Statistical Analysis Plan

Title: A Phase 1, Randomized, Double-Blind, Single Ascending Dose Study to Determine the Safety, Tolerability, and Pharmacokinetics of CD388 Subcutaneous Administration in Healthy Japanese Subjects

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STATISTICAL ANALYSIS PLAN

For:

Cidara Therapeutics Inc.

PROTOCOL No. CD388.SQ.1.03

A Phase 1, Randomized, Double-Blind, Single Ascending Dose Study to Determine the Safety, Tolerability, and Pharmacokinetics of CD388 Subcutaneous Administration in Healthy Japanese Subjects

Altasciences Project No. CID-P2-387

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STATISTICAL ANALYSIS PLAN APPROVAL

We have carefully read this statistical analysis plan and agree it contains the necessary information required to handle the statistical analysis of study data.

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VERSION CONTROL

Version	Date	Author	Description of Changes
1.0	2023/06/29	Logan Kowallis	N/A

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ABBREVIATIONS

λz	elimination rate constant
ADA	Anti-drug antibody
AE	adverse event
AESI	adverse event of special interest
ANOVA	analysis of variance
ATC	anatomical therapeutic chemical
BMI	body mass index
CI	confidence interval
CRF	case report form
CSR	clinical study report
CV%	coefficient of variability
DMP	data management plan
ECG	electrocardiogram
EOS	end of study
ET	early termination
HEENT	head, eyes, ears, nose, throat
HR	heart rate
ICF	informed consent form
ICH	International Conference on Harmonisation
ln	natural log
MedDRA	Medical Dictionary for Regulatory Activities
PCS	potentially clinically significant
PI	Principal Investigator
PK	pharmacokinetic(s)
PP	per protocol
PT	preferred term
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SE	standard error
SOC	system organ class
SOP	standard operating procedure
SQ	subcutaneous
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
WHO-DDE	World Health Organization Drug Dictionary- Enhanced

1 INTRODUCTION

This study is a randomized, double-blind, single ascending dose study to determine the safety, tolerability, and pharmacokinetics of CD388 subcutaneous administration in healthy Japanese subjects.

This statistical analysis plan (SAP) provides a detailed description of the statistical methods and procedures to be implemented for the analyses of data from protocol CD388.SQ.1.03. Pre-planning of analyses reduces the potential for bias and often reduces disputes between sponsor and the regulatory authority regarding the validity of the results. The same principles apply to supportive and/or sensitivity analyses. These analyses must be prospectively specified. (Good Review Practice: Clinical Review of Investigational New Drug Applications, December 2013).

The analyses described in the SAP are based upon the final protocol version, Amendment 1, dated 2022/12/12.

2 STUDY OBJECTIVES

The objectives of the study and corresponding study endpoints are detailed in Table 1.

Table 1: Objectives and Related Endpoints

Objective	Endpoint	Analysis
Primary		
To evaluate safety and tolerability of CD388 in healthy Japanese adult subjects	Adverse events (AEs) vital signs, electrocardiograms (ECGs), and physical exam	Refer to Section 8
Secondary		
To determine the plasma pharmacokinetic (PK) profile of CD388 Injection when dosed by SQ (subcutaneous) administration as a single dose to healthy Japanese adult subjects	The following PK parameters for CD388 in plasma will be evaluated: C_{max}, T_{max}, $AUC_{0\text{-last}}$, $AUC_{0\text{-}\infty}$, $t_{1/2}$, CL/F, and V_z/F	Refer to Section 7.1
Exploratory		
To evaluate the PK profile of CD388 in upper respiratory tract after SQ administration as a single dose to healthy Japanese adult subjects	The following PK parameters for CD388 in nasopharyngeal samples will be evaluated: C_{max}, T_{max}, $AUC_{0\text{-last}}$	Refer to Section 7.1
To evaluate biomarkers that may be associated with safety, reactogenicity, and immunogenicity after CD388 Injection	Results of the analyses of exploratory biomarkers (including but not limited to cytokines, chemokines, acute phase reactants, etc.)	Refer to Section 9

Objective	Endpoint	Analysis
To evaluate CD388 immunogenicity	Anti-drug antibody (ADA) titers in blood (plasma or serum)	Refer to Section 10

3 STUDY DESIGN

3.1 General Description

Cohort 1 will have 7 subjects receiving CD388 Injection and 2 subjects receiving placebo. If Cohort 2 is deemed appropriate to recruit, it will also have 7 subjects receiving CD388 Injection and 2 subjects receiving placebo. If Cohort 3 is deemed appropriate to recruit, it will follow the same process as Cohorts 1 and 2 and will have 7 subjects receiving CD388 Injection and 2 subjects receiving placebo.

Cohort 1 receives 50 mg of study drug injected subcutaneously (SQ). Cohort 2 receives 150 mg of study drug injected subcutaneously. Cohort 3 receives 450 mg of study drug injected subcutaneously.

A total possible 27 subjects will be enrolled in this study; 21 to receive CD388 Injection and 6 to receive placebo. No formal sample size calculation was used in determining sample size.

Subjects exhibiting Respiratory Tract Infection symptoms and who visit outpatient facilities for care will also have those visits summarized in addition to scheduled visits.

3.2 Investigational Product

The following will be administered to subjects based on the randomization schedule:

- **CD388 (Investigational product)**

  CD388 Injection is a clear to lightly opalescent liquid essentially free of particulate matter containing the active pharmaceutical ingredient, CD388. CD388 Injection is supplied as a frozen sterile solution in single-use vials.

- **Placebo**

  Normal saline will be administered SQ as the placebo control.

3.3 Study Procedures

For complete details on the study assessments to be performed for each study period, refer to APPENDIX A.

3.4 Randomization and Unblinding Procedures

Within each dose level (Cohorts 1, 2, and 3), subjects will be randomized to receive a single dose of CD388 Injection or saline placebo (treatment assignment is blinded). The study site's pharmacist (or pharmacist designee) will obtain a computer-generated study drug assignment. A subject is considered randomized when a randomization transaction is appropriately recorded.

All blinded study personnel (including the Sponsor directly involved in study conduct, Investigator, and site personnel directly involved in study conduct) and subjects will remain blinded to study drug assignment until the study is completed and the final database is locked with the exception of the unblinded pharmacy personnel, pharmacy monitor, and unblinded Sponsor personnel (such as Data Review Committee, clinical supply manager, PK lead, and

quality manager) who may be unblinded to study medication at any time during study conduct. The pharmacy monitor will monitor study drug preparation and accountability during the study and cases in which unblinding is required due to a safety or tolerability issue. To maintain study blinding, study drug preparation will be performed by an unblinded site pharmacist (or qualified unblinded personnel at the study site not involved with study procedures or evaluations).

Only in the case of an emergency, when knowledge of the study drug is essential for the clinical management or welfare of a specific subject, may the Investigator unblind a subject's study drug assignment.

As soon as possible and without revealing the subject's study drug assignment (unless important to the safety of subjects remaining in the study), the Investigator must notify the Sponsor if the blind is broken for any reason. The Investigator will record in source documentation the date and reason for revealing the blinded study drug assignment for that subject.

As PK samples from subjects assigned to placebo treatment will not be analyzed for determination of CD388 concentrations, the bioanalytical laboratory will receive the randomization list to allow for correct selection of the samples. Unblinding of the randomized treatment assignment will be performed at the bioanalytical laboratory. Specific procedures will be in place to ensure that randomized treatment assignment will not be revealed to anyone involved in the execution of the study.

4 ANALYSIS POPULATIONS

The following populations are defined for this study:

- **Enrolled Population**

  All subjects who provided informed consent and are randomized, regardless of whether or not the subject received study drug.

- **Safety Population**

  The safety population includes all subjects who receive any amount of study drug.

- **Pharmacokinetic (PK) Population**

  The PK population will include all subjects who have received CD388 injection with at least 1 post dose time point. Subjects who do not complete the sampling schedule may be included in the PK analysis for only the PK parameters that are judged not to be affected by the missing sample(s).

5 STUDY SUBJECTS

Unless otherwise specified, all available data will be listed and summary tables for disposition and protocol deviations will be presented for the safety population as described in Table 2.

Table 2: Data presentations for study subject information

Data	Variables	Presentation
Disposition and analysis population	Subject completion status (i.e., completed or withdrawn), reason for withdrawal, analysis population determination	Listings: • Disposition • Analysis population • Randomization Summary table including: • Number of subjects enrolled • N and % of subjects who completed the study • N and % of subjects discontinued from the study by primary reason for discontinuation and overall
Protocol deviations	Protocol deviations	Listings: • General deviations • Pharmacokinetic (PK) sample collection time deviations • Major deviations

5.1 Disposition

Subject disposition will be summarized for all subjects in the Enrolled population. The percentages will be calculated using the number of subjects in each cohort and study drug group in the Enrolled population as the denominator.

A listing of subject's disposition will be provided. A listing of subjects included in each of the analysis populations will also be provided. The randomization scheme listing will also be provided.

5.2 Protocol Deviations

Deviations will be collected by the clinic and presented as entered in a general protocol deviation listing. For PK sampling time deviations, information will be derived programmatically and presented in a separate listing. Major deviations will also be listed in their own listing.

6 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Unless otherwise specified, all available data will be listed and summary tables for demographics and other baseline characteristics will be presented for the Safety population as detailed in Table 3.

Table 3: Data presentations for demographic and other baseline characteristics

Data	Variables	Presentation
Demographics and other Baseline characteristics	Sex, age, ethnicity, race, height (cm), body weight at screening (kg), and body mass index (BMI) (kg/m^2)	Listing Summary Table
Medical history	All medical history findings	Listing Note: includes coded terms (system organ class [SOC] and preferred term [PT])
Prior medications	All medications taken 30 days prior to study drug administration (including prescription medications, nonprescription medications, dietary supplements, vitamins, or herbal medications)	Listing Note: includes coded terms (anatomic therapeutic chemical [ATC] level 4 and preferred name)
Lifestyle	Drinking habits	Listing
Contraception	Contraceptive method	Listing

The medical history at screening will include all queries by the medical and clinical staff related to the subject's well-being and history of relevant past medical events/experiences. Medical history will be coded to Medical Dictionary of Regulatory Activities (MedDRA) terms version 25 and listed by subject.

Prior medication will be coded using the World Health Organization Drug Dictionary Global dated March 2022 and will be listed by subject.

7 PHARMACOKINETIC ANALYSIS

The PK analysis will be carried out according to Altasciences Standard Operating Procedures (SOPs).

7.1 Pharmacokinetic Analysis

7.1.1 Missing Values

The lack of concentration values due to failure to collect the sample, a lost or compromised sample or due to the subject's early termination from the study will be termed "missing" in the dataset, and no imputation will be done. Predose samples collected can be set to 0.

If the actual collection time of a postdose PK sample is unknown, but a valid concentration value has been measured, the sample will be set to missing in the PK analysis; it will be presented in listing but excluded from descriptive statistics.

7.1.2 Measurements Below the Lower Limit of Quantitation

Concentration values below the LLOQ associated with predose and postdose collection times up to the first quantifiable sample will be assigned a value of zero, and with postdose collection times after first quantifiable sample will be replaced with missing for the non-compartmental analyses (NCA), mean PK profile representations as well as for descriptive statistic calculations.

Descriptive statistics will not be determined for time points with more than 1/3rd of points missing.

7.1.3 Actual Time

The unknown and duplicate actual time will be managed as per Altasciences SOPs.

The plasma NCA analysis will be based on the actual sampling times, except for predose samples, which will always be reported as zero, regardless of time deviations, provided that they were collected prior to dosing. A scheduled pre-dose sample collected after dosing will be set to missing in the PK analysis and its actual time will not be used and documented as appropriate. The individual plasma concentration/time profiles will be presented using actual sampling times whereas the mean plasma concentration/time profiles and tables presenting summary statistics of concentration-time series will be presented using nominal sampling times.

Actual times of the plasma samples will be listed in the report.

7.1.4 Non-Compartmental Analysis

The following configuration for the NCA analysis (with Phoenix® WinNonlin® version 8, or higher) will be used:

Data:	Serial sampled data
Model/Dose options Type:	Plasma (200 202)/Extravascular
AUC Calculation Method:	Linear up/Log down
Lambda z (λ_z) calculation:	Best fit method for λ_z Linear-Log regression

Reasons for excluding PK parameters will include the following:

- AUC: AUC parameters will not be estimated if less than 3 consecutive measurable concentrations are observed.
- PK parameters requiring λz estimation (eg, $AUC_{0-\infty}$, CL/F, V_Z/F, and $t_{1/2}$) will be set to Not Reported (NR) in the tables and listings if they meet the following:
  - Less than 3 points for λ_z estimation
  - $R^2 < 0.8$

A list of PK Parameter terms and definitions are found in Table 4.

Table 4: PK Parameter Term Definitions

PK Parameter	Definition
Plasma PK	
C_{max}	Maximum observed plasma concentration
t_{max}	Time to reach the maximum plasma concentration; if it occurs at more than onetime point, T_{max} is defined as the first time point with this value

PK Parameter	Definition
$AUC_{0\text{-last}}$	Area under the plasma concentration-time curve from time 0 to time of the last quantifiable concentration
$AUC_{0\text{-}\infty}$	Area under the plasma concentration-time curve from time 0 to infinite time, calculated as the sum of AUC_{last} and C_{last}/λ_z, in which C_{last} is the last observed quantifiable concentration
CL/F	Apparent clearance, calculated as Dose/AUC_∞
V_z/F	Apparent Volume of distribution, calculated as Dose/λ_z *AUC_∞
$t_{1/2}$	Terminal elimination half-life, calculated as 0.693/λ_z
Upper Respiratory Tract (Nasopharyngeal) PK	
C_{max}	Maximum Nasopharyngeal concentration
T_{max}	Time to reach the maximum Nasopharyngeal concentration; if it occurs at more than onetime point, T_{max} is defined as the first time point with this value
$AUC_{0\text{-last}}$	Area under the Nasopharyngeal concentration-time curve from time 0 to time of the last quantifiable concentration
The following plasma PK parameters will be used for PK calculation and presented in the PK listings only	
T_{last}	Time of last measurable observed concentration
C_{last}	Observed concentration corresponding to T_{last}
λ_Z	Terminal slope (λ_z) of the semi-logarithmic drug concentration-time curve
$\lambda_{Z\ Upper}$	Upper limit on time for values included in the calculation of λ_z
$\lambda_{Z\ Lower}$	Lower limit on time for values included in the calculation of λ_z
R^2	Goodness of fit for the terminal elimination phase
AUC%extrap	Extrapolated area (i.e., percentage of AUC_∞ due to extrapolation from T_{last} to infinity)

7.1.5 Pharmacokinetic Statistical Methodology

All PK tables, figures and listings (TFLs), when appropriate, will be stratified by cohort. Individual and mean plasma concentration-time profiles will be presented on linear and semi-log scales.

7.1.6 Summary Statistics

Summary statistics of the plasma and nasopharyngeal concentration data and derived parameters will be calculated for the PK population, unless otherwise indicated. Summary statistics will be calculated for concentration at each individual time point and for all PK parameters.

Concentration data will be summarized by cohort using the following statistics: number of observations (N), arithmetic mean (mean), standard deviation (SD), minimum (min), median, maximum (max), and coefficient of variation (CV%). PK parameters will be summarized using these same statistics, as well as geometric mean and geometric mean CV.

If a PK parameter value is reportable in less than 3 subjects for a cohort, then SD, CV%, and geometric mean CV will be considered not reportable.

8 SAFETY ANALYSIS

Unless otherwise specified, all available data will be listed and summary tables for safety assessments will be presented for the safety population as detailed in Table 5.

Table 5: Data Presentations for Safety Assessments

Data	Variables	Presentation
Adverse events	Adverse event (AE) description, date (study day) and time of onset and resolution, severity, relationship to study drug, action taken, and outcome (e.g., study discontinuation)	Listings: • Reported AEs, • Serious adverse events (SAEs), • Adverse events of special interest (AESIs) Summary tables, including number and percentage of subjects experiencing: • Treatment-emergent adverse events (TEAEs), • TEAEs by severity, • TEAEs by relationship to study treatment (i.e., related or unrelated) • Serious TEAEs, • TEAEs leading to withdrawal • TEAEs with an outcome of death. Overall summary will include: • At Least One TEAE • At Least One Drug-Related TEAE • Maximum Severity by grading 1 through 5 • At Least One SAE • At Least One Drug-Related SAE • Deaths Note: includes coded terms (system organ class [SOC] and preferred term [PT])
Concomitant medications	All medications taken during the study (as defined in the protocol and including prior medications that are continued), dose, units, route, indication/ reason taken, and date and time	Listing Note: includes coded terms (anatomic therapeutic chemical [ATC] level 4 and preferred name)
Extent of exposure	Study drug administration dose, date, time,	Listing
Clinical laboratory evaluations	Laboratory results (see Table 6 for categories)	Listings • all laboratory values by category,

Data	Variables	Presentation
		• Subjects with a potentially clinically significant (PCS) laboratory value by category Summary tables • Summary tables of laboratory values and change from baseline by visit • Number and percentage of subjects with at least one postbaseline laboratory value that is deemed as PCS by parameter • Number and percentage of subjects with a laboratory value that is deemed PCS, for each scheduled postbaseline assessment time point
Vital signs	Blood pressure, pulse, respiration rate, and body temperature	Listings • all vital signs values • PCS vital sign values Summary table • Summary tables of vital signs values and change from baseline by visit and timepoint. • Number and percentage of subjects with at least one post baseline PCS value will be summarized for the worst post baseline value. • Number and percentage of subjects with a vital sign value that is PCS, for each scheduled postbaseline assessment time point
Physical examination	Physical examination findings	Listings • all physical examination findings
Electrocardiograms (ECGs)	ECG interpretations and findings	Listings • all ECGs • clinically significant ECGs Summary table • Summary tables of ECGs parameters values and change

Data	Variables	Presentation
		from baseline by visit and timepoint. • Categorical QTCF presentation of outliers by visit and timepoint.
Reactogenicity/Injection Site Inspection		Summary table • all reactions overall and by severity Listing • all reactions

Note: Sub-bullets denote individual listings or tables to be generated.

8.1 Adverse Events

An AE is defined as any untoward medical occurrence in a clinical investigation subject administered an investigational product and which does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including a clinically significant abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product.

Treatment emergent adverse events (TEAEs) are AEs not present prior to the exposure to study treatment or AEs already present that worsen in intensity or frequency following exposure to study treatment. All AEs with a start date on or after exposure to study treatment are considered TEAEs. All summary tables (except where noted) will present TEAEs. If a subject has more than one TEAE with the same PT, it is counted once in the summary tables at the strongest relationship to study drug and at the highest severity.

Frequency tables summarizing all TEAEs, TEAEs by relationship, TEAEs by severity, Serious TEAEs, TEAEs leading to withdrawal, and TEAEs with an outcome of death (including SOC and PT) will be presented by treatment (with all placebo subjects pooled) and cohort as described in Table 5.

A listing of subjects with AESI anaphylaxis will be provided.

8.2 Clinical Laboratory Evaluations

See Table 5 for details on listings related to laboratory data. Categories of laboratory data include hematology, coagulation, serum chemistry, and urinalysis.

Specific hematology, clinical chemistry, urinalysis, coagulation, and serology parameters are listed in Table 6.

Table 6: Clinical Laboratory Evaluations

Laboratory Test Category	Specific Laboratory Tests	
Hematology:	Hemoglobin	Neutrophils (absolute)
	Hematocrit	Monocytes (absolute)

Laboratory Test Category	Specific Laboratory Tests	
	Erythrocyte (red blood count [RBC]) count	Eosinophils (absolute)
	Quantitative platelet count	Lymphocytes (absolute)
	Total leukocyte (white blood cell [WBC]) count	Basophils (absolute)
	Mean corpuscular hemoglobin (MCH)	Mean corpuscular volume (MCV)
Serum Chemistry:	Aspartate aminotransferase (AST)	Calcium
	Alanine aminotransferase (ALT)	CO_2 or bicarbonate
	Alkaline phosphatase (ALP)	Blood urea nitrogen (BUN) or urea
	Albumin	Creatinine
	Total bilirubin (if total bilirubin is ≥2 × ULN with no evidence of Gilbert's syndrome, then fractionate into direct and indirect bilirubin)	Glucose
	Sodium	Chloride
	Potassium	Lipase
	Total protein	Amylase
	Phosphorus	Lactate dehydrogenase (LDH)
	Creatinine Clearance (Cockcroft-Gault)	Complement C3, C4, CH50
Lipids:	Triglycerides	Low Density Lipoproteins (LDL)
	Cholesterol, Total	
Coagulation:	Activated partial thromboplastin time (aPTT)	International normalized ratio for prothrombin time (INR/PT)
Urinalysis:	pH	Occult blood
	Protein	Specific gravity
	Glucose	Ketones
	Appearance	Color
	Bilirubin	Leukocyte esterase
	Nitrite	Microscopic reflex if protein, nitrite, blood or leukocyte esterase are positive (WBC, RBC, epithelial cells, bacteria, casts, other findings)
Serology:	Hepatitis B surface antigen (HBsAg)	Human immunodeficiency virus (HIV) antibody
	Hepatitis C antibody	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR)
Pregnancy	Serum beta human chorionic gonadotropin (β-hCG) pregnancy test for females of childbearing potential (screening and Day 120 only), urine or serum test at all other specified visits	Follicle-stimulating hormone (FSH), if applicable to confirm postmenopausal status, is only required once

Laboratory Test Category	Specific Laboratory Tests
Other	Drug (opioids, benzodiazepines, barbiturates, cocaine metabolites, cannabinoids, methamphetamines, phencyclidine, amphetamine, cotinine) and alcohol screen

Values for continuous laboratory categories (hematology, chemistry, urinalysis, and coagulation) will be summarized by visit and for the change from baseline using descriptive statistics. The number and percentage of subjects with at least one post baseline PCS value and value that is PCS, for each scheduled post baseline of each laboratory parameter will also be presented. Serology, alcohol/drug screen, and pregnancy test results will be presented in separate listings.

Data listings will include out-of-range flags (L (low), H (high)) and whether the abnormal values are clinically significant or not (based on the PI determination) and an indication of whether the value meets the PCS criterion.

Potentially clinically significant laboratory values (as defined in Table 7, Table 8, Table 9, Table 10, and Table 11) will be listed by category.

Table 7: PCS Values for Hematology

Laboratory Parameter (Unit)	Normal Reference Range	Potentially Clinically Significant Range
White blood cell count, thou/µL	4.3 - 11.0	< 2.0, >25.0
Absolute basophils, cells/µL	0 - 150	> 400
Absolute eosinophils, cells/µL	0 - 500	> 800
Absolute lymphocytes, cells/µL	1200 - 3700	< 700, > 6000
Absolute monocytes, cells/µL	20 - 1000	< 10, > 2100
Absolute neutrophils, cells/µL	1800 - 7200	< 1000, > 9000
Platelet count, thou/µL	150 - 450	< 30, > 700
Red blood cell count million/uL		
Male	4.3 - 5.7	< 3.8 , > 6.4
Female	3.9 - 5.2	< 3.3, > 5.5
Hematocrit, %		
Male	40.0 – 51.0	< 20.0, > 60.0
Female	34.0 - 45.0	< 20.0, > 60.0
Hemoglobin, g/dL		
Male	13.5 – 17.5	< 7.0, > 18.0
Female	11.0 – 15.5	< 7.0, >18.0

Table 8: PCS Values for Serum Chemistry

Laboratory Parameter (Unit)	Normal Reference Range	Potentially Clinically Significant Range
Alanine aminotransferase, U/L		
Female	0 – 40	> 58
Male	0 – 55	> 92

Laboratory Parameter (Unit)	Normal Reference Range	Potentially Clinically Significant Range
Albumin, g/dL	3.5 – 5.2	< 1.5, >6.0
Alkaline phosphatase, U/L		
Female	35 – 104	
Male	40 – 129	
Amylase	28 – 100	
Aspartate aminotransferase, U/L		
Female	0 – 35	
Male	0 – 50	
Carbon dioxide , mmol/L	22 – 32	< 10, > 40
Bilirubin total, mg/dL	0 – 1.4	> 7.0
Blood urea nitrogen, mg/dL	6 – 21	>70
Calcium, mg/dL	8.4 – 10.6	< 6.9, > 12.6
Chloride, mmol/L	96 – 108	< 65, > 130
Creatinine, mg/dL		
Female	0.4 – 1.1	> 7.4
Male	0.5 – 1.2	> 7.4
Creatinine Clearance (Cockcraft-Gault)	> 80	
Direct Bilirubin, direct (conjugated), mg/dL	0 – 0.3	
Glucose, nonfasting, mg/dL	60 – 99	< 40, >400
Lactate dehydrogenase U/L		
Female	135 – 214	
Male	135 – 225	
Lipase	7 – 60	> 200
Magnesium mg/dL	1.3 – 2.5	< 0.9, > 3.5
Phosphorus mg/dL	2.6 – 4.5	< 1.4 , > 6.6
Potassium, mmol/L	3.4 – 5.4	< 3.0, > 6.5
Protein, total g/dL	6.3 – 8.3	< 3.0, > 9.0
Sodium, mmol/L	133 – 145	< 120, > 160

Table 9: PCS Values for Lipids

Laboratory Parameter (Unit)	Normal Reference Range	Potentially Clinically Significant Range
Low Density Lipoproteins	100 – 129	< 30, > 150
Cholesterol, Total	120 – 199	> 200
Triglycerides	35 – 149	> 149

Table 10: PCS Values for Coagulation

Laboratory Parameter (Unit)	Normal Reference Range	Potentially Clinically Significant Range
Partial thromboplastin time, activated, sec	24 – 35	< 10, > 100
Prothrombin time – INR	0.9 – 1.1	> 5.0

Table 11: PCS Values for Urinalysis

Laboratory Parameter (Unit)	Normal Reference Range	Potentially Clinically Significant Range
Bilirubin	Negative	1+
Glucose	Negative	1+
Ketones	Negative	1+
Leukocyte Esterase		
Male	Negative	1+
Female	Negative	1+
Nitrite	Negative	1+
Occult Blood		
Male	Negative	Trace
Female	Negative	Trace
Protein	Negative	1+
Specific Gravity	1.003 – 1.035	< 1.000 > 1.037
pH, Urine	5.0 – 8.0	NA

NA = not applicable.

8.3 Vital Signs

Vital signs will include systolic and diastolic blood pressure, body temperature, pulse, and respiratory rate.

Absolute and change from baseline values in vital signs measurements will be summarized descriptively by visit, and timepoint. A summary table of subjects with PCS values at any post baseline visit will be presented by visit.
Potentially clinically significant vital signs values (as defined in Table 12) will be listed by parameters.

Table 12: PCS Values for Vital Signs

Parameter (Unit)	Potentially Clinically Significant Range
Systolic Blood Pressure (mmHg)	<= 90, >= 140
Diastolic Blood Pressure (mmHg)	<= 60, >= 90
Pulse Rate (beats/min)	<= 50, >= 100
Body Temperature (ºC)	<= 36, > 38
Respiratory Rate (breaths/min)	<= 12, >= 20

Data listings will identify if values are “abnormal, clinically significant” or “abnormal, not clinically significant” and an indication of whether the value meets the PCS criterion.

8.4 Physical Examination Findings

The physical examination will include a general review of the following body systems: general appearance, head, eyes, ears, nose, throat (HEENT), neck / thyroid, respiratory, cardiovascular, gastrointestinal, genitourinary, neurological, musculoskeletal / extremities, skin and other. Physical examination results, with abnormal and clinically significant abnormal findings flagged will be listed.

8.5 Electrocardiogram

ECG parameters to be listed include HR, PR, QRS, and QTcF. ECG results will be summarized descriptively by visit and timepoint and change from baseline will be presented. Data listings will identify if values are “abnormal, clinically significant” or “abnormal, not clinically significant”.
Outliers with respect to QTcF will also be tabulated for the following categories:

Absolute value > 450 msec and ≤ 480 msec

Absolute value > 480 msec and ≤ 500 msec

Absolute value > 500 msec

Increase from baseline >= 30 msec and < 60 msec

Increase from baseline >= 60 msec

8.6 Reactogenicity/Injection Site Inspection

Reactogenicity/Injection Site Inspection will be summarized descriptively by CD388 dose, pooled placebo, visit, and time point. Also, worst severity score after each study drug injection will be summarized by CD388 dose and pooled placebo. Additionally, data listings will be provided.

9 PHARMACOGENOMICS AND BIOMARKER EVALUATIONS

Additional blood samples will be collected for pharmacogenomics and exploratory biomarker evaluation.
Analyses of DNA and biomarkers may be conducted at the Sponsor’s discretion and reported separately from the study report.

10 ANTIDRUG ANTIBODIES

Analysis of the ADA results will be determined and may include determination of subjects’ positive/negative ADA status at baseline, treatment-emergent ADA in subjects with a negative baseline, as well as post-baseline increase in titer for subjects with positive ADA at baseline.

11 DATA HANDLING AND PRESENTATION

All safety and statistical outputs will be generated using SAS software, version 9.4. Pharmacokinetic outputs will be generated using WinNonlin version 8.0 or higher.

All programs used to generate statistical analyses will be validated according to Altasciences’s standard operating procedures (SOPs).

The analyses described in this plan are considered a priori, in that they have been defined prior to database lock and prior to breaking the blind. Any analyses performed subsequent to database lock and breaking the blind that are not described within the present plan will be considered post hoc and exploratory. Post hoc analyses will be labeled as such in the corresponding statistical output and identified in the clinical study report (CSR).

11.1 Safety Analysis Presentation

Adverse events and medical history will be classified using the Medical Dictionary for Regulatory Activities (MedDRA) terminology version 25.0.

Prior and concomitant medications will be coded with the World Health Organization Drug Dictionary (WHODrug) version dated March 2022.

In general, the data listings will include all enrolled subjects up to the point of study completion or discontinuation; exceptions will be listings pertaining to a subset of subjects only (e.g., subjects with protocol deviations) or a subset of records/events (e.g., abnormal laboratory values).

For categorical variables, n and percentages will be presented. For continuous variables, mean, SD, median, min and max will be presented.

The following general comments also apply to all statistical analyses and data presentations:

- Duration variables will be calculated using the general formula: (end date - start date) +1.
- If the reported value of a clinical laboratory parameter cannot be used in a statistical summary table (e.g., a character string is reported for a parameter of the numerical type), a coded value must be appropriately determined and used in the statistical analyses. In general, a value for lower and upper limit of normal range such as ‘<10’ or ‘≤5’ will be treated as ‘10’ or ‘5’ respectively, and a value such as ‘>100’ will be treated as ’100’. However, the actual values as reported in the database will be presented in data listings.
- When assessments are repeated for a given time point, only the result which is the closest to the dosing time will be included in summary tables.
- If there is an unscheduled assessment, the result will only be utilized for a given time point if it falls within the analysis window and there is no scheduled assessment at the given time point.

In general, summary statistics for raw variables (i.e., variables measured at the study site or central laboratory) will be displayed as follows:

- Minima and maxima will be displayed to the same number of decimal places as the raw data.
- Means, medians, and quartiles will be displayed to 1 additional decimal place.
- Standard deviations will be displayed to 2 additional decimal places.
- Percentages will be displayed to 1 decimal place. Percentages between 0 and 0.1 (exclusive) will be displayed as ‘<0.1’.

- Derived variables (i.e., variables that are not measured by the study site but are calculated for analysis based on other measured variables) will be displayed to 1 decimal place. Values between 0 and 0.1 (exclusive) will be displayed as '<0.1'.

11.2 Pharmacokinetic Analysis

In general, all PK summary tables will be presented for the PK population.

Individual raw PK concentrations will be displayed with the same precision as received from the bioanalytical laboratory.

Precision for individual PK parameters will be displayed as follows:

- C_{max}, AUCs, CL/F and V_Z/F will be displayed with the same precision as the raw PK concentration data,
- Parameters associated with time (e.g., time of maximum concentration [T_{max}] and terminal elimination half-life [$t_{1/2}$]) will be displayed with 2 decimal places,
- Percentages will be displayed with 2 decimal places,
- Coefficient of determination (R2) and elimination rate constant (λ_z) will be displayed with 4 decimal places.

Summary statistics for concentration and PK parameters will be displayed with the same precision as the individual values, with the exception of number of observations (N) and CV% which will be presented with 0 and 1 decimal place, respectively.

11.3 Analysis Timepoints

Unless otherwise specified, the baseline value will be defined as the last non-missing evaluation prior to the first dose of study medication.

11.4 Methods for Handling Missing Data

No imputations of values for missing data (i.e., blank, "Not Done", "Not Applicable", etc.) will be performed and data presentations will reflect the data point as it appears in the case report form (CRF) or electronic data file.

12 INTERIM ANALYSES AND DATA SAFETY MONITORING

After 50% of Cohort 1 subjects have completed study drug administration and have undergone protocol-specified procedures and assessments for ≥10 days, the Principal Investigator (PI) and Sponsor will review blinded safety data in tables and listings: AEs (including systemic reactogenicity/injection site reactions, hypersensitivity reactions, and AESIs), vital signs, 12-lead ECGs, and clinical laboratory results (hematology, coagulation, serum chemistry, urinalysis) to determine the safety and tolerability of the study drug. The incidence and severity of AEs, and any adverse changes in vital signs, clinical laboratory findings, and ECGs will be considered when determining safety and tolerability of study drug. If the dose is determined to be safe and well tolerated ≥10 days after dosing, Cohort 2 will be enrolled. Enrollment of the remaining 50% of Cohort 1 will continue while the safety data of the first 50% of Cohort 1 is being reviewed.

Cohort 3 will be evaluated for enrollment using the same rules for evaluating Cohort 2.

13 GENERAL INFORMATION RELATED TO DATA PRESENTATIONS

The formats and layouts of TFLs are provided in a separate document and are common displays. Their numbering and general content follow the International Conference on Harmonisation (ICH) E3 guidelines. Actual formats and layouts may be altered slightly from those presented as necessary to accommodate actual data or statistics. Minor format changes will not require updates to the SAP, rather they may be documented in a Running Note to SAP.

APPENDIX A STUDY SCHEDULE(S)

	Screening	Clinical Research Unit (CRU) Inpatient Stay								Outpatient CRU Visits				
Day (Window)	-28 to -2	-1	1	2	3–6	7	9	11	14	30 (±3)	45 (±3)	60 (±5)	90 (±7)	120/165 [a] (±14)
Informed consent	X													
Inclusion/Exclusion criteria	X	X												
Medical history/demographics	X													
Complete physical with vital signs (BP, RR, HR, oral temperature, height, weight, BMI)	X													
Targeted physical with vital signs (BP, RR, HR, oral temperature, weight [b])		X	X [c]	X	X	X			X	X	X	X	X	X
Safety ECG [d]	X	X	X			X			X	X				X
Laboratory evaluations (CBC with platelets, coagulation, serum chemistry, urinalysis)	X	X		X	X [e]	X			X	X	X	X	X	X
Virology screening (HBV, HCV, HIV)	X													
Virology screening (SARS-CoV-2)		X												
Serum/urine pregnancy test [f]	X	X								X		X	X	X
FSH (if applicable to confirm postmenopausal status)	X													
Drug/alcohol screen [g]	X	X												
Randomization		X												
Dosing of study drug			X											
Reactogenicity/injection site inspection [h]			X	X	X									
PK sample collection [i]			X	X	X	X	X	X	X	X	X	X	X	X
Pharmacogenomics blood sample [j]			predose											
Exploratory biomarker samples			predose		X [e]									
Anti-drug antibodies			predose						X	X	X	X	X	X
Nasopharyngeal swab collection [k]			predose	X	X	X	X	X	X	X				
Assess and record AEs [l]	←													→
Concomitant medications/procedures review [m]	←													→

Abbreviations: AEs = adverse events; BMI = body mass index; BP = blood pressure, CBC = complete blood count; COVID-19 = coronavirus disease 2019; CRU = clinical research unit; DAR = drug-antibody ratio; ECG = electrocardiogram; FSH = follicle-stimulating hormone; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; HR = heart rate; hr = hour; ICF = informed consent form; PK = pharmacokinetic; RR = respiration rate; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

a. The timing of this visit is Day 120 for Cohort 1 and Day 165 for Cohorts 2 and 3. For subjects who discontinue study early, the Day 120/165 procedures should be performed.
b. Weight should be measured at each of the outpatient visits (Days 30, 45, 60, 90, 120/165).
c. On Day 1, the targeted physical examination should be performed predose. Vital signs collection will occur predose, 6 hours postdose, and as clinically indicated, and will be measured with the subject in a seated position for at least 3 minutes prior to measurement.
d. A triplicate 12-lead ECG is to be performed at screening, at CRU check-in on Day -1, predose (immediately prior to study drug administration) and 6 hours postdose (±10 minutes) on Day 1, and as indicated in the schedule. Subjects are to be resting (at least 5 minutes) and semi-recumbent when ECG is being conducted.
e. Laboratory evaluations (including exploratory biomarker samples) need to be performed once during the Day 3–6 interval on Day 4.
f. A sensitive serum pregnancy test (β-human chorionic gonadotropin) is required at screening and Day 120/165 for females of childbearing potential. Urine pregnancy test may be performed at all other time points.
g. Drug and alcohol screen is to be performed during the outpatient visits if vital signs are abnormal (see Appendix 2 of the protocol).
h. At indicated visits, inspection of administration site and surrounding area will be performed twice daily (once between approximately 2–4 hours postdose, and once approximately 8–12 hours postdose, then twice daily on other indicated study days at least 6 hours apart), with any abnormal findings reported as AEs. Reactions will be rated according to the scale provided in Table 5 of the protocol.
i. Blood samples for PK analysis will be collected predose (-24 hour window); post-dose at 2, 4, and 12 hours (each ±10 minute window); 24 hours (±30 minute window); 48 hours (±1 hour window); 72, 96, 120 hours (each ±2 hour window); and in the morning on Days 7, 9, 11, 14. Postdose samples collected at outpatient CRU visits at Days 30, 45, 60, 90, and 120/165 have the same windows (i.e., in ±days) as the visits.
j. A mandatory pharmacogenomic (DNA) blood sample will be collected once, preferably on Day 1 (collection at another time point is allowed if necessary) to allow for pharmacogenomic research related to CD388.
k. Nasopharyngeal swab samples will be collected predose on Day 1, and on Days 2, 5, 7, 9, 11, 14, and 30.
l. Adverse events (including influenza-like illness which will be tested for both COVID-19 and flu) will be collected for all subjects from the time of signing the ICF through 7 months after study drug dosing.
m. Concomitant medication and procedures, including those used to treat an AE, will be recorded from 28 days prior to the CD388 Injection/placebo administration until the final study visit.

ALTASCIENCES

TABLE, FIGURE, AND LISTING SHELLS ADDENDUM TO SAP

For:

Cidara Therapeutics Inc.

PROTOCOL No. CD388.SQ.1.03

A Phase 1, Randomized, Double-Blind, Single Ascending Dose Study to Determine the Safety, Tolerability, and Pharmacokinetics of CD388 Subcutaneous Administration in Healthy Japanese Subjects

Altasciences Project No. CID-P2-387

Prepared by:

Altasciences Inc.
575 Armand-Frappier Boulevard
Laval, Quebec
Canada, H7V 4B3

Version: 1.0

Date: 2023/06/29

ALTASCIENCES

VERSION CONTROL

Version	Date	Author	Description of Changes
1.0	2023/06/29	Logan Kowallis	N/A

ALTASCIENCES

TABLE OF CONTENTS

INTRODUCTION

The table, figure, and listing (TFL) shells describe the TFLs that will be programmed during the analysis and reporting of CD388.SQ.1.03.

These TFLs are common data displays. The numbering and general content follow the International Conference on Harmonisation (ICH) E3 guidelines and they are organized as they will appear in the Clinical Study Report (CSR).

The TFL shells should be read in conjunction with the Clinical Study Protocol, Case Report Form (CRF), and Statistical Analysis Plan (SAP). This version of the shells has been developed using Clinical Study Protocol version Amendment 1, dated 12-DEC-22 and CRF version 2.0, dated 19-JAN-23. Finalization and approval of the SAP prior to the planned database lock is considered to cover the finalization and approval of the TFL shells as well.

Modifications may be necessary to the planned TFL shell presentation to accommodate data collected during the study conduct. Significant changes, as deemed appropriate, will be documented in a Running Note to SAP.

Common Presenation

The following common presentation will be considered as default unless otherwise defined.

Page Size and Margins

Tables, figures, and listings will be displayed on letter size paper, 8.5 inches by 11 inches, with the following margins (in inches):

Orientation	Top	Bottom	Left	Right
Landscape	0.75	0.5	0.5	0.5
Portrait	0.5	0.5	0.75	0.5

Font Type and Size

Courier New, size 8

Header and Footer

The following header and footer will be presented in each TFL, unless otherwise specified:

CIDARA THERAPEUTICS INC.		Altasciences
Project # CID-P2-387 / CD388.SQ.1.03		Page 1 of x
Contents		
Date: VERSION – YYYY-MM-DD	Data Source: XXXX	Program Source: XXXXX.sas

Footnote

In footnote section, present in the following order, as applicable:

- Abbreviations
- Note(s)
- Numbered or lettered footnotes, eg, [1], [2], [a], [*], …

Treatment/Group Presentation

The following treatment or group termes will be presented, unless otherwise specified:

Treatment Description	Code	Shortened Term	
Cohort 1: 50 mg CD388	A	50 mg CD388	
Cohort 2: 150 mg CD388	B	150 mg CD388	
Cohort 3: 450 mg CD388	C	450 mg CD388	
Placebo	D	Pooled Placebo	
All subjects, IP or Placebo given	E	Overall or All Subjects	

Alignment

Where applicable, the following alignment in data presentation will be followed:

n	xx
Mean (SD)	xx.x (xx.xx)
Median	xx.x
Min, Max	xx, xx

n (%)	20 (100.0)
	10 (50.0)
	1 (5.0)

TABLE, FIGURE, AND LISTING SHELLS

14 Clinical Study Report Tables and Figures

14.1 Demographic Data

14.1.1.1.1 *Table* Template Disposition

Table 14.1.1 Subject Disposition (All Subjects)

		50 mg CD388	150 mg CD388	450 mg CD388	Pooled Placebo	Overall
Subjects Screened (n)						xx
Subjects Randomized (Enrolled Population) (n)		xx	xx	xx	xx	xx
Subjects who Received Study Drug [n(%)]		xx (100.0)	xx (100.0)	xx (100.0)	xx (100.0)	xx (100.0)
Subject Completed the Study [n(%)]	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
If No, Reason(s) of Study Discontinuation [n(%)]	Reason 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Reason 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects Included in Each Analysis Population [n(%)]	Safety Population	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Pharmacokinetic Population	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note(s): Percentages are based on the number of subjects who received at least one dose of study drug.
Safety population is defined as includes all subjects who receive any amount of study drug.

Pharmacokinetic population is defined as all subjects who have received CD388 injection with at least 1 dose and have at least one post-dose time point available.

14.1.2 Demographics

14.1.2.1.1 *Table* Template: Demographics

Table 14.1.2.1 Summary of Demographic and Baseline Characteristics (Safety Population)

		50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)	Overall (N=XX)
Age (years)	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Sex [n(%)]	Male	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Female	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity [n(%)]	Hispanic/Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not Hispanic/ Not Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race [n(%)]	Race1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Race2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Weight (kg)	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Height (cm)	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Body Mass Index (kg/m^2)	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Table 14.1.2.2 Summary of Demographic and Baseline Characteristics (Pharmacokinetic Population)

<Similar presentation as Table 14.1.2.1>

14.2 Pharmacokinetic, Pharmacodynamic, and Efficacy Data

14.2.1 Pharmacokinetic Data

14.2.1.1 Pharmacokinetic Concentration Summaries

Table 14.2.1.1.x Summary Statistics of CD388 Plasma Concentration Data Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

Analyte	Cohort	Dose (mg)		Nominal Time (h)						
				0	2.00	4.00	X.XX	X.XX	X.XX	2856.00/3936.00
CD388	<COHORT>	<DOSE>	n							
			Mean							
			SD							
			Min							
			Median							
			Max							
			CV (%)							

Programming Note(s):

- Nominal Time to be presented with 2 decimals

Numbering scheme:

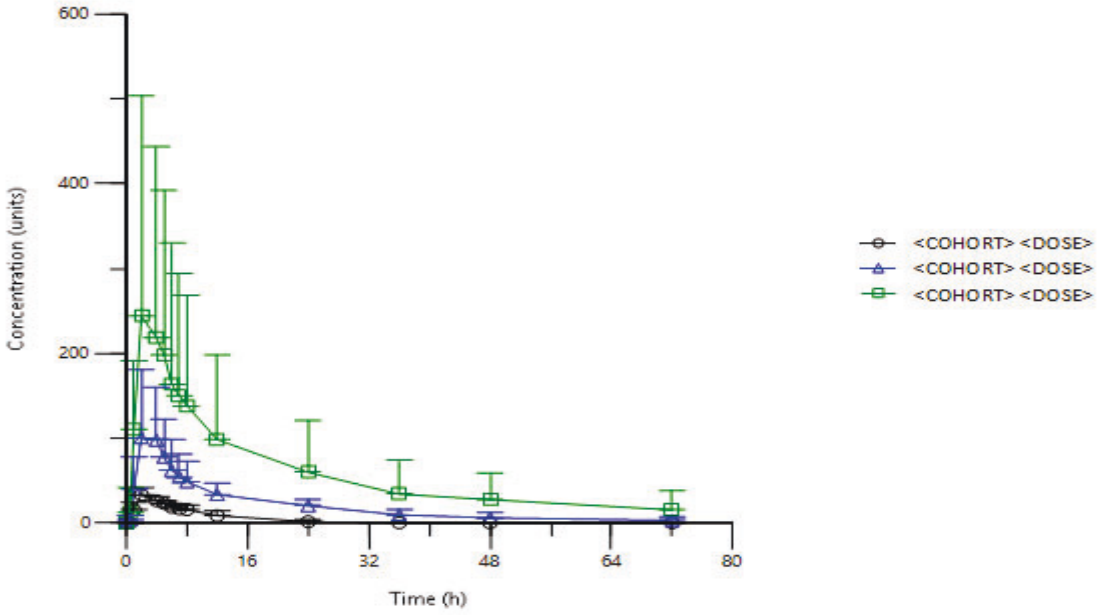
x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

Similar tables:

Table 14.2.1.2.x: Summary Statistics of CD388 Nasopharyngeal Concentration Data Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

Where, x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

Figure 14.2.1.1.x: Mean (+SD) Plasma Concentration-Time Profiles of CD388 Following Single Subcutaneous Administration of CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population (Pharmacokinetic Population)



Programming Note(s):

- X and Y-axis will match the scaling of the data.
- Linear and Semi-Log Scale will be provided

Numbering scheme:

x=1 for Linear scale and x=2 for semi-log scale

Similar figures:

Figure 14.2.1.1.x: Mean (+SD) Nasopharyngeal Concentration-Time Profiles of CD388 Following Single Subcutaneous Administration of CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population (Pharmacokinetic Population)

Where, x=1 for Linear scale and x=2 for semi-log scale

14.2.1.2 Pharmacokinetic Parameter Summaries

Table 14.2.1.2.1: Summary Statistics of Plasma PK Parameters of CD388 Following a Single Subcutaneous Administration of CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

PK Parameter	Cohort 1 (N=XX)	Cohort 2 (N=XX)	Cohort 3 (N=XX)
C_{max} (unit)			
n			
Mean (SD)			
Median (min,max)			
CV%			
Geometric mean (Geometric CV%)			
t_{max} (unit)			
n			
Median			
Min, Max			
…. (unit)			
n			
Mean (SD)			
Median (min,max)			
CV%			
Geometric mean (Geometric CV%)			

Programming Note(s):

- All PK parameters noted in the SAP will appear in the table.

Similar Tables:

Table 14.2.1.2.2: Summary Statistics of Nasopharyngeal PK Parameters of CD388 Following a Single Subcutaneous Administration of CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

14.2.1.3 Statistical Analysis of Pharmacokinetic Data

Table 14.2.1.3.1 Statistical Analysis for Dose Proportionality of *AnalyteName* Pharmacokinetic Parameters (Pharmacokinetic Population)

Parameter (unit)	n	Intercept (α)	Slope (β)	95% CI of Slope		R-squared
				Lower Bound	Upper Bound	
C_{max} (unit)	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
AUC_{0-inf} (unit)	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
AUC_{0-last} (unit)	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx

Abbreviation(s): CI = confidence interval.

Note(s): Proportionality analysis was performed using a power model: $\ln(\text{PK parameter}) = \alpha + \beta \cdot \ln(\text{Dose}) + \varepsilon$.

14.3 Safety Data

14.3.1 Adverse Events

14.3.1.1 Adverse Event Summary

Table 14.3.1.1 Summary of Adverse Events (Safety Population)

	50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)
Number of AEs Reported (n)	xx	xx	xx	xx
Number of TEAEs Reported (n)	xx	xx	xx	xx
Subjects With at Least One TEAE [n(%)] [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects With At Least One Drug-Related TEAE [n(%)] [1] [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
TEAEs by Relationship [3]				
Related [n(%)] [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Unrelated [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
TEAEs by Severity [3]				
Mild [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Moderate [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Severe [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Treatment-Emergent SAEs Reported (n)	xx	xx	xx	xx
Subjects With at Least One Treatment-Emergent SAE [n(%)][1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject with at Least One Drug-Related Treatment-Emergent SAE [n(%)] [1] [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject with TEAE Leading to Discontinuation [n(%)] [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death [n(%)] [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Abbreviation(s): AE = adverse event; TEAE = treatment-emergent adverse event; SAE = serious adverse event.
[1] Percentages are based on the number of subjects in the Safety population in each treatment group.

[2] TEAE that was reported as: "Definitely Related", "Probably Related", or "Possibly Related".
[3] Percentages are based on the number of TEAEs reported in each treatment group.

14.3.1.2 TEAE by SOC

Table 14.3.1.2 Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class MedDRA Preferred Term	50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)
Subjects with at least one TEAE [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 12 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 13 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 2 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 21 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 22 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 23 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Abbreviation(s): MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment-emergent adverse event.
Note(s): Each TEAE is counted only once for each subject within each System Organ Class and MedDRA Preferred Term.

Programming Note(s):

- SOC and PT are sorted alphabetically.

14.3.1.3 Drug-Related TEAE Summary by SOC and PT

Table 14.3.1.3 Summary of Drug-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class MedDRA Preferred Term	50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)
Subjects With at Least One Drug-Related TEAE [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 12 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 13 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 2 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 21 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 22 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MedDRA Term 23 [n(%)]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Abbreviation(s): MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment-emergent adverse event.

Note(s): Each TEAE is counted only once for each subject within each System Organ Class and MedDRA Preferred Term. A drug-related TEAE is a TEAE that was reported as: "Definitely Related", "Probably Related", or "Possibly Related".

Programming Note(s):

- SOC and PT are sorted alphabetically.

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 14.3.2.1 Listing of Death, Other Serious and Significant Adverse Events (Safety Population)

<Similar presentation as Listing 16.2.7.1>

14.3.4 Safety Assessments

14.3.4.1 Out of Range Lab

Table 14.3.4.1.1 Listing of Out-of-Range Laboratory Values (Safety Population)

Category/ Parameter (Unit)	Subject ID	Cohort/ Treatment	Visit	Date/Time	Value	Reference Range	Reference Range Flag	Safety Review
Lab Category 1								
Lab Test 11	xxx	xxxxxx	xxxxxx	YYYY-MM-DD/HH:MM	xxx	xxx-xxx	Low	NCS
	xxx	xxxxxx	xxxxxx	YYYY-MM-DD/HH:MM	xxx	xxx-xxx	High	CS
Lab Test 12								
Lab Category 2								

Abbreviation(s): CS = clinically significant; NCS = not clinically significant; RPT = repeated; TBC = to be controlled.

Table 14.3.4.1.2 Listing of Clinically Significant Laboratory Values

<Similar presentation as Table 14.3.4.1.1>

14.3.4.2 Summary Lab

Table 14.3.4.2.1.1 Summary of General Biochemistry (Safety Population)

Parameter (Units)	Visit			50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)
Albumin (g/dL)	Baseline [1]	Value	n	xx	xx	xx	xx
			Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
			Median	xx.x	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Day 2	Value	n	xx	xx	xx	xx
			Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
			Median	xx.x	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
		Change from baseline	n	xx	xx	xx	xx
			Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
			Median	xx.x	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Etc.							

Abbreviation(s):
[1] Baseline is defined as the last non-missing evaluation prior to the first dose of study drug.

Programming Note(s):

- Parameters are sorted alphabetically.

Table 14.3.4.2.2.1 Summary of Hematology (Safety Population)

Table 14.3.4.2.3.1 Summary of Coagulation (Safety Population)

Table 14.3.4.2.4.1 Summary of Urinalysis (Safety Population)

Table 14.3.4.2.4.1 Summary of Lipids (Safety Population)

<Similar presentation as Table 14.3.4.2.1.1>

Table 14.3.4.2.2.2 Summary of Subjects with Potentially Clinically Significant General Biochemistry (Safety Population)

Table 14.3.4.2.2.2 Summary of Subjects with Potentially Clinically Significant Hematology (Safety Population)

Table 14.3.4.2.3.2 Summary of Subjects with Potentially Clinically Significant Coagulation (Safety Population)

Table 14.3.4.2.4.2 Summary of Subjects with Potentially Clinically Significant Urinalysis (Safety Population)

Table 14.3.4.2.5.2 Summary of Subjects with Potentially Clinically Significant Lipids (Safety Population)

<Similar presentation as Table 14.3.5.3>

14.3.5 Vital Signs Data

14.3.5.1 Clinically Significant Vital Signs

Table 14.3.5.1 Listing of Clinically Significant Vital Signs Values

Parameter (Units)	Subject ID	Cohort/ Treatment	Visit	Timepoint	Date/Time	Value	Safety Review
Vital Sign Test 1	xxx						CS
	xxx						CS
Vital Sign Test 2	xxx						
	xxx						
Etc.	xxx						

Abbreviation(s): CS = clinically significant; DBP = diastolic blood pressure; SBP = systolic blood pressure.

14.3.5.2 Vital Signs Summary

Table 14.3.5.2 Summary of Vital Signs (Safety Population)

Parameter (Units)	Visit	Timepoint			Drug A 10 mg (N=XX)	Drug A 20 mg (N=XX)	Etc (N=XX)	Pooled Placebo (N=XX)
DBP (mmHg)	Baseline [1]		Value	n	xx	xx	xx	xx
				Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
				Median	xx.x	xx.x	xx.x	xx.x
				Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Day 1	1 h	Value	n	xx	xx	xx	xx
				Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
				Median	xx.x	xx.x	xx.x	xx.x
				Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
			Change from baseline	n	xx	xx	xx	xx
				Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
				Median	xx.x	xx.x	xx.x	xx.x
				Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Etc.								

Abbreviation(s): DBP = diastolic blood pressure; SBP = systolic blood pressure.
[1] Baseline is defined as the last non-missing evaluation prior to the first dose of study drug.

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Table 14.3.5.3 Summary of Subjects with Potentially Clinically Significant Vital Signs (Safety Population)

Parameter (Units) PCS Criteria	Visit	Timepoint			50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)
DBP (mmHg)	Baseline [1]		Value	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
	Day 1	1 h	Value	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)

Etc.

Abbreviation(s): DBP = diastolic blood pressure; SBP = systolic blood pressure.
[1] Baseline is defined as the last non-missing evaluation prior to the first dose of study drug.

14.3.6 Electrocardiogram Data

Table 14.3.6.1 Listing of Clinically Significant Electrocardiogram Assessments (Safety Population)

Subject ID	Cohort/ Treatment	Visit	Timepoint	ECG #	Date/Time	Parameter	Result	Safety Review
xxxxx	xxxxxx	Screening		1	YYYY-MM-DD/ HH:MM	Interpretation	Abnormal	CS
		Day 1	1 h	3	YYYY-MM-DD/ HH:MM	Interpretation	Abnormal	CS

Abbreviation(s): CS = clinically significant.

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14.3.6.1 ECG Summary

Table 14.3.6.2 Summary of Electrocardiogram (Safety Population)

Parameter (Units)	Visit	Timepoint			50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)
PR (msec)	Baseline [1]		Value	n	xx	xx	xx	xx
				Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
				Median	xx.x	xx.x	xx.x	xx.x
				Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Day 1	1 h	Value	n	xx	xx	xx	xx
				Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
				Median	xx.x	xx.x	xx.x	xx.x
				Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
			Change from baseline	n	xx	xx	xx	xx
				Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
				Median	xx.x	xx.x	xx.x	xx.x
				Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Etc.								

Abbreviation(s):
[1] Baseline is defined as the average of triplicates prior to the first dose of study drug.

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Table 14.3.6.3 Summary of Electrocardiogram Outliers (Safety Population)

Visit	Parameter	Category	50 mg CD388 (N=XX)	150 mg CD388 (N=XX)	450 mg CD388 (N=XX)	Pooled Placebo (N=XX)
Baseline [1]	QTcF Absolute Values	n	xx	xx	xx	xx
		> 450 msec and ≤ 480 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		> 450 msec and ≤ 500 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		> 500 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Day 1	QTcF Absolute Values	n	xx	xx	xx	xx
		> 450 msec and ≤ 480 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		> 450 msec and ≤ 500 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		> 500 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	QTcF Increases from Baseline	n	xx	xx	xx	xx
		> 30 msec and ≤ 60 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		> 60 msec	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Etc.						

Abbreviation(s):
[1] Baseline is defined as the average of triplicates prior to the first dose of study drug.

14.3.7 Other Safety Data

Table 14.3.7.1 Listing of Clinically Significant Physical Examination (Safety Population)

Body System	Subject ID	Cohort/ Treatment	Visit	Date/Time	Result	Safety Review	Abnormal Finding
					Abnormal	CS	

Abbreviation(s): CS = clinically significant.

Table 14.3.7.1 Summary of Reactogenicity/Injection-Site Inspection (Safety Population)

<Similar presentation as Table 14.3.6.1>

16 Appendices

16.1.7 Randomization Scheme and Codes

Listing 16.1.7 Randomization (Safety Population)

Subject ID	Date	Randomization Number	Cohort	Treatment

16.2 Subject Data Listings

16.2.1 Discontinued Subjects

Listing 16.2.1 Study Disposition (Safety Population)

Subject ID	Cohort/ Treatment	Date of Completion or Discontinuation	Completion Status	Reason for Discontinuation	If due to AE, specify AE #/ If due to death, specify date

Abbreviation(s): AE = adverse event.

16.2.2 Protocol Deviations

Listing 16.2.2.1 Protocol Deviations (Safety Population)

Subject ID	Cohort/ Treatment	Category	Date	Deviation Number	Deviation Code	Description	Severity

Listing 16.2.2.2 Major Protocol Deviations (Safety Population)

<Similar presentation as Listing 16.2.2.1>

16.2.3 Subjects Excluded from the Analysis

Listing 16.2.3 Analysis Populations (Safety Population)

Subject ID	Cohort/ Treatment	Safety Population	Pharmacokinetic Population	Reason if Excluded from Pharmacokinetic Population

16.2.4 Demographic Data

16.2.4.1 Demographic Characteristics

Listing 16.2.4.1 Demographic Characteristics (Safety Population)

Subject ID	Cohort/ Treatment	Age	Sex	Ethnicity	Race	Other Race	Weight (kg)	Height (cm)	BMI (kg/m^2)

16.2.4.2 Medical History

Listing 16.2.4.2 Medical History (Safety Population)

Subject ID	Cohort/ Treatment	MH#	System Organ Class	MedDRA Preferred Term	Description	Start Date	End Date

Abbreviation(s): MedDRA = Medical Dictionary for Regulatory Activities; MH = medical history.

16.2.4.3 Prior and Concomitant Medications

Listing 16.2.4.3 Prior and Concomitant Medication (Safety Population)

Subject ID	Cohort/ Treatment	CM #	Prior Y/N	Related to AE#/MH#	ATC Level 1/ Preferred Name/ Medication Name	Indication	Dose (unit)	Frequency	Route	Start Date	End Date

Abbreviation(s): AE = adverse event; ATC = Anatomical Therapeutic Chemical; CM = concomitant medication; MH = medical history.

16.2.5 Compliance and/or Drug Concentration Data

Listing 16.2.5 Investigational Product Administration (Safety Population)

Subject ID	Cohort/ Treatment	Date/Time	Dose Administered

16.2.6 Individual Response Data

16.2.6.1 Pharmacokinetic Data

Table 16.2.6.1.x Individual CD388 Plasma Concentration Data Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

Analyte	Cohort	Dose (mg)	Subject ID	Nominal Time (h)						
				0	2.00	4.00	X.XX	X.XX	X.XX	2856.00/3936.00
CD388	<COHORT>	<DOSE>	XX							
			XX							
			XX							

Programming Note(s):

- Nominal Time to be presented with 2 decimals and will be based on cohort sampling

Numbering scheme:

x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

Similar tables:

Table 16.2.6.2.x Individual CD388 Nasopharyngeal Concentration Data Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

Where, x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

16.2.6.1.1 Individual PK Parameters

Listing 16.2.6.1.x Individual Plasma PK Parameters of CD388 Following Single Subcutaneous Administration of CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

Subject ID	Cmax (unit)	t_{max}(unit)
XXX	XXX	
XXX	XXX	
XXX	XXX	
XXX	XXX	
XXX	XXX	
XXX	XXX	

Programming Note(s):

- All PK parameters noted in the SAP will appear in the listing.

Similar Listings:

Listing 16.2.6.2.x Individual Nasopharyngeal PK Parameters of CD388 Following Single Subcutaneous Administration of CD388 to Healthy Japanese Adult Subjects(Pharmacokinetic Population)

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16.2.6.1.2 PK Sampling Times

Listing 16.2.6.1.3.1.x Actual Pharmacokinetic Plasma Sampling Times Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects (Pharmacokinetic Population)

Analyte	Cohort	Dose (mg)	Subject	Nominal Time (unit)						
				0	2.00	4.00	X.XX	X.XX	X.XX	2856.00/3936.00
<ANALYTE>	<COHORT>	<DOSE>	<SUBJID>							
			<SUBJID>							
			<SUBJID>							
			<SUBJID>							
			….							

Programming Note(s):

Nominal Time to be presented with 2 decimals

Numbering scheme:

x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

Similar Listings:

Listing 16.2.6.1.3.2.x Actual Pharmacokinetic Nasopharyngeal Sampling Times Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects (Pharmacokinetic Population)

Where, x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

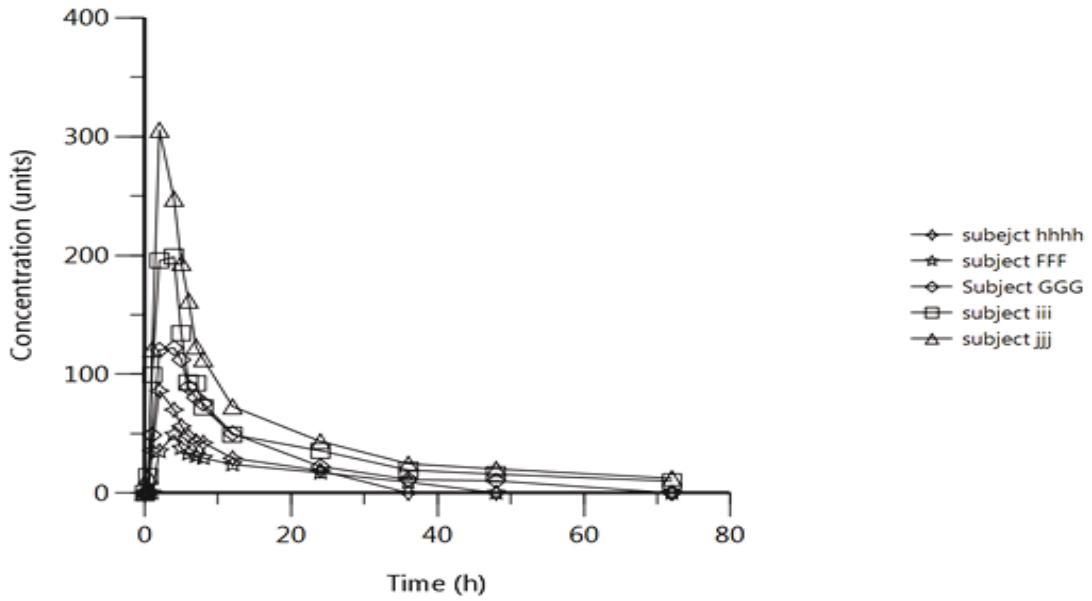
Listing 16.2.6.1.3.3.x Deviations for Actual Pharmacokinetic Plasma Sampling Times Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects (Pharmacokinetic Population)

Where, x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

Listing 16.2.6.1.3.4.x Deviations for Actual Pharmacokinetic Nasopharyngeal Sampling Times Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects (Pharmacokinetic Population)

Where, x=1 for cohort 1, x=2 for cohort 2, x=3 for cohort 3

Figure 16.2.6.1.x.y Individual Plasma Concentration-Time Profiles of CD388 Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects (Pharmacokinetic Population)



Programming Note(s):

- X and Y-axis will match the scaling of the data.
- All subjects per Cohort will appear on this figure.
- Linear and Semi-Log Scale will be provided

Numbering scheme:

x=1 for cohort 1, x=2 for cohort 2, upto x=3 for cohort 3
y=1 for linear scale, y=2 for semi-log scale

Similar Listings:

Listing 16.2.6.2.x.y Individual Nasopharyngeal Concentration-Time Profiles of CD388 Following a Single Subcutaneous Administration of <DOSE> mg CD388 to Healthy Japanese Adult Subjects (Pharmacokinetic Population)

Whwre, x=1 for cohort 1, x=2 for cohort 2, upto x=3 for cohort 3
y=1 for linear scale, y=2 for semi-log scale

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16.2.7 Adverse Event Listings

Listing 16.2.7.1 Adverse Events (Safety Population)

Subject ID	Cohort/ Treatment	AE#/ TEAE?	SOC/ PT/ Description of AE	Study Day of Onset	Resolution Date/Time (Duration)	I:Maximal Severity R:Causality Assessment E:Expectedness	O:Outcome S:Serious AE D:AE leading to Discontinuation	A: Action Taken with Study Treatment OA:Other Action(s) Taken C: Concomitant Given

Abbreviation(s): AE = adverse event; PT = preferred term; SOC = system organ class; TEAE = treatment-emergent adverse event.

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16.2.8 Listing of Individual Laboratory Measurements by Subject

Listing 16.2.8.1 General Biochemistry (Safety Population)

Subject ID	Cohort/ Treatment	Parameter (Units)	Reference Range	Visit	Date/Time	Value	Reference Range Flag	Safety Review
xxxxx	xxxxxx			Day -1 [1]				

Abbreviation(s): CS = clinically significant; PCS = potentially clinically significant; RPT = repeated; TBC = to be controlled.

[1] Baseline is defined as the last non-missing evaluation prior to the first dose of study drug.

Programming Note(s):

- Add [1] (or proper number) to indicate baseline in Visit.

Listing 16.2.8.2 Hematology (Safety Population)

Listing 16.2.8.3 Serology (Safety Population)

Listing 16.2.8.4 Urine Drug Screen (Safety Population)

Listing 16.2.8.5 Urinalysis (Safety Population)

Listing 16.2.8.6 Other Laboratory Tests (Endocrinology) (Safety Population)

<Similar presentation as Listing 16.2.8.1 (to update per protocol definition)>

16.2.9 Listing of Other Individual Measurements by Subject

16.2.9.1 Vital Signs

Listing 16.2.9.1 Vital Signs (Safety Population)

Subject ID	Cohort/ Treatment	Visit	Timepoint	Date/Time	Parameter (Units)	Value	Safety Review
xxxxx	xxxxxx	Day 1	Predose [1]				

Abbreviation(s): CS = clinically significant; PCS = potentially clinically significant; NCS = not clinically significant.

[1] Baseline is defined as the last non-missing evaluation prior to the first dose of study drug.

Programming Note(s):

- Add [1] (or proper number) to indicate baseline in Timepoint.

Listing 16.2.8.7 Reactogenicity/Injection Site Inspection (Safety Population)

<Similar presentation as Listing 16.2.9.1 >

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16.2.9.2 ECG

Listing 16.2.9.2 Electrocardiogram Assessments (Safety Population)

Subject ID	Cohort/ Treatment	Visit	Timepoint	ECG #	Date/Time	Parameter (Unit)	Value	Safety Review
xxxxx	xxxxxx	Screening		1	YYYY-MM-DD/ HH:MM	ECG Parameter 1	xx.x	
						ECG Parameter 2	xx.x	
						Etc.		
						Interpretation		Abnormal NCS
				2				
				3				
				Average				
		Day 1	Predose	1	YYYY-MM-DD/ HH:MM	ECG Parameter 1	xx.x	
						ECG Parameter 2	xx.x	
						Etc.		
						Interpretation		Abnormal NCS
				2				
				3				
				Average [1]				

Abbreviation(s): CS = clinically significant; NCS = not clinically significant.
[1] Baseline is defined as the average of triplicates prior to the first dose of study drug.

Programming Note(s):

- Add [1] (or proper number) to indicate baseline;
- Column of "ECG #" could be removed if only one assessment at a timepoint;
- Safety review only applicable to Interpretation row.

16.2.9.3 Physical Examination

Listing 16.2.9.3 General Physical Examination (Safety Population)

Subject ID	Cohort/ Treatment	Visit	Date/Time	Body System	Result	Safety Review	Abnormal Finding

Abbreviation(s): CS = clinically significant; NCS = not clinically significant.

DocuSign

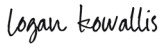
Certificate Of Completion

Envelope Id: 84E2F9D96DF84EB99D1916BBD2784F87
Status: Completed
Subject: CD388-JBS_CID-P2-387_SAP and TFL Shells_V1 Final_29JUN23
Source Envelope:
Document Pages: 81
Signatures: 3
Certificate Pages: 3
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Disabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
Joaquin Sosa
6310 Nancy Ridge Dr
STE 101
San Diego, CA 92121
jsosa@cidara.com
IP Address: 136.49.202.34

Record Tracking

Status: Original
6/29/2023 10:25:16 AM
Holder: Joaquin Sosa
jsosa@cidara.com
Location: DocuSign

Signer Events	Signature	Timestamp
Logan Kowallis lkowallis@altasciences.com Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 32C40A31-4D82-4E9E-86AF-69AB8FF04815 Using IP Address: 208.127.232.217 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 6/29/2023 10:36:21 AM Viewed: 6/29/2023 10:46:58 AM Signed: 6/29/2023 10:47:33 AM
Electronic Record and Signature Disclosure: Accepted: 8/29/2022 12:06:12 PM ID: f1fb397e-e3e9-4740-93ac-5e23a9cdf767		
Ozlem Equils, MD oequils@cidara.com Security Level: Email, Account Authentication (Required)	 Signature Adoption: Drawn on Device Signature ID: 8C319F80-E19A-475B-8904-4981B91CEB55 Using IP Address: 98.207.229.100 Signed using mobile With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 6/29/2023 10:36:22 AM Viewed: 6/29/2023 10:37:22 AM Signed: 6/29/2023 10:37:52 AM
Electronic Record and Signature Disclosure: Accepted: 6/29/2023 10:37:22 AM ID: 86aa6ff1-38b5-4e5c-a0a8-22f51c00e252		

Signer Events	Signature	Timestamp
Prabhjot Kaur pkaur@altasciences.com Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 4F5ABB3C-ED1F-4591-873C-19D04B0CB290 Using IP Address: 208.127.227.63 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I am the author of this document	Sent: 6/29/2023 10:36:22 AM Viewed: 6/30/2023 12:20:09 PM Signed: 6/30/2023 12:21:26 PM
Electronic Record and Signature Disclosure: Accepted: 6/30/2023 12:20:09 PM ID: da776d4a-3ec4-4389-98d2-be31c119691b		
In Person Signer Events	**Signature**	**Timestamp**
Editor Delivery Events	**Status**	**Timestamp**
Agent Delivery Events	**Status**	**Timestamp**
Intermediary Delivery Events	**Status**	**Timestamp**
Certified Delivery Events	**Status**	**Timestamp**
Carbon Copy Events	**Status**	**Timestamp**
Marie-Cordia Mayoyo Kabamba mcmayoyo@altasciences.com Security Level: Email, Account Authentication (Required) **Electronic Record and Signature Disclosure:** Not Offered via DocuSign	COPIED	Sent: 6/29/2023 10:36:22 AM
Witness Events	**Signature**	**Timestamp**
Notary Events	**Signature**	**Timestamp**

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	6/29/2023 10:36:23 AM
Certified Delivered	Security Checked	6/30/2023 12:20:09 PM
Signing Complete	Security Checked	6/30/2023 12:21:26 PM
Completed	Security Checked	6/30/2023 12:21:26 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

ELECTRONIC RECORD AND SIGNATURE DISCLOSURE

By accepting this notice, I am documenting that I understand and approve the following:

1. When I sign documents or data electronically, I am accountable and responsible for all items thus signed.
2. I am to be held responsible for all actions initiated under my electronic signature.
3. I will use my electronic signature only for those assigned tasks that I have the education, training, and experience to perform.

I will comply with the US FDA 21 CFR Part 11 and EU Annex 11 security rules for Cidara Therapeutics use of electronic signatures as follows:

1. I will not share passwords and/or identification codes used to log into a system or to manifest an electronic signature for Cidara Therapeutics documents.
2. I will immediately notify Cidara Therapeutics of any loss of misuse of passwords and/or identification codes which may have been used to log into a system or to manifest an electronic signature for Cidara Therapeutics documents.