintained in the Investigator's study files and a copy given to the study subject. In addition, if a protocol is amended and the amendment(s) impact the content of the informed consent, the informed consent document must be revised. Study subjects participating in the study when the amended protocol is implemented must be re-consented with the revised version of the

informed consent document. The revised informed consent document signed and dated by the study subject and by the person consenting the study subject must be maintained in the Investigator's study files and a copy given to the study subject.

11.4 Confidentiality

The Sponsor (Altor BioScience), affirms the subject's right to protection against invasion of privacy and to be in compliance with ICH and other local regulations (whichever is most stringent). The Sponsor requires the Investigator to permit the Sponsor and/or their designated representatives and, when necessary, representatives from regulatory authorities, to review and/or copy any medical records relevant to the study in accordance with local laws.

Should direct access to medical records require a waiver or authorization separate from the subject's signed informed consent document, it is the responsibility of the Investigator to obtain such permission in writing from the appropriate individual.

Subjects will be identified only by initials and unique subject numbers in CRFs.

11.5 Protocol Amendment

Protocol modifications, except those intended to reduce immediate risk to study subjects, may be made only by Altor BioScience. A protocol change intended to eliminate an apparent immediate hazard to subjects may be implemented immediately, provided the IRB/IEC is notified within 5 days.

Any permanent change to the protocol must be handled as a protocol amendment. The written amendment must be submitted to the IRB/IEC and the Investigator must await approval before implementing the changes. Altor BioScience will submit protocol amendments to the appropriate regulatory authorities for approval.

If in the judgment of the IRB/IEC, the Investigator, and/or Altor BioScience, the amendment to the protocol substantially changes the study design and/or increases the potential risk to the subject and/or has an impact on the subject's involvement as a study participant, the currently approved written informed consent form will require similar modification. In such cases, informed consent will be renewed for subjects enrolled in the study before continued participation.

11.6 Institutional Review Board/Independent Ethics Committee Review and Approval

The Investigator must obtain IRB/IEC approval for the investigation. Initial IRB/IEC approval, and all materials approved by the IRB/IEC for this study, including the subject consent form and recruitment materials, must be maintained by the Investigator and made available for inspection.

The final study protocol, including the final version of the Informed Consent Form, must be approved or given a favorable opinion in writing by an IRB or IEC as appropriate. The Investigator must submit written approval to Altor BioScience before he or she can enroll any subject into the study.

The Investigator is responsible for informing the IRB or IEC of any amendment to the protocol in accordance with local requirements. In addition, the IRB or IEC must approve all advertising used to recruit subjects for the study. The protocol must be re-approved by the IRB or IEC upon receipt of amendments and annually, as local regulations require.

The Investigator is also responsible for providing the IRB or IEC with reports of any reportable serious adverse drug reactions from any other study conducted with the investigational product. Altor BioScience will provide this information to the Investigator.

Progress reports and notifications of serious adverse drug reactions will be provided to the IRB or IEC according to local regulations and guidelines

11.7 Closure of Study

Altor BioScience reserves the right to terminate this study at any time for reasonable medical or administrative reasons. Any premature discontinuation will be appropriately documented according to local requirements (e.g., IRB/IEC, regulatory authorities).

In addition, the Investigator or Altor BioScience has the right to discontinue a single site at any time during the study for medical or administrative reasons such as:

- Unsatisfactory enrollment.
- GCP noncompliance.
- Inaccurate or incomplete data collection.
- Falsification of records.
- Failure to adhere to the study protocol.

12 DATA HANDLING AND RECORD KEEPING

12.1 Data/Documents

The Investigator must ensure that the records and documents pertaining to the conduct of the study and the distribution of the investigational product are complete, accurate, filed, and retained. Examples of source documents include hospital records, clinic and office charts, laboratory notes, memoranda, subject's diaries or evaluation checklists, dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiche, X-ray film and reports, and records kept at the pharmacy and the laboratories, as well as copies of CRFs or CD-ROM.

12.2 Data Capture and Management

The data for this study is being captured in an electronic data capturing (EDC) system. Training and access will be provided to the study sites prior to subject screening and enrollment. For new study personnel requiring access to the EDC, contact Altor BioScience. The Electronic Case Report Form (eCRF) Completion Guidelines are provided as a separate document. Study data will be collected via the EDC system and will be managed through the use of programmed electronic edit checks. Data discrepancies will be brought to the attention of the clinical team and research site personnel, if necessary. An audit trail of the resolution of data discrepancies will be maintained in the EDC system.

12.3 Inspection of Records

Altor BioScience will be allowed to conduct site visits to the investigation facilities for the purpose of monitoring any aspect of the study. The Investigator agrees to allow the monitor to inspect the drug storage area, study drug stocks, drug accountability records, subject charts and study source documents, and other records relative to study conduct.

12.4 Retention of Records

Essential documents must be retained by the Investigator for a minimum of 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region, or at least 2 years have elapsed since the formal notification to regulatory authorities of discontinuation of clinical development of the study drug; and for a period of at least 3 years after the Sponsor notifies the Investigator that the final report has been filed with regulatory authorities. The Investigator must retain these documents for the time period described above or according to local laws or requirements, whichever is longer. Essential documents include, but are not limited to, the following:

- Signed informed consent documents for all subjects.
- Subject identification code list, and the screening and enrollment log (Section 16.8).
- Record of all communications between the Investigator and the IRB/IEC.
- Composition of the IRB/IEC.

- Record of all communications between the Investigator, Sponsor, and their authorized representative(s).
- List of Sub-Investigators and other appropriately qualified persons to whom the Investigator has delegated significant study-related duties, together with their roles in the study, curriculum vitae, and their signatures.
- Copies of CRFs (if paper) and of documentation of corrections for all subjects.
- Study drug accountability records.

If it becomes necessary for Altor BioScience or the Regulatory Authority to review any documentation relating to the study, the Investigator must permit access to such records.

13 QUALITY CONTROL AND QUALITY ASSURANCE

All aspects of the study will be carefully monitored by the Sponsor or its authorized representative(s) for compliance with applicable government regulations with respect to current GCP and SOPs.

13.1 Study Monitoring

Before the research site can enter a subject into the study, a representative of Altor BioScience will:

- Determine the adequacy of the facilities.
- Discuss with the Investigator(s) and other personnel their responsibilities with regard to protocol adherence and the responsibilities of Altor BioScience or its representatives. This will be documented in a Clinical Study Agreement between Altor BioScience and the Investigator.

During the study, a monitor from Altor BioScience or representative will have regular contacts with the research site, for the following:

- Provide information and support to the Investigator(s).
- Confirm that facilities remain acceptable.
- Confirm that the research team is adhering to the protocol, data are being accurately recorded in the case report forms, and investigational product accountability checks are being performed.
- Perform source data verification. This includes a comparison of the data in the case report forms with the subject's medical records at the hospital or practice and other records relevant to the study. This will require direct access to all original records for each subject (e.g., clinic charts).
- Record and report any protocol deviations not previously sent to Altor BioScience
- Confirm AEs and SAEs have been properly documented on CRFs and confirm any SAEs have been forwarded to Altor BioScience and those SAEs that met criteria for reporting have been forwarded to the IRB/IEC.

The monitor will be available between visits if the Investigator(s) or other staff needs information or advice.

13.2 Deviations

Deviations are defined as any departure from the IRB-approved protocol and significant non-compliance with good clinical practices (GCP). Deviations may lead to increased risk to the study participant and may jeopardize the study data integrity. All protocol deviations discovered by the site must be submitted to Altor within 10 working days for review and approval. Use the Protocol Deviation Guidelines to determine the deviation code and classification and submit the **Protocol Deviation Notification Form** (Section 16.7) to Altor BioScience. Altor will notify the site to confirm that the deviation is properly coded, classified (Major or Minor) and is approved for entry

into the applicable CRF. If a CRA/Monitor discovers a protocol deviation, the CRA/Monitor will provide instructions to the site for entry into the applicable CRF. If the Protocol Deviation is determined to be Major, the site should report it to their IRB of record in accordance with the IRB's reporting requirements. The Principal Investigator (PI) will be responsible for the final determination of IRB reportability. The following are examples of major protocol deviations:

- Not adhering to inclusion/exclusion criteria for subject eligibility/enrollment
- Missed dose of ALT-803 administration (unless held for safety)
- Failure to report serious adverse events (SAE)
- Failing to obtain informed consent prior to performing any study procedures
- Working under an expired professional license/certification
- Failure to collect immunogenicity sample from all study participants at the site

Minor protocol deviations should be reported as required to the site's IRB of record (most minor deviations will not require IRB reporting). The following are examples of minor protocol deviations:

- The study staff did not collect a sample for a lab test required by the protocol
- Subject failure to return General Health Questionnaires
- Study visit out of timeframe
- Failure to collect immunogenicity sample at one study visit for a subject

In the event that the Investigator deviates from the protocol in the interest of subject safety, the PI should notify the Sponsor within 24 hours of the site's knowledge of the deviation using the **Protocol Deviation Notification Form** (Section 16.7). All other deviations should be reported to the Sponsor within 10 working days.

Protocol Deviation Guidelines

DEVIATION CODE	DEVIATION DESCRIPTION	CLASSIFICATION (MAJOR/MINOR)	IRB REPORTABLE	Verify site staff has been Re-educated/ Re-Trained
1-INFORMED CONSENT	Use of an outdated / expired consent form (provided the updated information does not affect subject safety), or Delay in re-consenting the subject using the most current ICF version.	Major	Reportable	Y
	Informed consent signed by someone other than the individuals authorized to signed consent, (e.g. someone other than an Investigator or delegated study personnel).	Major	Reportable	Y
	Inappropriate documentation of informed consent, including: 1) A missing subject signature 2) Failure to provide a copy to the subject signing the form 3) Missing date on either subject's signature or person obtaining consent's signature	Major	Reportable	Y
	Informed consent obtained after initiation of any other study specific procedures.	Major	Reportable	Y
	Signature of person conducting the Informed Consent is missing	Major	Reportable	Y
	Inappropriate documentation of informed consent, including: 1) Someone other than the subject dated the ICF 2) Missing initials on one or more of the consent pages 3) Mismatched signature dates (PI/subject)	Minor	Non-reportable	Y
2-INCLUSION / EXCLUSION CRITERIA	Enrollment of a subject who did not meet all inclusion/exclusion criteria.	Major	Reportable	Y
	Enrollment of a subject who did not meet an inclusion/exclusion criteria but obtained a successful waiver from the Sponsor prior to entry	Major	Reportable	N
3-SUBJECT DOSING	Failure to follow Dose Preparation / Administration Instructions.	Major	Reportable	Y
4-ADVERSE EVENT	Failure to report reportable serious adverse event to the IRB and / or Sponsor.	Major	Reportable	Y
	Failure of Investigator to gather adverse event data from subject.	Major	Reportable	Y

DEVIATION CODE	DEVIATION DESCRIPTION	CLASSIFICATION (MAJOR/MINOR)	IRB REPORTABLE	Verify site staff has been Re-educated/ Re-Trained
5-DRUG ACCOUNTABILITY	Destruction of IP on site without CRA verification	Minor	Non-reportable	Y
	Any documented record of temperature of IP being outside the labeled and protocol defined temperature range and approved for use by Sponsor.			
	Any documented record of temperature of IP being outside the labeled and protocol defined temperature range, not approved for used and administered to a subject.	Major	Reportable	
6-CONCOMITANT MEDICATION	Administration of Prohibited Medication	Major	Reportable	Y
7-VISIT/ ASSESSMENT	Study assessment / lab test missing or not performed at the scheduled visit not effecting the Primary/secondary endpoints.	Minor	Non-reportable	Y
	Study assessment / lab test performed out of the protocol specified timeframe.	Minor	Non-reportable	Y
	Any missed visits or clinical/laboratory assessments as a result of being hospitalized or indisposed due to an SAE.	N/A	NOT A DEVIATION	
8-GCP NON-COMPLIANCE	Breaches of subject confidentiality.	Major	Reportable	Y
	Site personnel conducting study specific procedure prior to having task appropriately delegated and documented.	Minor	Non-reportable	Y
	Repeated or continued negligence in performance of study procedures / Lack of Principal Investigator Oversight.	Major	Reportable	Y
	Performance of any study specific procedures not approved by the IRB	Major	Reportable	Y
	Failure of Investigator to sign signature pages within reasonable timeframe following protocol/Investigator Brochure amendments.	Minor	Non-reportable	Y
	Failure to submit continuing review application to the IRB before study expiration.	Minor	Non-reportable	Y

13.3 Audits and Inspections

Authorized representatives of Altor BioScience, a regulatory authority, or an IRB/IEC may visit the site to perform audits or inspections, including source data verification. The purpose of an Altor BioScience 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, GCP guidelines of the ICH, and any applicable regulatory requirements. The Investigator is required to permit direct access to the facilities where the study took place, source documents, CRFs, and applicable supporting records of study subject participation for audits and inspections by company authorized representatives, regulatory authorities, and IRB/IECs. The Investigator should make every effort to be available for the audits and/or inspections. The Investigator should contact Altor BioScience immediately if contacted by a regulatory agency about an inspection.

14 STUDY REPORT AND PUBLICATIONS

Altor BioScience is responsible for preparing and providing the appropriate regulatory authorities with clinical study reports according to the applicable regulatory requirements.

The publication policy of Altor BioScience is discussed in the Investigator's Clinical Research Agreement.

15 CONFIDENTIALITY

All information generated in this study is considered highly confidential and must not be disclosed to any person or entity not directly involved with the study unless prior written consent is gained from Altor BioScience. However, authorized regulatory officials, IRB/IEC personnel, Altor BioScience and its authorized representatives are allowed full access to the records.

Identification of subjects and CRFs shall be by initials, screening and treatment numbers only. If required, the subject's full name may be made known to an authorized regulatory agency or other authorized official.

16 REFERENCES

Bessard A, Solé V, Bouchaud G, Quéméner A, Jacques Y. High antitumor activity of RLI, an interleukin-15 (IL-15)-IL-15 receptor alpha fusion protein, in metastatic melanoma and colorectal cancer. Mol Cancer Ther. 2009 Sep;8(9):2736-45.

Cheever MA. Twelve immunotherapy drugs that could cure cancers. Immunol Rev. 2008 Apr;222:357-68.

Han KP, Zhu X, Liu B, Jeng E, Kong L, Yovandich JL, et al. IL-15:IL-15 receptor alpha superagonist complex: high-level co-expression in recombinant mammalian cells, purification and characterization. Cytokine 2011; 56 (3):804-810.

Mocci G, Marzo M, Papa A, et al. Dermatological adverse reactions during anti-TNF treatments: Focus on inflammatory bowel disease. J Crohns Colitis. 2013 Nov;7(10):769-79. doi: 10.1016/j.crohns.2013.01.009. Epub 2013 Mar 1

Rhode PR, Egan JO, Xu W, Hong H, Webb GM, Chen X, et al. Comparison of the Superagonist Complex, ALT-803, to IL15 as Cancer Immunotherapeutics in Animal Models. Cancer Immunol Res 2016;4(1):49-60.

Xu W, Jones M, Liu B, Zhu X, Johnson CB, Edwards AC, Kong L, Jeng EK, Han K, Marcus WD, Rubinstein MP, Rhode PR, Wong HC. Efficacy and mechanism-of-action of a novel superagonist interleukin-15: interleukin-15 receptor αSu/Fc fusion complex in syngeneic murine models of multiple myeloma. Cancer Res. 2013 May 15;73(10):3075-86.

Ward A, Anderson M, Craggs RI, Maltby J, Grahames C, Davies RA, Finch D, Pattison D, Oakes H, Mallinder PR. E. coli expression and purification of human and cynomolgus IL-15. Protein Expr Purif. 2009 Nov;68(1):42-8.

Zhu X, Marcus WD, Xu W, Lee HI, Han K, Egan JO, Yovandich JL, Rhode PR, Wong HC. Novel human interleukin-15 agonists. J Immunol. 2009 Sep 15;183(6):3598-607.

Tan, Aaron & Goh, Debbie & Farhatnia, Yasmin & G, Natasha & Lim, Jing & Teoh, Hin & Rajadas, Jayakumar & Alavijeh, Mohammad & Seifalian, Alexander. An Anti-CD34 Antibody-Functionalized Clinical-Grade POSS-PCU Nanocomposite Polymer for Cardiovascular Stent Coating Applications: A Preliminary Assessment of Endothelial Progenitor Cell Capture and Hemocompatibility. 2013 Oct. PloS one. 8. e77112. 10.1371/journal.pone.0077112.

APPENDICES

16.1 APPENDIX I – ALT-803 Injection Site Reaction Subject Diary

STUDY NUMBER: _____

Patient Number*		**Date of Study Drug Injection***	____/____/____	*To be completed by the site.

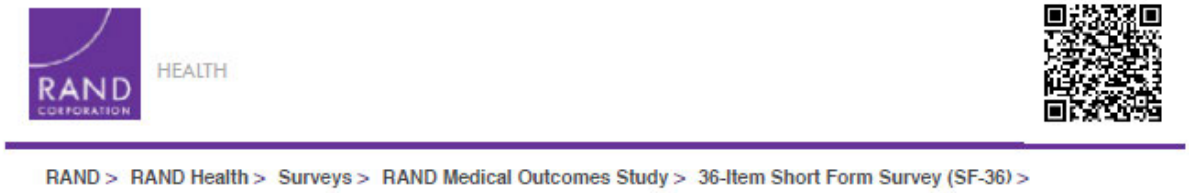
Please answer all questions below daily for 7 days, beginning with day of treatment. Be sure to bring back this completed diary to your next clinic visit.

	Instructions	**Day of Study Drug Injection** ___/___/_____	**Day 1 Post Injection** ___/___/_____	**Day 2 Post Injection** ___/___/_____	**Day 3 Post Injection** ___/___/_____	**Day 4 Post Injection** ___/___/_____	**Day 5 Post Injection** ___/___/_____	**Day 6 Post Injection** ___/___/_____
1. Is there redness at the injection site?	Check: ☐Yes or ☐No If yes, measure longest diameter in cm	☐Yes ☐No _____cm	☐Yes ☐No _____cm	☐Yes ☐No _____cm	☐Yes ☐No _____cm	☐Yes ☐No _____cm	☐Yes ☐No _____cm	☐Yes ☐No _____cm
2. Is there firmness or swelling at the injection site?	Check: ☐Yes or ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
3. Have you experienced any pain or itching at the injection site?	Check: ☐Yes or ☐No If yes, tell us if the pain and/or itching is mild, moderate or severe	☐ Pain ☐ Itch Mild Mild Mod Mod Severe Severe	☐ Pain ☐ Itch Mild Mild Mod Mod Severe Severe	☐ Pain ☐ Itch Mild Mild Mod Mod Severe Severe	☐ Pain ☐ Itch Mild Mild Mod Mod Severe Severe	☐ Pain ☐ Itch Mild Mild Mod Mod Severe Severe	☐ Pain ☐ Itch Mild Mild Mod Mod Severe Severe	☐ Pain ☐ Itch Mild Mild Mod Mod Severe Severe
4. Have you taken or applied any medication for injection site pain or itching?	Check: ☐Yes or ☐No Provide name of medication(s)	☐Yes ☐No Name(s):	☐Yes ☐No Name(s):	☐Yes ☐No Name:	☐Yes ☐No Name:	☐Yes ☐No Name:	☐Yes ☐No Name:	☐Yes ☐No Name:
5. Have you experienced any chills?	Check: ☐Yes or ☐No If yes, tell us if the chills are mild, moderate or severe	☐Yes ☐No Mild Moderate Severe	☐Yes ☐No Mild Moderate Severe	☐Yes ☐No Mild Moderate Severe	☐Yes ☐No Mild Moderate Severe	☐Yes ☐No Mild Moderate Severe	☐Yes ☐No Mild Moderate Severe	☐Yes ☐No Mild Moderate Severe
6. Record your daily temperature upon waking (do not drink anything 5 minutes before taking your temperature)	Check: ☐Yes or ☐No If your temperature is 101°F for more than 24 hours, call your doctor.	☐Yes ☐No _____°F Time: ____:____ AM / PM	☐Yes ☐No _____°F Time: ____:____ AM / PM	☐Yes ☐No _____°F Time: ____:____ AM / PM	☐Yes ☐No _____°F Time: ____:____ AM / PM	☐Yes ☐No _____°F Time: ____:____ AM / PM	☐Yes ☐No _____°F Time: ____:____ AM / PM	☐Yes ☐No _____°F Time: ____:____ AM / PM

Grading Injection Site Pain or Itching
Mild – Noticeable, does not interfere with activity
Moderate – Interferes with activity, limiting activities of daily living
Severe – Severely limiting self-care activities of daily living, incapacitating

Grading Chills
Mild – Mild sensitive of cold, shivering, chattering of teeth
Moderate – Moderate tremor of entire body, medication taken
Severe – Prolonged or severe, does not respond to medication

16.2 APPENDIX II – General Health Questionnaire (RAND SF 36)



RAND > RAND Health > Surveys > RAND Medical Outcomes Study > 36-Item Short Form Survey (SF-36) >

36-Item Short Form Survey Instrument (SF-36)

RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:

- 1 - Excellent
- 2 - Very good
- 3 - Good
- 4 - Fair
- 5 - Poor

2. **Compared to one year ago**, how would you rate your health in general **now**?

- 1 - Much better now than one year ago
- 2 - Somewhat better now than one year ago
- 3 - About the same
- 4 - Somewhat worse now than one year ago
- 5 - Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	○ 1	○ 2	○ 3
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	○ 1	○ 2	○ 3
5. Lifting or carrying groceries	○ 1	○ 2	○ 3
6. Climbing **several** flights of stairs	○ 1	○ 2	○ 3
7. Climbing **one** flight of stairs	○ 1	○ 2	○ 3
8. Bending, kneeling, or stooping	○ 1	○ 2	○ 3
9. Walking **more than a mile**	○ 1	○ 2	○ 3
10. Walking **several blocks**	○ 1	○ 2	○ 3
11. Walking **one block**	○ 1	○ 2	○ 3
12. Bathing or dressing yourself	○ 1	○ 2	○ 3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	Yes	No
13. Cut down the **amount of time** you spent on work or other activities	○ 1	○ 2
14. **Accomplished less** than you would like	○ 1	○ 2
15. Were limited in the **kind** of work or other activities	○ 1	○ 2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	○ 1	○ 2

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	Yes	No
17. Cut down the **amount of time** you spent on work or other activities	○ 1	○ 2
18. **Accomplished less** than you would like	○ 1	○ 2
19. Didn't do work or other activities as **carefully** as usual	○ 1	○ 2

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- ○ 1 - Not at all
- ○ 2 - Slightly
- ○ 3 - Moderately
- ○ 4 - Quite a bit
- ○ 5 - Extremely

21. How much **bodily** pain have you had during the **past 4 weeks**?

- ○ 1 - None
- ○ 2 - Very mild
- ○ 3 - Mild
- ○ 4 - Moderate
- ○ 5 - Severe
- ○ 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- ○ 1 - Not at all
- ○ 2 - A little bit
- ○ 3 - Moderately
- ○ 4 - Quite a bit
- ○ 5 - Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	1	2	3	4	5	6
24. Have you been a very nervous person?	1	2	3	4	5	6
25. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
26. Have you felt calm and peaceful?	1	2	3	4	5	6
27. Did you have a lot of energy?	1	2	3	4	5	6
28. Have you felt downhearted and blue?	1	2	3	4	5	6
29. Did you feel worn out?	1	2	3	4	5	6
30. Have you been a happy person?	1	2	3	4	5	6
31. Did you feel tired?	1	2	3	4	5	6

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- 1 - All of the time
- 2 - Most of the time
- 3 - Some of the time
- 4 - A little of the time
- 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	1	2	3	4	5
34. I am as healthy as anybody I know	1	2	3	4	5
35. I expect my health to get worse	1	2	3	4	5
36. My health is excellent	1	2	3	4	5

ABOUT

The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest.

1776 Main Street
Santa Monica, California 90401-3208

RAND® is a registered trademark. Copyright © 1994-2016 RAND Corporation.

16.3 APPENDIX III – SAE REPORT FORM AND COVER SHEET

ALTOR BIOSCIENCE AND NANTBIOSCIENCE, INC.

SERIOUS ADVERSE EVENT REPORT

Send the completed form to Email: SAE@altorbioscience.com (an identical copy of email sent to Altor will be automatically generated and sent to Nant Safety)

Reporter Name:	Report Date (DD/MMM/YYYY):
Investigator Name:	Site Name:
Address:	Country:
Telephone:	Email:
☐ Initial Report ☐ Follow-up Report #:	Awareness Date (DD/MMM/YYYY):

Subject Identifiers and Demographics

Subject Initials	Subject Study ID	Gender	DOB: (DD/MMM/YYYY)	Weight (kg):	Height (cm):
		☐ M ☐ F			

Seriousness (Check all that apply)

☐ Insubject hospitalization or prolongation of hospitalization		Date of admission:_____(DD/MMM/YYYY) Date of discharge:_____(DD/MMM/YYYY)	
☐ Results in death	Date of death:_____ (DD/MMM/YYYY): Cause of death:_____	Death certificate? ☐ No ☐ Yes (*attach redacted*)	Autopsy? ☐ No ☐ Yes (*attach redacted*)
☐ Life-Threatening	☐ Persistent or Significant Disability/Incapacity	☐ Congenital Anomaly/Birth Defect	
☐ Important Medical Event, explain:			

Event Information

Adverse Event *(One entry only for event term)*	SAE Start Date (DD/MMM/YYYY)	SAE Stop Date (DD/MMM/YYYY)	Check if Ongoing
			☐
	SAE Start Time *(24 hour clock)*	SAE Stop Time *(24 hour clock)*	

Severity Grade *(NCI CTCAE Version 4.03)*	Relationship to ALT-803	Outcome of Event
☐ Grade 1 Mild ☐ Grade 2 Moderate ☐ Grade 3 Severe ☐ Grade 4 Life-Threatening ☐ Grade 5 Death	☐ Suspected ☐ Not suspected	☐ Not recovered/Not Resolved ☐ Recovered/Resolved ☐ Recovered/Resolved with sequelae ☐ Recovering/Resolving ☐ Fatal ☐ Unknown

SAMPLE

Site ID: 067 **Subject Study ID & Initials: _____**

Study Medication Data

Date of First Dose (DD/MMM/YYYY)	Date of Last Dose prior to SAE (DD/MMM/YYYY)	Dose Amount & unit	# of Doses Received	Study Medication	Lot #
				ALT-803	

Action Taken with Study Medication

Action taken with ALT-803 due to this event:	☐ Dose not changed ☐ Dose interrupted ☐ Drug withdrawn ☐ Dose reduced ☐ Not applicable ☐ Dose Increased ☐ Unknown	If study medication was stopped or interrupted, did the event abate?	☐ No ☐ Yes ☐ N/A
		If study medication was stopped or interrupted, did the event reappear after reintroduction?	☐ No ☐ Yes ☐ N/A
		If study medication was stopped or interrupted, did the event reappear after reintroduction?	☐ No ☐ Yes ☐ N/A

Describe event fully. Include baseline medical status including relevant medical history, signs and symptoms, diagnosis, diagnostic test results, clinical course, treatment (all drugs/procedures used as interventions for SAE), outcome, hospital course for hospitalizations, etc. Attach relevant de-identified test results and hospital records when submitting this form. Provide rationale for causality assessments. Document other potential causes of the event. ***Complete AE, Medical History, applicable Study Treatment Administration, and Concomitant Medications eCRFs as soon as possible.***

Relevant medical hx:

Con meds rec'd 2 weeks prior to SAE:

Investigator's Name (print)	*Date* (DD/MMM/YYYY)
Investigator's Signature	*Date* (DD/MMM/YYYY)

SAMPLE

Altor BioScience

NANTWORKS

SAMPLE

SAE FAX COVERSHEET

If the SAE Form cannot be emailed to SAE@altorbioscience.com, please fax to 954-443-8610 and use the SAE Fax Coversheet.

From: Email: Fax No: ( ) - Tel No: ( ) -	To: 954-443-8610
Date:	Number of pages:
Study Reference #:	QUILT 3.055 (CA-ALT-803-02-17)
Site/Patient #:	DRUG NAME: ALT-803 + PD-1 Checkpoint Inhibitor
SAE:	
Onset Date:	

Please find attached SAE data for the above referenced study.

(If this SAE has been reported to regulatory authorities, please provide the authority reported to, date reported and authority confirmation of report receipt information)

Kind Regards,

16.4 APPENDIX IV – Immune Cells Storage Log

Immune Cells Specimen Storage Log
(Immune Cell Assays)
Clinical Protocol CA-ALT-803-03-17

Subject ID No.: _____ Subject Initials: _____

# of tubes*	Visit	Time Point	Date of collection (dd/mmm/yyyy)	Time of collection (hh:mm;0-23:0-59)	Processed by (initials)
	Day 1	**Pre-dose**			
	Day 2	**N/A**			
	Day 3	**N/A**			
	Day 4	**N/A**			
	Day 5	**N/A**			
	Day 6	**N/A**			
	Day 7	**N/A**			
	Day 9	**N/A**			
	Day 15	**Pre-dose**			
	Day 16	**N/A**			
	Day 17	**N/A**			
	Day 18	**N/A**			

	Day 19	**N/A**			
	Day 20	**N/A**			
	Day 21	**N/A**			
	Day 22	**N/A**			
	Day 23	**N/A**			
	Day 29	**N/A**			

*****Should be 2 aliquots (2 freezer tubes) per time point ^Collected the next day.

Please follow proper documentation guidelines (i.e. corrections should be made by crossing out the error with a single line, entering the correct information above the crossed-out data and initialing and dating next to it. Also, blank fields should be crossed out with a single line, 'N/A' should be entered next to or above the line and initial and date next to it.)

Date of Local Pick-Up (dd/mmm/yyyy): _____

Package Prepared By (initials): _____

16.5 APPENDIX V – PK, Cytokine and Immunogenicity Storage Log

PK, Cytokine and Immunogenicity Specimen Storage Log
(Samples for PK, Cytokine and Immunogenicity Assays)
Clinical Protocol CA-ALT-803-03-17

Subject ID No.: _____ Subject Initials: _____

# of tubes*	Visit	Time Point	Date of collection (dd/mmm/yyyy)	Time of collection (hh:mm;0-23:0-59)	Processed by (initials)
2	**Day 1, Baseline, Study Period 1**	**Pre-dose (+/- 5 min)**			
1	**Day 1, Study Period 1**	**60 min (+/- 5 min)**			
1	**Day 1, Study Period 1**	**4hr (+/- 15 min)**			
2	**Day 2, Study Period 1**	**24 hr (+/- 60 min)**			
2	**Day 3, Study Period 1**	**48 hr (+/- 60 min)**			
2	**Day 4, Study Period 1**	**72 hr (+/- 60 min)**			
2	**Day 5, Study Period 1**	**96 hr (+/-60 min)**			
2	**Day 6, Study Period 1**	**120 hr (+/- 120 min)**			
2	**Day 7, Study Period 1**	**144 hr (+/-120 min)**			
2	**Day 8, Study Period 1**	**168 hr (+/-120 min)**			
2	**Day 9, Study Period 1**	**192 hr (+/-120 min)**			

2	**Day 1, Baseline, Study Period 2**	**Predose (+/- 5 min)**			
1	**Day 1, Study Period 2**	**60 min (+/- 5 min)**			
1	**Day 1, Study Period 2**	**4 hr (+/- 15 min)**			
2	**Day 2, Study Period 2**	**24 hr (+/- 60 min)**			
2	**Day 3, Study Period 2**	**48 hr (+/- 60 min)**			
2	**Day 4, Study Period 2**	**72 hr (+/- 60 min)**			
2	**Day 5, Study Period 2**	**96 hr (+/- 60 min)**			
2	**Day 6, Study Period 2**	**120 hr (+/- 120 min)**			
2	**Day 7, Study Period 2**	**144 hr (+/- 120 min)**			
2	**Day 8, Study Period 2**	**168 hr (+/- 120 min)**			
2	**Day 9, Study Period 2**	**192 hr (+/- 120 min)**			
1	**End of Study Visit**	**N/A**			

*****Should be 2 aliquots (2 freezer tubes) per red top tube collected per time point

Please follow proper documentation guidelines (i.e. corrections should be made by crossing out the error with a single line, entering the correct information above the crossed-out data and initialing and dating next to it. Also, blank fields should be crossed out with a single line, 'N/A' should be entered next to or above the line and initial and date next to it.)

Date of Local Pick-Up (mm/dd/yyyy): _____

Package Prepared By (initials): _____

16.6 APPENDIX VI – Pregnancy Questionnaire

Initial Pregnancy Questionnaire

Altor BioScience and NantBioScience					**Protocol: CA-ALT-803-03-17**	
Site ID: 067		Subject Study ID: Gender: ☐ F ☐ M			Subject's Date of Birth:	
Current Pregnancy Details						
Date of Last Menstrual Period:					Date of positive pregnancy test:	
Was a serum BHCG performed?		☐ Yes ☐ No			Date:	Result:
Ultrasounds performed?		☐ Yes ☐ No			Date:	Result:
Findings:						
Estimated Date of Conception:					Estimated Date of Delivery:	
Previous Pregnancies:						
Gravidity (number of pregnancies)						
Parity (number of pregnancies carried to viable gestational age): _		Full Term: _	Premature: _	Abortions: _		Now Living: _
Maternal Health Status						
Diabetes during or prior to pregnancy?				☐ Yes ☐ No		
Hypertension during or prior to pregnancy				☐ Yes ☐ No		
Other maternal medical problems? If yes to any of the above, please provide details.						
Social Habits During this Pregnancy:						
Smoking?		☐ Yes ☐ No			If yes, please list number of cigarettes per day:	
Alcohol Consumption?		☐ Yes ☐ No			If yes, please provide the number of drinks per week:	
Any problems in pregnancy due to alcohol?		☐ Yes ☐ No			If yes, describe:	
Drug Use?		☐ Yes ☐ No			If yes, provide details:	
Comments (Provide any additional information pertinent to the pregnancy):						

Study Site Personnel:
Complete this form with all known information initially and add to the form any follow-up information as it becomes available. Please initial and date any new information or changes. At the end of the pregnancy, complete the Pregnancy Outcome form. Please submit these to Email: SAE@AltorBioscience.com (an identical copy of email sent to Altor will be automatically generated and sent to Nant Safety).

Signature/Title:_____ **Date**:_____

Follow-up Pregnancy Questionnaire

Altor BioScience and NantBioScience			**Protocol: CA-ALT-803-03-17**	
Site ID: 067		Subject Study ID: Gender: ☐ F ☐ M	Subject's Date of Birth:	

Pregnancy Outcome
☐ Normal delivery → Date: _____ ☐ Early delivery → Date: _____ ☐ Elective Abortion → Date:_____ ☐ Miscarriage → Date: _____
Findings and/or complications regarding the pregnancy outcome (Provide details regarding the outcome of the pregnancy including complications, vaginal versus C-section, miscarriage details, etc.):

Details regarding child			
Gender: ☐ M ☐ F	Weight: ☐ lbs ☐ kg	Apgars at 1 minute:	Apgars at 5 minutes:
Gestational Age of Child:	weeks		
Were there any congenital anomalies or health issues with the child while hospitalized for the birth? ☐ Yes → Describe details ☐ No			
Were there any congenital anomalies or health issues with the child up to 6 months of age? ☐ Yes → Describe details ☐ No			

Study Site Personnel:
Complete this form with all known information initially and add to the form any follow-up information as it becomes available. Please initial and date any new information or changes. If any event meets SAE criteria, submit an SAE form within 24 hours and collect all medical records for the event. Please submit these to Email: SAE@AltorBioscience.com (an identical copy of email sent to Altor will be automatically generated and sent to Nant Safety).

Signature/Title:_____Date:_____

16.7 APPENDIX VII – Protocol Deviation Notification

Subject Study ID											
0	3	1	7	-				-			

Subject Initials		

Site No.

PROTOCOL DEVIATION NOTIFICATION

This notification is completed because a protocol deviation occurred and Sponsor review is required prior to taking any further action.

Deviation Code (check one):

☐ **1-Informed Consent** ☐ **2-Inclusion/Exclusion Criteria** ☐ **3-Subject Dosing**

☐ **4-Adverse Event** ☐ **5-Drug Accountability** ☐ **6-Concomitant Medication**

☐ **7-Visit/Assessment** ☐ **8-GCP Non-Compliance**

The Protocol Deviation is classified as (check one):

☐ **Major**

☐ **Minor**

Please note that final classification is determined by Altor BioScience.

Protocol Deviation Narrative (explain details of the protocol deviation):

SAMPLE

Instructions:
Complete this form and send to: mstone@altorbioscience.com or Fax: (954) 443-8610 and wait for further instructions.

16.8 APPENDIX VIII – Screening and Enrollment Log

Principal Investigator Name:									**Site ID: 067**
Screening								**Enrollment**	
Date Screened (dd/mmm/yyyy)	**Screening ID**	**Current Status**	**PT Initials**	**Protocol Version**	**ICF Version**	**Date ICF Signed (dd/mmm/yyyy)**	**Reason(s) for Screen Failure (E1 to E4)**	**Subject Study ID**	**Date of First Dose (dd/mmm/yyyy)**
Current status codes: 1-Recruit pending 2-Recruit failed 3-Screening pending 4-Screening failed 5-Enrolled									

Instructions: Send the Screening and Enrollment Log when requested to: mstone@altorbioscience.com or Fax: (954) 443-8610

16.9 APPENDIX IX – Notification of Enrollment and Dosing

Subject Screening ID										
S	0	3	1	7				-		

Subject Initials		

Site No.

NOTIFICATION OF ENROLLMENT & DOSING

Date of First Dose:

Subject Study ID:

Group (circle one): **Group A** **Group B**

The Investigator approved the subject for enrollment on __ __ / __ __ __ / __ __ __ __
(DD / MMM / YYYY)
Date of enrollment approval

SAMPLE

Instructions:

- Complete this form after the subject is enrolled and the first dose is administered.
- Send no later than 2 days after first dose administration to: mstone@altorbioscience.com or Fax: (954) 443-8610

Completed by: _____

Name Signature Date

Notification Form Version 1.0 Date 06/07/2017 Confidential Page 1 of 1

16.10 APPENDIX X – Study Medication Inventory/Tracking Form (SMIT)

Study Medication Inventory/Tracking Form (SMIT)

Protocol #: CA-ALT-803-03-17 Study Medication Name: ALT-803

Site Name: _____ Site #: _____

Total No. of Vials @	No. of Vials Used $	Lot No.	Conc. (mg/mL)	Date * Pick-up	Prepared by (initials)	Date * Received	Received by (initials)	Date * Dispensed	Dispensed by (initials)	Subject Study ID No.	Dose (ug)	Date * Returned	Returned by (initials)	Returned To

SAMPLE

16.11 APPENDIX XI – Study Medication Shipping Notice/ Receipt Form (SMSNR)

ALTOR BIOSCIENCE
Study Medication Notice/Receipt Form (SMSNR)
Form: CA-607-F3, Page 1 of 1

SENDER SECTION

Protocol #: _____ Name of study medication: _____

Principal Investigator: _____ Site #: _____

Type of temperature monitor: color-indicators TempTale S/N: _____ (circle one)

Study Medication Lot Number	Number of vials

Delivered by: _____ (sign & print) Date delivered: _____

RECIPIENT & RETURN SECTION

Please complete & sign this section as soon as you open the contents of the package.

TempTale: Press and hold the **STOP BUTTON** for 3 seconds until the "Stop sign" icon appears in the upper right corner of the display. Notate the time turned off and if an alarm symbol is visible below:

Digital recorder description	Circle alarm status
TempTale monitor (Time **TURNED OFF**: _____)	Alarm symbol: yes no (if yes, call Altor immediately)

The contents agree with the information stated in the **Sender Section.** Yes _____ No _____

All the study medication vials are intact and have no noticeable damage. Yes _____ No _____

After observing the contents of all vials, the study medication is **not** frozen. Yes _____ No _____

If the answer to any of the above questions is **No**, please notify Altor immediately at (954) 443-8600

Extension _____ or _____ for further instructions. Otherwise, sign and date below:

Package opened and inspected by: _____(sign & print)

Date opened: _____ Time opened: _____ am/pm (circle one)

Email this form immediately to MikeFenn@altorbioscience.com and cc mstone@altorbioscience.com
or fax to: (954) 443-8610 Attn: Mike Fenn

Return the TempTale to Altor designee

DO NOT USE THE STUDY MEDICATION UNTIL RECEIVING ALTOR'S NOTIFICATION

FOR ALTOR USE ONLY

Was the same temperature monitor returned (i.e. TempTale)? Yes _____ No _____ N/A _____

Temperature conditions met the requirements and the study medication vials are acceptable for clinical use.

_____(sign & print) Date: _____

16.12 APPENDIX XII – Study Medication Shipping Requisition Form (SMSR)

Protocol #: CA-ALT-803-03-17

Site Name: _____ Site #: _____

ALT-803 (please select one):	Number of Vials	Reason for Request
2 mL vial containing 1.2 mL of ALT-803 at a concentration of 1.0 mg/mL		
2 mL vial containing 0.6 mL at a concentration of 2.0 mg/mL		

Requested By: _____ (sign & print) Date: _____

Date Study Medication Needed By (dd/mmm/yyyy): _____

E-mail this form to:
MikeFenn@altorbioscience.com and cc mstone@altorbioscience.com
or Fax to: (954) 443-8610 Attn: Mike Fenn

16.13 APPENDIX XIII – Study Treatment Preparation Worksheet

ALT-803 Study Treatment Preparation Worksheet (Page 1 of 2)

Subject Study ID:	**Subject Initials:**
Subject Weight prior to 1st dose: kg	**Treatment Preparation Date:**
ALT-803 Lot No.:	**ALT-803 Concentration:**
No. of ALT-803 Vials Used (for this weight)**:**	**ALT-803 Dose Level (circle one please):** 10 µg/kg 20 µg/kg

Documentation:

For each subject, complete this form for the first study dose. The Study Coordinator will provide the subject information to complete the top of the form. ALT-803 dosing will be calculated using a weight obtained within 5 days prior to the first dose. The dose will be re-calculated at the beginning of each subsequent cycle in the event of a 10% or greater weight change, complete a new form for each instance this occurs.

Each vial of ALT-803 will either contain 1.2 mL of study drug at 1 mg/mL (1000 µg/mL) or will contain 0.6 mL of study drug at 2 mg/mL (2000 µg/mL). Refer to the vial label to confirm the correct lot no. and concentration.

A. ALT-803 treatment preparation for 1 mg/mL concentration vials

1. Use the following instructions to prepare each study medication dose using **1 mg/mL** concentration vials (*Skip to Section B if 2 mg/mL concentration vials are used*):
    1. Calculate the *ALT-803 dose volume* (mL) as follows:

= [20 µg/kg (ALT-803 Dose level) X _____ kg] ÷ 1000 µg/mL
Subject weight

Note: multiple vials may need to be used for each dose.

2. Once subject is confirmed to meet dosing eligibility, withdraw the *ALT-803 dose volume* from the study drug vial(s) directly into a syringe(s) for subcutaneous injection.
3. Label the syringe(s) at minimum with the Subject Initials and Study ID No. (or other applicable subject identifying information), and Date Prepared.
4. Distribute for subject treatment.
5. Skip to Section C to complete this form.

B. ALT-803 treatment preparation for 2 mg/mL concentration vials

2. Use the following instructions to prepare each study medication dose using **2 mg/mL** concentration vials. ALT-803 will be diluted (1:1 dilution) to a concentration of **1 mg/mL** after confirming the volume needed.

1. Calculate the *ALT-803 dose volume* (mL) at **1 mg/mL** as follows:

= [20 µg/kg (ALT-803 Dose level) X _____ kg] ÷ 1000 µg/mL
Subject weight

ALT-803 Study Treatment Preparation Worksheet (Page 2 of 2)

Note: multiple vials may need to be used for each dose.

2. Once subject is confirmed to meet dosing eligibility, add saline using a 1:1 dilution (0.6 mL) to the study drug vial or to multiple vials depending on the *ALT-803 dose volume* required per step 1 above.
3. Withdraw the *ALT-803 dose volume* from the study drug vial(s) after dilution directly into a syringe(s) for subcutaneous injection.
4. Label the syringe(s) at minimum with the Subject Initials and Study ID No. (or other applicable subject identifying information), and Date Prepared.
5. Distribute for subject treatment.
6. Proceed to Section C to complete this form.

C. Signature and record keeping

1. Record the No. of ALT-803 Vials Used (for this particular weight) at the top of this form.
2. Sign and date at the bottom of this page and file in the pharmacy binder along with the updated **SMIT Form** (or equivalent accountability log). These documents will be inspected and copies will be reviewed during on-site monitoring visits or will be requested for off-site review via fax or email.
3. Used vials can be disposed of according to standard site guidelines. Maintain disposal/destruction records for inspection by Altor or Altor representative to review at a later time.

Pharmacist (or designee) signature: _____ Date: _____

Please follow proper documentation guidelines (i.e. corrections should be made by crossing out the error with a single line, entering the correct information above the crossed-out data and initialing and dating next to it. Also, blank fields should be crossed out with a single line, 'N/A' should be entered next to or above the line and initial and date next to it.)

16.14 APPENDIX XIV – Temperature Excursion Form

Protocol #: CA-ALT-803-03-17 Date of Report: _____

Principal Investigator: _____ Site #: _____

Investigational Product: _____ Lot Number(s): _____

Was a subject dosed with the affected medication? ☐ Yes ☐ No	If Yes: Subject Study ID: _____ Subject Initials: _____ Number of doses: _____ Additional Information: _____

Information on excursion (please include temperature logs with the report)

Excursion Location (e.g. refrigerator ID): _____

What was the known duration of the excursion: _____

What was product's minimum temperature: _____

What was product's maximum temperature: _____

Cause of Excursion: _____

Corrective Action Taken: _____

Completed by: _____
Printed Name Signature Date

Temperature Excursion Assessment (For Altor BioScience Use Only)

☐ Investigational Product is acceptable for use

☐ Investigational Product is not acceptable for use (Altor will provide a replacement and will provide further instructions for the quarantined vials)

Completed by: _____ (sign & print) Date: _____

QA Reviewed/Approved: _____ (sign & print) Date: _____

Clinical Reviewed/Approved: _____ (sign & print) Date: _____

16.15 APPENDIX XV – Names of Study Personnel

Sponsor:	Altor BioScience 2810 North Commerce Parkway Miramar, Florida 33025 954-443-8600
Medical Monitor:	John Wrangle, MD, MPH 173 Ashley Ave, BSB suite 102 Charleston, SC 29425 Phone: 843-792-4271 FAX: 843-792-0644 Wrangle@musc.edu
Sponsor Study Project Manager:	Monica Stone, MD, MSc. Altor BioScience 2810 North Commerce Parkway Miramar, Florida 33025 954-443-8600 mstone@altorbioscience.com
Sponsor Contact (budgets):	Monica Jones Director, Regulatory Affairs & Quality Assurance Altor BioScience 2810 North Commerce Parkway Miramar, Florida 33025 954-443-8600 monicajones@altorbioscience.com
Sponsor Contact (Supplies):	Mike Fenn Clinical Operations Specialist II Altor BioScience (954) 443-8600 ext. 838 mikefenn@altorbioscience.com

16.16 APPENDIX XVI – Declaration of Helsinki

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles

for

Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly

Helsinki, Finland, June 1964

and amended by the

29th WMA General Assembly, Tokyo, Japan, October 1975

35th WMA General Assembly, Venice, Italy, October 1983

41st WMA General Assembly, Hong Kong, September 1989

48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996

and the

52nd WMA General Assembly, Edinburgh, Scotland, October 2000

A. INTRODUCTION

The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my subject will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the subject's interest when providing medical care which might have the effect of weakening the physical and mental condition of the subject."

Medical progress is based on research, which ultimately must rest in part on experimentation involving human subjects.

In medical research on human subjects, considerations related to the wellbeing of the human subject should take precedence over the interests of science and society.

The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the etiology and pathogenesis of disease. Even the best-proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

Appropriate caution must be exercised in the conduct of research, which may affect the environment, and the welfare of animals used for research must be respected.

The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the Investigator, the Sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring

information to the committee, especially any SAEs. The researcher should also submit to the committee, for review, information regarding funding, Sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a subject of the research, even though the subject has given consent.

Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

The subjects must be volunteers and informed participants in the research project.

The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the subject’s information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under

duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the Investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the Investigator must obtain that assent in addition to the consent of the legally authorized representative.

Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

Both authors and publishers have ethical obligations. In publication of the results of research, the Investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the subjects who are research subjects.

The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

At the conclusion of the study, every subject entered into the study should be assured of access to the best-proven prophylactic, diagnostic and therapeutic methods identified by the study.

The physician should fully inform the subject which aspects of the care are related to the research. The refusal of a subject to participate in a study must never interfere with the subject-physician relationship.

In the treatment of a subject, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the subject, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.