CELLTRION Inc.
CT-P13 1.6

An Open-Label, Randomized, Parallel-Group, Phase I Study to Evaluate Pharmacokinetics, Efficacy and Safety between Subcutaneous CT-P13 and Intravenous CT-P13 in Patients with Active Crohn's Disease and Active Ulcerative Colitis

25th October 2019
Statistical Analysis Plan

Part 2 – Final Version 2.1

Prepared by:

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Approved by: _____ Date: ____/____/____

[redacted]

Upon review of this document, including table, listing and figure shells, the undersigned approves the final statistical analysis plan. The analysis methods and data presentation are acceptable, and the table, listing and figure production can begin.

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List of Abbreviations

Abbreviation	Definition
ARR	Administration-Related Reaction
ADA	Anti-Drug Antibody
ADR	Adverse Drug Reaction
AE	Adverse Event
ANCOVA	Analysis of Covariance
ATC	Anatomical Therapeutic Chemical
AUC_{τ}	Area Under the Concentration-Time Curve at Steady State
AZA	Azathioprine
BA	Bioavailability
BLQ	Below the Lower Limit of Quantification
BMI	Body Mass Index
CD	Crohn's Disease
CDAI	Crohn's Disease Activity Index
CI	Confidence Interval
CL	Clearance
C_{max}	Observed Maximum Serum Concentration
CRP	C-Reactive Protein
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
C_{trough}	Trough Concentration
CT-P13	Infliximab (CELLTRION, Inc.)
CV%	Percent Coefficient of Variation
DRM	Data Review Meeting
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
EOI	End of Infusion
eCRF	Electronic Case Report Form
EOS	End-of-Study
ESR	Erythrocyte Sedimentation Rate
FC	Fecal Calprotectin
GCL	Global Central Lab
HBcAb	Hepatitis B Core Antibody
HBsAb	Hepatitis B Surface Antibody
HBsAg	Hepatitis B Surface Antigen
HBV-DNA	Hepatitis B Virus DNA
HIV	Human Immunodeficiency Virus
HLGT	High Level Group Term
HLT	High Level Term
ICF	Informed Consent Form
IGRA	Interferon Gamma Release Assay
IRR	Infusion-Related Reaction
ISR	Injection Site Reaction
ITT	Intent-to-treat
IV	Intravenous
IWRS	Interactive Web Response System
LLN	Lower Limit of Normal
LLT	Lowest Level Term
LLoQ	Lower Limit of Quantification

MedDRA	Medical Dictionary for Regulatory Activities
MRT	Mean Residence Time
MSS	Mayo Scoring System
MTX	Methotrexate
N/A	Not Applicable
Nab	Neutralizing Antibody
NCA	Non-compartmental Analysis
NONNEM	Non-linear Mixed Effect Model
NRR	Not Reported Result
NYHA	New York Heart Association
PD	Pharmacodynamic
PFS	Pre-filled Syringe
PK	Pharmacokinetic
PT	Preferred Term
SADR	Serious Adverse Drug Reaction
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SC	Subcutaneous
SD	Standard Deviation
SE	Standard Error
SES-CD	Simplified Endoscopic Activity Score for Crohn's Disease
SI	System International
SIBDQ	Short Inflammatory Bowel Disease Questionnaire
SIR	Systemic Injection Reaction
SOC	System Organ Class
SOI	Start of Infusion
TB	Tuberculosis
TEAE	Treatment-Emergent Adverse Event
TESAE	Treatment-Emergent Serious Adverse Event
TLF	Table, Listing and Figure
UC	Ulcerative Colitis
ULN	Upper Limit of Normal
VAS	Visual Analogue Scale
WHO	World Health Organization
6-MP	6-mercaptopurine

1. ADMINISTRATIVE STRUCTURE

This study is being conducted under the sponsorship of CELLTRION, Inc. The clinical monitoring and medical writing are being performed under contract with [redacted], in collaboration with CELLTRION, Inc. Pharmacokinetics analysis is being performed under contract with [redacted], in collaboration with CELLTRION, Inc. The data management and statistical analysis are being performed by CELLTRION, Inc.

2. INTRODUCTION

This statistical analysis plan (SAP) defines the statistical methods and data presentations to be used by CELLTRION Clinical Statistics team in the analysis and presentation of data for Part 2 of CELLTRION study number CT-P13 1.6, entitled as "An Open-label, Randomized, Parallel-Group, Phase I Study to Evaluate Pharmacokinetics, Efficacy and Safety between Subcutaneous CT-P13 and Intravenous CT-P13 in Patients with Active Crohn's Disease and Active Ulcerative Colitis".

The following clinical study reports (CSR) will be generated during entire Study Period:

- A report of all pharmacokinetics (PK), efficacy, pharmacodynamics (PD), and safety data up to and including Week 30. The following data will be included.

<table>
<tr><th></th><th>Ongoing at Week 30</th><th>Withdrawal prior to Week 30 administration</th></tr>
<tr><td>Scheduled Visit (including EOS)</td><td>Up to and including Week 30</td><td>All available data</td></tr>
<tr><td>Unscheduled Visit</td><td>On or before date of Week 30 administration* for each patient</td><td rowspan="2">All available data up to the latest date of the all patient's Week 30 administration date*.</td></tr>
<tr><td>Non-visit based data (e.g. adverse events and medications)</td><td>All available data having a start date/or imputed start date on or before the date of Week 30 administration* for each patient.</td></tr>
</table>

* If the date of Week 30 administration is missing, the date of Week 30 visit is used for cut-off date.

- A report of all PK, efficacy, PD, and safety data up to and including Week 54. The data will be included using the same rule applied for Week 30 report (replacing Week 30 with Week 54)

- A report of all PK, efficacy, PD, and safety data after completion of all visits and safety follow-ups according to Section 5.5.11.2 of the protocol for all patients.

This SAP covers all specified analysis and is based on the following documents:

- Study Protocol Version 3.0 – 9th January 2018
- Unique CRF for Part 2 Version 2.0 – 26th January 2019

Table, Listing and Figure (TLF) mock shells will be presented as an addendum to this document.

3. STUDY OBJECTIVES

Primary, secondary and tertiary objectives are described as below.

3.1. Primary Objective

The primary objective of this study for Part 2 is to demonstrate that CT-P13 SC is noninferior to CT-P13 IV in terms of PK, as determined by the $C_{trough,week22}$ (pre-dose level at Week 22).

3.2. Secondary Objective

- The secondary objective of this study for Part 2 is to evaluate efficacy, PK, PD and overall safety of CT-P13 SC in comparison with CT-P13 IV over the first 30 weeks.
- The secondary objective of this study for Part 2 is to evaluate efficacy, PK, PD and overall safety of CT-P13 SC up to Week 54.

3.3. Tertiary Objective

- The tertiary objective of this study for Part 2 is to evaluate biomarkers (genotypes [optional] and amino acids) and patient overall satisfaction of CT-P13 IV and CT-P13 SC

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This study is an open-label, randomized, multicenter, parallel group, phase I study designed to evaluate PK, PD, efficacy and safety between CT-P13 SC and CT-P13 IV in patients with active Crohn's Disease (CD) and active Ulcerative Colitis (UC).

For Part 2, minimum 130 male or female patients with active CD or active UC will be randomly assigned at Week 6 in a 1:1 ratio to 1 of 2 treatment groups, CT-P13 SC and CT-P13 IV (approximately 65 patients per treatment group) as presented in Table 1.

Table 1. Study Arm

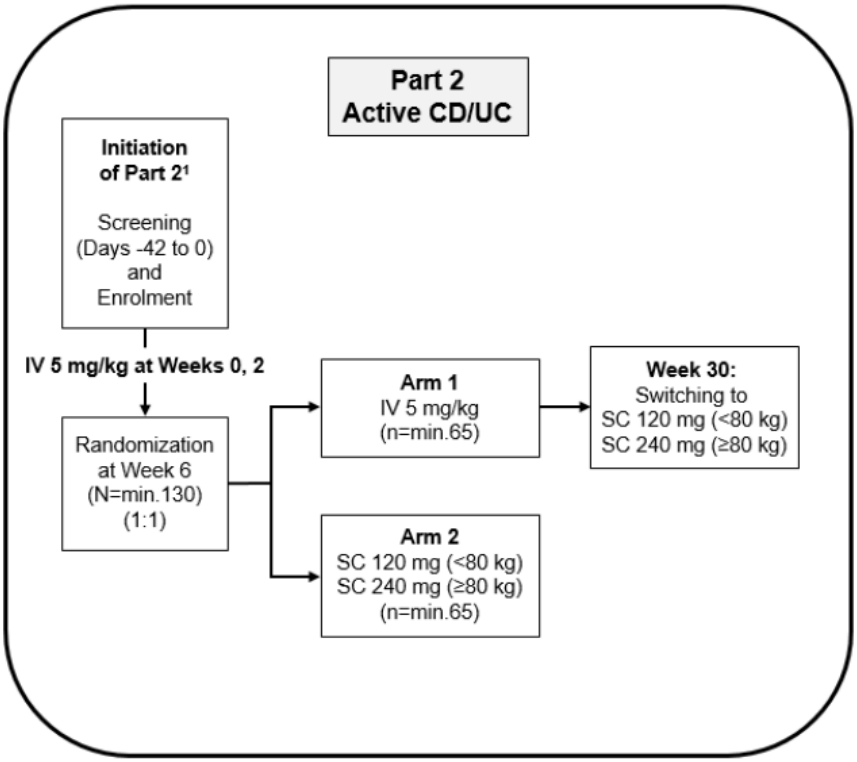
Arm Number	Dosage	Investigational Product	Method of Administration

Arm 1[1]	5 mg/kg	CT-P13 IV 100 mg/vial	2-hour IV infusion
Arm 2[2]	120 mg (<80 kg)	CT-P13 SC 120 mg/PFS	Single SC injection
	240 mg (≥80 kg)	CT-P13 SC 120 mg/PFS	Double SC injection

IV, intravenous; PFS, pre-filled syringe; SC, subcutaneous
[1]CT-P13 IV will be switched to CT-P13 SC at Week 30. The dosage of CT-P13 SC will be determined based on the patient's body weight at Week 30.
[2]The dosage of CT-P13 SC will be determined based on the patient's body weight at Week 6.

The overview of study design for Part 2 is illustrated in Figure 1.

Figure 1. Overview of Study Design for Part 2



IV, intravenous; SC, subcutaneous; CD, Crohn's disease; UC, Ulcerative Colitis;

The study will comprise 3 study periods including Screening, Treatment Period (Dose-Loading Phase and Maintenance Phase) and the End-of-Study.

Screening: Screening will take place between Days –42 and 0, prior to the first administration of the study drug.

Treatment Period: On Day 0, Week 0, patients who meet all inclusion criteria and none of the exclusion criteria will be enrolled in the study. Initially, CT-P13 IV will be given to

all enrolled patients at Weeks 0 and 2 and patients who received two full doses and have no safety concern based on investigator's discretion will be randomly assigned to receive either CT-P13 SC or CT-P13 IV before treatment on Day 42, Week 6.

Patients may also be premedicated 30 to 60 minutes prior to the start of study treatment administration and any premedications such as but not limited to antihistamine (at equivalent dose of 2 to 4 mg of chlorpheniramine), hydrocortisone, paracetamol, and/or nonsedating antihistamine (at equivalent dose of 10 mg of cetirizine) can be given at the investigator's discretion. Patients will comply with all appropriate visits and assessments.

The Dose-Loading Phase will consist of 2 doses of CT-P13 IV infusion. All patients (Arm 1 and 2) will receive a 2-hour CT-P13 IV infusion at Week 0 and Week 2.

The Maintenance Phase of the study will consist of further doses of study treatment with the last dose administered no later than Week 54.

- **Arm 1:** further 3 doses of CT-P13 IV will be administered at Week 6 and every 8 weeks thereafter up to Week 22 (Weeks 14 and 22). CT-P13 IV will be then switched to CT-P13 SC at Week 30 with CT-P13 SC dose based on body weight at Week 30. Further doses of study treatment with CT-P13 SC will be given every 2 weeks up to Week 54.

- **Arm 2:** CT-P13 SC dose based on body weight at Week 6 will be administered by PFS at Week 6 and then every 2 weeks up to Week 54.

For patients receiving CT-P13 SC 120 mg every 2 weeks, dose escalation to CT-P13 SC 240 mg every 2 weeks will be allowed since Week 30 if the patient initially responded but then lost response at Week 30, 38, 46 or 54 visit. Dose escalation will not be allowed for patients receiving CT-P13 SC 240 mg every 2 weeks. Loss of response is defined as need of the initiation of a new treatment for active CD or UC, or as following:

- For Crohn's disease, if patient has an increase in CDAI ≥70 points from the lowest CDAI score with a total score ≥220

- For Ulcerative colitis, if patient meets (1) and either of (2) or (3);

  (1) an increase in rectal bleeding subscore ≥1 point from the lowest score with actual value of >1 point

  (2) an increase in partial Mayo score ≥2 points from the lowest score with actual value of ≥4 points

  (3) an increase in endoscopic subscore ≥1 point from the lowest score with actual value of >1 point

Patients will return to the site at predefined time intervals for clinical assessments and blood sampling. At each visit, patients will be questioned about AEs and concomitant medications and will be monitored for the clinical signs and symptoms of TB.

The primary pharmacokinetic endpoint evaluation will be conducted during the Maintenance Phase at Week 22, and secondary pharmacokinetic endpoint evaluations will be conducted during the Treatment Period up to Week 54, with blood samples for analysis obtained at the time points specified in the schedule of events.

Efficacy, pharmacodynamics, biomarkers and safety assessments will be performed at the time points specified in the schedule of events.

The patient assessment Overview for Part 2 is illustrated in Figure 2.

Figure 2. Patient Assessment Overview for Part 2

	Dose-loading		Maintenance[1]													
Week	**0**	**2**	**6**	**14**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**38**	**46**	**54**
Visit[2]	X	X	X	X	X	X	X	X[3]	X	X[3]	X	X[3]	X	X	X	X
Evaluation																
Primary Pharmacokinetic					X											
Efficacy	X	X	X	X	X								X	X	X	X
Secondary Pharmacokinetic	◄															►
Pharmacodynamic	X	X	X	X	X								X	X	X	X
Safety Evaluation	◄															►

1. Additional visits will only be made by patients who need extra training for CT-P13 SC injection.
2. A visit window of ±3 days is allowed throughout the study period, including the End-of-Study Visit.
3. Only patients from Arm 2 will make visits for additional pharmacokinetic assessment.

CT-P13 SC will be injected by a healthcare professional at each site visit (Weeks 6, 14, 22, 30, 38, 46, 54 and Weeks 24, 26, 28 for patients who will make PK sampling visits). After proper training in injection technique, patients may self-inject with CT-P13 SC if their investigator determines that it is appropriate at any other scheduled administration weeks.

End-of-Study Visit: The End-of-Study Visit will occur 2 weeks after the last dose is received. For patients with early discontinuation before switching to CT-P13 SC at Week 30 in Arm 1 or before randomization at Week 6 in Arm 2, the End-of-Study Visit will occur 8 weeks after the last dose of CT-P13 IV is received.

The schedule of events is presented in Appendix 1.

5. GENERAL STATISTICAL CONSIDERATIONS

Continuous data will be summarized using descriptive statistics: n, mean, standard deviation (SD), minimum, median and maximum unless otherwise specified. The

descriptive statistics will be calculated using raw data before rounding although rounded values are listed. The following rules will be followed with regard to the number of decimal places:

- Minimum and maximum will be displayed without rounding from values in the source listing.
- Mean, median, geometric mean and percent coefficient of variation (CV%) will be rounded to one more decimal place than the maximum decimal place of values in the source listing.
- SD will be rounded to one more decimal place than mean.
- Point estimate and confidence intervals (CI) obtained from statistical procedures will be displayed to two decimal places.

Categorical data will be summarized using numbers and percentages of patients. Percentages will be rounded to one decimal place and will be suppressed when the count is zero. The denominator for all percentages will be the number of patients within the treatment group for the population of interest, unless otherwise specified.

All statistical analysis excluding primary endpoint analysis (ANCOVA) will be conducted by each disease (CD and UC) and overall. Primary endpoint analysis (ANCOVA) will be conducted by overall.

EOS and unscheduled visit will not be summarized in visit-based tables, unless otherwise specified. But, all data will be displayed in listings. Unless otherwise specified, listings will be sorted by the treatment group, patient number, and visit, if applicable. In cases where more ordering is required, other variables will be included in the sort order as applicable.

For the purpose of summarization, any numeric values recorded below the lower limit or above the upper limit of quantification will be set to the respective limit for all related summaries. In listings, original results containing inequality sign will be displayed, unless otherwise specified.

When combining data from eCRF and analytical facilities such as [redacted], discrepancy will be handled as following:

1) Recorded as collecting sample in eCRF but no corresponding results from analytical facility – listing will display only sample collection visit/date/time from eCRF;

2) No corresponding records in eCRF for results from analytical facility – listing will display only specimen collection visit/date and results from analytical facility;

3) Discrepancy in sample collection date from eCRF and analytical facility – listing will display results from analytical facility and visit/date/time from eCRF

if not missing; if sample collection date/time is missing in eCRF then use specimen collection visit/date from analytical facility.

All available results from analytical facilities will be included in the summary table.

5.1. Software

All analyses will be conducted using [redacted] Population PK model will be employed to estimate the individual subject PK parameters by a non-linear mixed effect PK model using [redacted]. PK parameters which are not derived using NONMEM will be calculated by noncompartmental methods using the appropriate validated software such as [redacted].

5.2. Sample Size

The primary endpoint is the $C_{trough,week22}$ (pre-dose level at Week 22). A sample size of 104 subjects (52 subjects each in the CT-P13 SC and CT-P13 IV treatment groups) provide 90% power to demonstrate noninferiority of CT-P13 SC to CT-P13 IV based on the 95% one-sided confidence interval for the geometric mean ratio of CT-P13 SC to CT-P13 IV in $C_{trough,week22}$. In the sample size calculation, noninferiority margin of 80%, one-sided alpha level 5%, expected ratio of 1.3 and CV of 100% were assumed. Considering 20% drop-out rate, total 130 patients (65 patients each in the CT-P13 SC and CT-P13 IV treatment groups) will be required.

A reassessment of sample size accounting for the actual ratio of geometric means and CV was made using the result from Part 1. The sample size was not to be decreased from the initial 130 total sample size but could be increased up to 200 patients in case that actual ratio of geometric means decreases to 1.18 or actual CV increases up to 140%. Sample size was determined as initial 130 total considering DSMB's recommendation based upon the review of PK, efficacy, PD and safety data found over the first 30 weeks from Part 1 of the study.

5.3. Randomization, Stratification, and Blinding

An Interactive Web Response System (IWRS) will be used for the randomization. Clinical Statistics team will generate the randomization schedule for IWRS, which will link sequential patient randomization numbers to treatment codes. The randomization at Week 6 will be stratified by current use of treatment with azathioprine (AZA) or 6-mercaptopurine (6-MP) or methotrexate (MTX) (used or not used), disease (Crohn's disease or Ulcerative colitis), clinical response at Week 6 (responder or non-responder by CDAI-70 for Crohn's disease or partial Mayo score for Ulcerative colitis), and body

weight at Week 6 (<80 kg or ≥80 kg). The randomization numbers will be blocked, and within each block the same number of patients will be allocated to each arm. The block size will not be revealed. Blinding is not included in this study because it is an open-label study.

5.4. Population of Analysis

Population to be used in analysis will be specified in related sections. The following patient populations are defined: Intent-to-Treat (ITT), All-randomized, Pharmacokinetic (PK), Pharmacodynamics (PD), Efficacy and Safety Populations. Patients who have any major protocol deviations (as defined in Section 5.6) may be excluded from analysis Population. The relevant decision will be taken at the Data Review Meeting (DRM).

Analysis of the ITT Population and All-randomized Population will be performed according to the treatment they were randomized to at Week 6. The other populations will be analyzed according to actual treatment group. The actual treatment group will be assigned according to their actual treatment, not according to the randomized arm, even if there is a discrepancy between the actual administered dose and the randomized arm. If there is a patient who has the discrepancy, the patient receiving at least one CT-P13 SC before Week 30 will be treated as CT-P13 SC treatment group. All other patients will be treated as CT-P13 IV treatment group.

For randomized patients, data before randomization at Week 6 will be displayed under the treatment group based on randomized or actual administered study drug. If a patient discontinues the study before the randomization at Week 6, the patient will be listed under treatment group of "Not Applicable" and will not be included in summary tables.

The number of patients in each population will be tabulated by the treatment group. A listing will also be produced displaying data on ITT Population.

5.4.1. Intent-to-Treat Population

The ITT Population will consist of all enrolled patients. A patient will be considered to be enrolled if the patient is successfully screened based on the 'Screening Pass YES/NO' page of the eCRF. In addition, a patient can be enrolled by an investigator's decision. Some of listings will be generated on the ITT Population to include patients who discontinued the study prior to randomization at Week 6.

5.4.2. All-randomized Population

The All-randomized Population will consist of all randomly assigned patients at Week 6, regardless of whether or not any study drug dosing was completed. This will therefore include all patients who have been allocated randomization ID at Week 6 based on 'Randomization' page of eCRF.

5.4.3. Pharmacokinetic Population

The PK Population will consist of the All-randomized Population who receive at least one full dose of study drug at Week 6 or thereafter and who have at least one PK concentration result after Week 6 treatment. The primary PK endpoint of $C_{trough,week22}$ (pre-dose level at Week 22) will be analyzed in patients who received all doses (full) of study drug up to Week 22 (prior to Week 22) in the PK Population. A patient will be considered as receiving full dose if the actual administered dose (mg) of the patient is greater than or equal to 95% of prescribed dose (mg) based on 'Study Drug Administration' page of eCRF. If a patient doesn't receive full dose, the patient will be discussed during the DRM to confirm whether the patient can be considered as receiving full dose or not.

5.4.4. Pharmacodynamic Population

The PD Population will consist of the All-randomized Population who receive at least one full dose (as defined in Section 5.4.3) of study drug at Week 6 or thereafter and who have at least one PD result (Fecal calprotectin [FC] or C-reactive protein [CRP]) after Week 6 treatment.

5.4.5. Efficacy Population

The Efficacy Population will consist of the All-randomized Population who receive at least one full dose (as defined in Section 5.4.3) of study drug at Week 6 or thereafter and who have at least one efficacy evaluation result after Week 6 treatment. A patient will be considered as having an efficacy evaluation result if the patient is recorded as performing at least one of any assessment of the followings.

For CD,

- CDAI
- Simplified Endoscopic Activity Score for Crohn's Disease (SES-CD)
- Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

For UC,

- Mayo Scoring System (MSS) assessment
- Flexible proctosigmoidoscopy (or colonoscopy)
- SIBDQ

5.4.6. Safety Population

The Safety Population will consist of all patients who receive at least one (partial or full) dose of study drug at Week 6 or thereafter. A patient will be considered to have received a study drug if the patient is recorded as study drug administered or if a date of administration is recorded on the 'Study Drug Administration' page of the eCRF.

5.4.7. CD Subsets

The Intent-to-Treat Population – CD, All-randomized Population – CD, Pharmacokinetic Population – CD, Pharmacodynamic Population – CD, Efficacy Population – CD and Safety Population– CD will consist of all patients who have diagnosis of CD on the 'Diagnosis of IBD' page of eCRF in each Population.

5.4.8. UC Subsets

The Intent-to-Treat Population – UC, All-randomized Population – UC, Pharmacokinetic Population – UC, Pharmacodynamic Population – UC, Efficacy Population – UC and Safety Population – UC will consist of all patients who have diagnosis of UC on the 'Diagnosis of IBD' page of eCRF in each Population.

5.5. Definition of Baseline

The baseline value will be considered to be the last non-missing value before the first administration. Post-baseline values will be considered to be all values collected after the first administration.

5.6. Protocol Deviations

Protocol deviation will be categorized as "major" or "minor". Category of protocol deviation will be identified during the DRM. A major protocol deviation is one that may affect the interpretation of study results or the patient's rights, safety or welfare.

Major protocol deviations and population to be excluded are defined as follows:

- Mis-randomizations (PK and/or Efficacy populations): defined as patients who received another treatment to which they were assigned at any point during the study. Patients with mis-randomizations at any time point during the study will be excluded from Efficacy population. Patients with mis-randomizations before Week 22 administration will be excluded from PK population.

- Significant GCP non-compliance (All populations): CELLTRION will identify the sites which have been closed or patients who have been affected due to suspected scientific misconduct and/or serious GCP non-compliance.

- Non-compliance of inclusion or exclusion criteria which affect the PK and/or efficacy result (PK and/or Efficacy population): CELLTRION will identify via review of data sourced from the site monitoring database.

- Dose skip (PK and Efficacy population): If a patient skipped dose (two or more consecutive for SC injections, or one or more for IV infusion) prior to Week 22,

then the patient will be excluded from PK and Efficacy population. CELLTRION will identify via review of exposure data.

- Overdose (PK population): If a patient receives overdose, the patient will be discussed during the DRM to confirm whether the patient will be excluded from PK population.

The major protocol deviations used for exclusion will be summarized for the All-randomized Population by treatment group. A listing of major protocol deviations for each patient will also be provided by treatment group for the ITT Population.

5.7. Outliers

Any outliers that are detected during the review of the data will be investigated and discussed during the DRM. In general, outliers will not be excluded. Sensitivity analyses and exploratory analyses may be conducted using imputation or excluding outliers to ensure robustness of study conclusions. Details of outliers detected will be presented in the footnotes of the relevant outputs.

6. PATIENT DISPOSITION

The total number of patients who were screened and screening failure will be displayed along with the primary reason for screening failure.

The reasons for screening failure will be displayed using the following categories and ordering:

- Inclusion/Exclusion Criteria Not Met
- Subject Withdrew Consent
- Others

A listing of patients reported as screening failures will be provided.

The number of patients who were enrolled, treated in each phase, randomized, discontinued in each phase and completed the study will also be displayed on the All-randomized Population along with percentage, if applicable.

Patient disposition will be defined as follows:

- A patient will be considered to have enrolled if the patient is successfully screened based on the ‘Screening Pass YES/NO’ page of the eCRF. In addition, a patient can be enrolled by an investigator’s decision.
- A patient will be considered to have been treated in the Dose-loading Phase if it is recorded as ‘Yes’ on the ‘Study Drug Administration’ page of the eCRF at Week 0 and/or Week 2.
- A patient will be considered to be randomized if the patient was allocated a randomization ID at Week 6 based on the ‘Randomization’ page of the eCRF.

- A patient will be considered to have been treated in the Maintenance Phase if it is recorded as 'Yes' on the 'Study Drug Administration' page of the eCRF on or after Week 6.
- A patient will be considered to have completed the study if it is recorded that they completed ('Yes' box checked) on the 'Study Treatment Termination' page of the eCRF. Conversely, a patient is considered to have discontinued the study if it is recorded in the 'Study Treatment Termination' page of the eCRF that they did not complete ('No' box checked). If the patient who is considered to have discontinued the study has received a study drug administration on or after Week 6, the patient will be considered to have discontinued in the Maintenance Phase, otherwise, in the Dose-loading Phase.

The total number of patients who discontinued the study in the Dose-loading Phase will be presented by primary reason. The number and percentage of patients who discontinued the study in the Maintenance Phase will also be displayed by primary reason for discontinuation and treatment group. The reasons for discontinuation will be displayed using the following categories and ordering:

- Patient develops signs of disease progression in the judgment of the investigator
- Patient withdraws consent or refuses to continue treatment and/or procedures/observations
- Patient has any AE that would compromise his or her safety if he or she continues to participate in the study
- Patient has a significant protocol violation
- Patient is lost to follow-up
- Patient died
- Pregnancy
- Investigator's decision
- Others

In addition, the time on study drug prior to discontinuation will also be summarized using descriptive statistics by treatment group, if applicable, for those patients who have discontinued study treatment prematurely in the Dose-loading Phase or Maintenance Phase, respectively. The treatment duration in days will be calculated as (Date of last administration - date of first administration + 1).

The date of first administration will be taken as the earliest date recorded on the 'Study Drug Administration' page of the eCRF. The date of last administration will be taken as recorded on the 'Study Treatment Termination' page of the eCRF.

The patient disposition data collected for the ITT Population will be listed by treatment group.

7. DEMOGRAPHICS, BASELINE, AND BACKGROUND CHARACTERISTICS

7.1. Demographics and Stratification Details

The following demographic measures will be summarized for the All-randomized Population by treatment group: Age (years); Sex (male, female); Female fertility status (Pre-Menarche, Surgically Sterilized, Post-Menopausal, Potentially Able to bear Children, Other); Race (Not allowed by investigator country regulations, Asian/Oriental, Caucasian/White, African/Black, Other); Ethnicity (Hispanic or Latino, Non-Hispanic or non-Latino, Unknown); Height (cm), Weight (kg) and Body Mass Index (BMI) (kg/m^2) as recorded at the screening visit.

Age will be automatically calculated in the eCRF system based on the date of the informed consent visit and the year of birth considering whether birth date has passed the informed consent date or not.

The following stratification details will also be summarized for the All-randomized Population by treatment group: current use of treatment with AZA or 6-MP or MTX (used or not used), disease (CD or UC), clinical response at Week 6 (responder or non-responder by CDAI-70 for CD or partial Mayo score for UC) and body weight at Week 6 (<80 kg or ≥80 kg). If there is a difference for data entered between IWRS and eCRF, the stratification factors will be summarized using the final data collected on the eCRF.

Demographics will be listed for the ITT Population by treatment group. Stratification details will be listed for the All-randomized Population by treatment group.

7.2. Congestive Heart Failure Assessment

Congestive heart failure will be assessed by New York Heart Association (NYHA) functional criteria at Screening. If a patient had cardiac disease, corresponding NYHA class will be selected. The criteria for congestive heart failure is defined as Table 2.

Table 2. New York Heart Association Functional Classification

Class	Symptoms
I (Mild)	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain
II (Mild)	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
III (Moderate)	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.

IV (Severe)	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased

All NYHA criteria assessment data will be presented in a listing by treatment group for the ITT Population. Patients who have no cardiac disease will be classed as "No Class" in the listing.

7.3. Hepatitis B and C and Human Immunodeficiency Virus 1 and 2

At Scheduled visit, the following assessments will be performed:

- Hepatitis B Surface Antigen (HBsAg)
- Hepatitis B Surface Antibody (HBsAb)
- Hepatitis B Core Antibody (HBcAb)
- Hepatitis B virus (HBV)- DNA
- Hepatitis C Antibody
- Human Immunodeficiency Virus (HIV) 1&2

Viral serology results will be summarized at Baseline (as defined in Section 5.5) by treatment group for the All-randomized Population. A listing will be produced by treatment group for the ITT Population. If confirmatory test is conducted, the result of the confirmatory test will be used for the summary. All collected results will be listed.

7.4. Medical History

Medical history is captured at Screening and will be coded using Medical Dictionary for Regulatory Activities (MedDRA Version 20.1 or higher). Medical history will be summarized by treatment group, system organ class (SOC) and preferred term (PT) for the All-randomized Population. The total number of medical history and the number and percentage of patients with at least one medical history will also be presented in the table by treatment group. Medical history will also be listed for the ITT Population by treatment group.

7.5. IBD History

IBD history is captured at the Screening visit. The time since IBD diagnosis will be tabulated for the All-randomized Population by treatment group at each disease. Time (years) since IBD diagnosis will be calculated as [(date of first administration – date of diagnosis)/365.25]. If an incomplete IBD diagnosis date is recorded for a patient this will be imputed using the latest possible date. That is, if the day is missing (i.e. XXMAR2018) the date will be the last day of the month (i.e. 31MAR2018). If the day and month are missing (i.e. XXXXX2018), the date will be set to the 31st December (i.e. 31DEC2018). If the imputed date is later than date of first administration, then it will be imputed using the date of first administration. If the whole date is missing, the date will not be imputed

and time since IBD diagnosis will not be calculated. IBD history will also be listed by treatment group for the ITT Population.

7.6. Inclusion and Exclusion Criteria

Details of inclusion and exclusion criteria can be found in Sections 4.2 and 4.3 of the protocol (CT-P13 SC 1.6 v3.0). Inclusion and Exclusion criteria for each patient will be presented in separate listings for the ITT Population by treatment group.

The listing will indicate which protocol the patient was recruited under and hence which criteria applied.

8. TREATMENTS AND MEDICATIONS

8.1. Prior and Concomitant Medications

All medications for the treatment of CD or UC, from the diagnosis of disease until the last assessment date or EOS visit, will be collected on the eCRF. All medications except for the treatment of CD or UC used during the study taken within 30 days before date of first administration and until the last assessment date or EOS visit will be collected on the eCRF. All concomitant medications also will be recorded when any Serious Adverse Drug Reactions (SADRs) (Adverse Drug Reaction [ADR] in Korea) occur after the End-of-Study visit. All medications will be coded according to the World Health Organization drug dictionary (WHO Drug Dictionary September 1, 2017 or later version).

Medications will be classed as either prior or concomitant. For the purpose of inclusion in prior or concomitant medication tables, incomplete medication start and stop dates will be imputed as follows:

If the stop date is incomplete the following rules will be applied:

- Missing day: Assume the last day of the month.
- Missing day and month: Assume December 31st.
- Missing day, month and year: Leave it as Missing.

In the case of the death of a patient, and the imputed end date is after the date of death, the end date will be imputed as the date of death.

If the start date is incomplete the following rules will be applied. If the stop date is incomplete, imputed end date will be used instead of reported end date:

- Missing day: Assume the first day of the month.
  However, if the partial date and the date of first administration (defined as the earliest date recorded on the “Study Drug Administration” page of eCRF) lie within the same month and year and the date of first administration is not after the stop date of the medication, set to the date of first administration. Otherwise, set to stop date of the medication.

- Missing day and month: Assume January 1st.
  However, if the partial date and the date of first administration lie within the same year and the date of first administration is not after the stop date of the medication, set to the date of first administration. Otherwise, set to stop date of the medication.

- Missing day, month and year: Assume date of first administration, if not after the stop date for the medication. Otherwise, set to stop date for the medication.

For the missing day imputation, the following examples should be used for reference:

- Example 1:
  Medication start: UNJUN2018
  Medication end: 20OCT2018
  Date of first administration: 16OCT2018
  Medication start imputed: 01JUN2018
- Example 2:
  Medication start: UNOCT2018
  Medication end: 20OCT2018
  Date of first administration: 16OCT2018
  Medication start imputed: 16OCT2018
- Example 3:
  Medication start: UNOCT2018
  Medication end: 20OCT2018
  Date of first administration: 24OCT2018
  Medication start imputed: 20OCT2018

A prior medication is defined as following, and all other medications will be defined as concomitant medication.

- A medication having actual/imputed stop date of medication before the first administration date, or

- A medication checked as yes to “Is stop date before the first injection of study drug (Week 0)?” on eCRF.

The prior medications will be summarized by treatment groups, drug class (using Anatomical Therapeutic Chemical [ATC] level 2), and PT along with the total number of prior medications and the number and percentage of patients with at least one prior medication for the Safety Population. The summaries will be repeated in separate tables for concomitant medications and just for concomitant medications in Maintenance Phase, respectively. A concomitant medication in Maintenance Phase is defined as a medication that has an actual or imputed stop date on or after the Week 6 administration date, marked as ongoing or missing in patients who are administered on or after Week 6.

All prior and concomitant medications will be listed separately by treatment group for the ITT Population.

8.2. Exposure to Study Drug

The number and percentage of patients with dose administered at each scheduled week will be summarized by treatment group for the Safety Population. For patients who are not administered with the study drug, the number and percentage of patients with each reason why the dose was not administered (AE, Other) will be displayed by visit. For patients who were administered the study drug, a table will be provided displaying descriptive statistics of the planned dose, prescribed dose and actual dose administered by treatment group at each scheduled dose.

Planned, prescribed and actual administered dose per weight (mg/kg) for IV infusion and planned, prescribed and actual administered dose (mg) for SC injection will be summarized. The dose per weight (mg/kg) for IV infusion will be calculated using the Prescribed Dose (mg) and Actual Administered Dose (mg) based on the 'Study Drug Administration' page of eCRF and Weight (kg) on the 'Vital Signs' page of eCRF. If weight is missing at the applicable visit, then weight at the last non-missing assessment before the applicable visit date (applicable administration date) for the patient will be used. Planned dose will be calculated with the patient's body weight at relevant visit as per protocol (no consideration of investigator's decision including dose escalation) as follows:

Table 3. Planned dose

<table>
<tr><th></th><th>SC 120/240mg</th><th>IV 5mg/kg</th></tr>
<tr><td>Week 0 and Week 2</td><td>Patient's body weight at each visit × 5mg/kg</td><td rowspan="2">Patient's body weight at each visit × 5mg/kg</td></tr>
<tr><td>Before Week 30</td><td rowspan="2">If patient's body weight at Week 6 < 80kg, set to 120mg. Otherwise, set to 240mg.</td></tr>
<tr><td>On or after Week 30</td><td>If patient's body weight at Week 30 < 80kg, set to 120mg. Otherwise, set to 240mg.</td></tr>
</table>

Note: no consideration of investigator's decision including dose escalation.

In addition, the total number of doses received and total administered dose (mg) of each patient during the Dose-loading Phase, Maintenance Phase and Maintenance Phase (on or after Week 30) will be summarized using descriptive statistics by treatment group for the Safety Population.

For patients receiving CT-P13 SC 120 mg every 2 weeks, dose escalation to CT-P13 SC 240 mg every 2 weeks will be allowed starting on Week 30 if the patient initially responded but then lost response at Week 30, 38, 46 or 54 visit. Dose escalation will not be allowed for patients receiving CT-P13 SC 240 mg every 2 weeks. The number of patients with escalated dose and descriptive statistics of prescribed dose (mg) will be displayed by treatment group at each scheduled dose (since Week 30) for the Safety Population. Since Week 30, descriptive statistics for total number of escalated dose and average administered escalated dose (mg) of each patient will be displayed along with the number of patients with at least 1 escalated dose for the Safety Population. A listing will be provided by treatment group for the ITT Population showing the details of study drug administration.

This listing will include all data collected on the "Study Drug Administration" page of eCRF.

9. PHARMACOKINETIC ANALYSIS

All pharmacokinetic tables, listings and figures will be generated using all data on the PK Population by treatment group unless otherwise specified.

9.1. Serum Concentrations

PK samples will be collected at pre-dose (prior to the beginning of the study treatment administration on dosing day) of the scheduled sampling time points. In addition, PK samples will also be collected at specific PK monitoring visit period (between Week 22 and Week 30) presented in Table 4.

All patients in Arm 2 will be randomly assigned at Week 14 in a 1:1:1:1 ratio in to one of group A, B, C or D to collect blood samples at the specified time points:

- Group A: frequent PK sampling at Week 22 (Arm 2A)
- Group B: frequent PK sampling at Week 24 (Arm 2B)
- Group C: frequent PK sampling at Week 26 (Arm 2C)
- Group D: frequent PK sampling at Week 28 (Arm 2D)

Table 4. Steady state PK sampling time points

Visit (Day)	Arm 1	Arm 2			
		Group A	Group B	Group C	Group D
Week 22 (Day 154)	• Pre-dose* • After EOI (+15 min) • 1 hr (±15 min) after EOI • 8 hr (±15 min) after SOI • 24 hr (±15 min) after SOI • 48±2 hr after SOI • 168±6 hr after SOI	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection	• Pre-dose**	• Pre-dose**	• Pre-dose**
Week 24 (Day 168)	• 14 days (±12 hr) after SOI at Week 22	• Pre-dose**	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection	• N/A	• N/A
Week 26 (Day 182)	• 28±1 days after SOI at Week 22	• N/A	• Pre-dose**	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection	• N/A

Visit (Day)	Arm 1	Arm 2			
		Group A	Group B	Group C	Group D
Week 28 (Day 196)	• 42±1 days after SOI at Week 22	• N/A	• N/A	• Pre-dose**	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection
Week 30 (Day 210)	• Pre-dose*	• Pre-dose**	• Pre-dose**	• Pre-dose**	• Pre-dose**

EOI, End of the infusion; hr, hours; min; minutes; N/A, not applicable; SOI, Start of the infusion.
*prior to the beginning of study treatment administration on dosing day (or 56 days after previous dosing day only if patient has not received study treatment on each relevant dosing day)
**prior to the beginning of study treatment administration on dosing day (or 14 days after previous dosing day only if patient has not received study treatment on each relevant dosing day)
Note: If a patient in Arm 2 is not able to attend any of the sampling visits, it should be discussed with the Sponsor in advance.

Individual serum concentrations, scheduled time, actual sampling time and deviations from scheduled time will be presented in a data listing by treatment group for the Safety Population.

Serum concentrations of Infliximab will be summarized using descriptive statistics (n, mean, SD, CV%, geometric mean, minimum, median, and maximum) by treatment group at each scheduled collection visit and time point for the PK Population. Geometric mean will not be reported if the dataset includes zero values. All concentrations below the lower limit of quantification (BLQ) will be indicated in the data listing.

For summary of serum concentration, BLQ prior to the first administration (Week 0, Dose 1) will be set to zero. All other BLQs after study drug exposure will be set equal to Lower Limit of Quantification (LLoQ).

Mean serum concentration versus scheduled sample time plots for study drugs will also be presented on both linear and semi-logarithmic scales by treatment group for the PK Population. Additional plots showing the data collected during the PK monitoring visit period will be provided separately for better comparison between treatment groups for the PK Population.

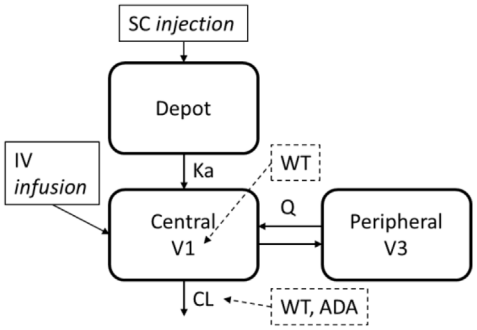
9.2. Pharmacokinetic Parameters

Individual serum concentration data over actual time data will be used to calculate PK parameters of infliximab. Due to the sparse PK sampling time points, a population PK model will be employed to estimate the individual subject PK parameters (except for $C_{trough,week22}$) by a non-linear mixed effect PK model using [redacted]. In case of $C_{trough,week22}$ and observed C_{trough}, standard non-compartmental method using [redacted], will be used.

For the calculation of $C_{trough,week22}$ and observed C_{trough} (derived by NCA [Non-compartmental analysis]), BLQ prior to the first administration (Week 0, Dose 1) will be set to zero. All other BLQs after study drug exposure will be set equal to LLoQ. For the

calculation of other secondary PK parameters (including model predicted C_{trough} at week 22, 24, 26 and 28), depending on the percentage of BLQ values alternative imputations methods may be explored and applied as deemed appropriate. A full dosing history will be used for PK parameter derivation.

Table 5. Pharmacokinetic Parameters for Infliximab

Primary Parameter: $C_{trough,week22}$ will be calculated at Week 22 for Arm 1 and Arm 2.	
$C_{trough,week22}$	Trough concentration, calculated from the pre-dose level at Week 22, if available. (calculated by NCA)
Secondary Parameters (calculated between Week 22 and Week 30, if data allows): Except for AUC_{ss8W}, secondary parameters will be calculated at Week 22 for Arm 1 and Arm 2A, Week 24 for Arm 2B, Week 26 for Arm 2C, and Week 28 for Arm 2D. **Figure 3. Final Population PK Model Equations and Model Diagram** 	
AUC_{τ}	Model predicted area under the concentration-time curve over the dosing interval (predicted [τ_{pre}]) at steady state. For Arm 2, frequent sampling visit will be considered predicted [τ_{pre}]. Predicted [τ_{pre}] is defined as the actual (not the nominal) inter-dose interval for each subject.
AUC_{ss8W}	AUC exposure normalized to an 8-week interval, calculated over dosing interval (predicted τ [τ_{pre}]), according to the following formula: AUC_{τ} [ng·h/mL]/ τ_{pre} [h]×1344 [h]
$C_{max,ss}$	Model predicted maximum serum concentration after dose administration
$T_{max,ss}$	Time of predicted maximum serum concentration
$T_{1/2}$	Terminal half life, calculated as: $\ln(2) / (0.5*(k_{13}+k_{31}+k - \text{sqrt}((k_{13}+k_{31}+k)^2-4*k_{31}*k)))$, where $k_{13} = Q/V_1$, $k_{31} = Q/V_3$ and $k = CL/V_1$. V_1, V_3, Q and CL are the central and peripheral volumes of distribution, inter-compartmental clearance and CL_{ss} or CL_{ss}/F (following IV and SC administration, respectively) obtained directly from the population PK model.
MRT	Mean residence time, calculated as: $MRT = (V_1*(1 + (V_3 / V_1))) / CL_{ss}$, where V_1, V_3 and CL_{ss} are the central and peripheral volumes of distribution and clearance obtained directly from the population PK model.

	MRT will only be reported for subjects receiving IV administration.
CL_{ss}	Clearance after IV dosing obtained directly from the population PK model.
CL_{ss}/F	Apparent clearance after SC dosing obtained directly from the population PK model.
$DNC_{max,ss}$	Dose normalized peak exposure, calculated as: $C_{max,ss}/DN = C_{max,ss}$/total dose administered
Secondary Parameter (obtained over Week 0 to Week 54)	
C_{trough}	Trough concentration, calculated by NCA (i.e. obtained directly from the observed pre-dose concentrations, if available.) In addition, model predicted C_{trough} will be reported at Weeks 22, 24, 26 and 28. Note) For IV, the patient will be administered at Week 22 and Week 30. C_{trough} for Week 22 will be the pre-dose level of Week 30. For SC Group A, the patient will be injected at Week 22, 24, 26, 28. Thus, C_{trough} for Week 22 will be the pre-dose level of Week 24 (not Week 30 pre-dose level), C_{trough} for Week 24 (and Week 26) will not be calculated and C_{trough} for Week 28 will be the pre-dose level of Week 30.

ss, steady state

The PK parameters will be presented in listings and summarized in tables by treatment group for the PK Population.

9.3. Statistical Analysis

For the primary pharmacokinetic endpoint, $C_{trough,week22}$ (pre-dose level at Week 22) will be analyzed using an analysis of covariance (ANCOVA) with treatment as fixed effect and current use of treatment with AZA or 6-MP or MTX (used or not used), disease (CD or UC), clinical response at Week 6 (responder or non-responder by CDAI-70 for CD or partial Mayo score for UC), body weight at Week 6 (<80 kg or ≥80 kg) fitted as covariates in patients who received all doses (full) of study drug up to Week 22 (prior to Week 22) for the PK population. The $C_{trough,week22}$ will be natural log transformed prior to analysis. Point estimates (geometric least square means and ratio of geometric least square means) will be calculated by back transforming the least squares means of the natural log transformed values of $C_{trough,week22}$ and difference in the least squares means. Two-sided 90% CI of the ratio geometric least square means will also be produced. The non-inferiority of CT-P13 SC to CT-P13 IV will be concluded if the lower bound of two-sided 90% CI for the ratio of geometric least square means is higher than 80%.

10. PHARMACODYNAMIC ANALYSIS

The CRP and FC will be recorded as numeric PD parameters. Any numeric values recorded below the lower limit of quantification or above the upper limit of quantification will be

set to the respective limit for all summaries. In listing, original results containing inequality signs will be displayed.

Descriptive statistics will be provided for the CRP and FC (actual value and change from baseline) for the PD population by treatment group at each scheduled visit. Descriptive statistics will consist of n, mean, SD, SE, CV%, geometric mean, minimum, median and maximum. All PD information will be listed by treatment group for the PD population. In addition, a plot will be presented showing the mean (±SE) concentration of the CRP and Fecal calprotectin at each scheduled visit for the PD Population by treatment group.

11. BIOMARKER ASSESSMENT

For amino acid assessments (including but not limited to tryptophan), blood samples and consumption time of foods or drinks containing protein will be collected at the time points specified. For genotype assessment (including VNTR2/VNTR3, VNTR3/VNTR3), blood samples of patients who sign a separate informed consent form will be collected.

Any numeric values for amino acid recorded below the lower limit of quantification or above the upper limit of quantification will be set to the respective limit of all summaries. In listing, original results containing inequality signs will be displayed. Descriptive statistics will be provided for the amino acid (actual value and change from baseline) for the Safety population by treatment group at each scheduled visit. The number and percentage of patients with each result for genotype will be summarized by treatment group, test and visit for the Safety population separately. A listing for biomarker assessment will also be generated for the ITT population. Biomarker assessment will be analyzed for the final report.

12. EFFICACY ANALYSIS

All efficacy data will be listed for the All-randomized Population by treatment group unless otherwise specified.

12.1. Active Crohn's Disease (CD)

Efficacy will be assessed by the evaluation of CDAI, SES-CD and SIBDQ for patients with CD. The efficacy tables will be generated using all data for the Efficacy Population - CD by treatment group unless otherwise specified.

12.1.1. Crohn's Disease Activity Index (CDAI)

CDAI score is comprised of patient's CDAI diary entries, hematocrit results, and assessments performed by site investigator including but not limited to physical examination, vital signs and weight. The components of CDAI and weighting factors are the following:

Table 6. Crohn's Disease Activity Index

No.	Items	Factor
1	Number of liquid or very soft stools[1]	×2
2	Abdominal pain[1] (0=none, 1=mild, 2=moderate, 3=severe)	×5
3	General well-being[1] (0=generally well, 1=slightly under par, 2=poor, 3=very poor, 4=terrible)	×7
4	Number of 6 listed categories patient now has: 1) Arthritis/arthralgia 2) Iritis/uveitis 3) Erythema nodosum/pyoderma gangrenosum/aphthous stomatitis 4) Anal fissure, fistula, or abscess 5) Other fistula 6) Fever over 100°F (37.8°C) during past week	×20
5	Taking lomotil/opiates for diarrhea (0=no, 1=yes)	×30
6	Abdominal mass (0=none, 2=questionable, 5=definite)	×10
7	Hematocrit[2] (Males: [47-hematocrit], Females: [42-hematocrit])	×6
8	Percentage deviation from standard weight[3] ([Standard weight – Patient weight]/Standard weight) × 100 (%)	×1

1. Sum of 7 days.
2. Only for CDAI assessment at Screening and during the study period, the hematocrit results from local laboratory within the 7 days prior to the CDAI score assessment will be used.
3. If the calculated subtotal is less than '-10', then it will be set to '-10'.
Source: Best et al.1976.

Descriptive statistics for actual and change from baseline of CDAI score at each scheduled visit will be calculated by treatment for the Efficacy Population – CD. If there is an incomplete component, CDAI score will not be calculated.

The number and percentage of patients achieving clinical response according to CDAI criteria (CDAI-70 or CDAI-100) will be summarized at each scheduled visit by treatment group for the Efficacy Population – CD. A patient is defined as having a CDAI-70 (or CDAI-100) response if there is a decrease in CDAI score of 70 points or more (100 points or more for CDAI-100 response) from the baseline value (as defined in Section 5.5).

The number and percentage of patients achieving clinical remission will be summarized at each scheduled visit by treatment group for the Efficacy Population – CD. Clinical remission is defined as an absolute CDAI score of less than 150 points.

All CDAI information will be listed by treatment group for the All-randomized Population – CD.

12.1.2. Simplified Endoscopic Activity Score for Crohn's Disease (SES-CD)

The degree of mucosal ulceration will be assessed by colonoscopy (endoscopic examination of luminal surface of gastrointestinal tract which may include the rectum, colon and terminal ileum) using the SES-CD. SES-CD is obtained as follows:

Table 7. SES-CD

		Rectum	Left Colon	Transverse Colon	Right Colon	Ileum	Subtotal SES-CD
Was this section of the intestine	Explored Resected Inaccessible						
Q1. Presence and size of ulcers	0 = None 1 = Aphthous ulcers (0.1 to 0.5 cm) 2 = Large ulcers (0.5 to 2 cm) 3 = Very large ulcers (> 2cm)						
Q2. Extent of ulcerated surface	0 = None 1 = < 10% 2 = 10 — 30% 3 = > 30%						
Q3. Extent of affected surface	0 = Unaffected segments 1 = < 50% 2 = 50 — 75% 3 = > 75%						
Q4. Presence and type of narrowing	0 = None 1 = Single, can be passed 2 = Multiple, can be passed 3 = Cannot be passed						
Total SES - CD							**Overall SES-CD**

Source: Daperno et al. 2004

Subtotal SES-CD consists of the sum of scores for all individual segments: Small Intestine (Ileum) and Large Intestine (Left Colon, Transverse Colon, Right Colon, Rectum) at each assessment. Total SES-CD consists of the sum of scores for all assessments (Q1, Q2, Q3, Q4) at each individual segments. Overall SES-CD consists of the sum of Subtotal SES-CD for each of the assessments (Q1, Q2, Q3, Q4).

Colonoscopy will be evaluated at local and central level. The SES-CD evaluated at central will be summarized and listed separately in all relative tables and listings as the scores evaluated at local. Centrally evaluated SES-CD will be analysed only for the final report.

Descriptive statistics for actual and change from baseline of overall SES-CD at each study visit will be calculated by treatment for the Efficacy Population – CD. At each visit, if any of the individual segments for a subject has an inaccessible or missing exploration result, then the subject's overall SES-CD will be excluded from this summary table. In addition, if subject has inaccessible or missing exploration result at baseline visit, then the subject's change from baseline for each visit will be excluded from summary table; but if any of the individual segments for a subject at each visit has a resected exploration result (provided that no inaccessible exploration results exist at that visit), then the overall SES-CD will be included in this summary table.

Endoscopic response is defined as a decrease in 50% or more of Overall SES-CD from the baseline value using colonoscopy date (as defined in Section 5.5) without inaccessible or missing exploration result. The number and percentage of patients achieving endoscopic

response will be summarized by treatment group for the Efficacy Population – CD in the following patients.

- Confirmed mucosal abnormality (Overall SES-CD > 0) without inaccessible or missing exploration result at baseline, and
- Having Overall SES-CD without inaccessible or missing exploration result at each visit

Endoscopic remission is defined as an absolute Overall SES-CD of 2 points or less without inaccessible or missing exploration result. The number and percentage of patients achieving endoscopic remission will be summarized by treatment group for the Efficacy Population – CD in the following patients having Overall SES-CD at each visit.

- Confirmed mucosal abnormality (Overall SES-CD > 0) regardless of exploration result at baseline, or
- Overall SES-CD of 0 with inaccessible exploration result or with missing exploration result at baseline

All SES-CD information will be listed by treatment group for the All-randomized Population- CD.

12.1.3. Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

The SIBDQ is a quality-of-life questionnaire for patients with inflammatory bowel disease. It has 10 questions measuring physical, social, and emotional status. Scores for this questionnaire range from 1 (poorest quality of life) to 7 (best quality of life). The total score will be the sum of the scores obtained for physical, social and emotional status for each patient and visit. Descriptive statistics for actual and change from baseline of SIBDQ total score at each study visit will be tabulated by treatment group for the Efficacy Population – CD. All SIBDQ information will be listed by treatment group for the All-randomized Population.

12.2. Active Ulcerative Colitis (UC)

Efficacy will be assessed by the evaluation of Mayo Scoring System (MSS), Mucosal Healing and SIBDQ for patients with UC. The efficacy tables will be generated using all data for the Efficacy Population – UC by treatment group unless otherwise specified.

12.2.1. Mayo Scoring System (MSS)

Clinical response and remission for the patients with UC will be assessed by evaluation of the MSS. MSS is defined as follows:

Table 8. Mayo Scoring System (MSS)

No.	Items	Score

1	**Stool frequency**[1]	
	Normal no. of stools for this patient	0
	1 to 2 stools more than normal	1
	3 to 4 stools more than normal	2
	5 or more stools more than normal	3
2	**Rectal bleeding**[2]	
	No blood seen	0
	Streaks of blood with stool less than half the time	1
	Obvious blood with stool most of the time	2
	Blood alone passes	3
3	**Findings of flexible proctosigmoidoscopy**[3]	
	Normal or inactive disease	0
	Mild disease (erythema, decreased vascular pattern)	1
	Moderate disease (marked erythema, absent vascular pattern, friability, erosions)	2
	Severe disease (spontaneous bleeding, ulceration)	3
4	**Physician's global assessment**[4]	
	Normal	0
	Mild disease	1
	Moderate disease	2
	Severe disease	3

Total Mayo score ranges from 0 to 12, with higher scores indicating more severe disease.

1. Each patient serves as his or her own control to establish the degree of abnormality of the stool frequency.
2. The daily bleeding score represents the most severe bleeding of the day.
3. Endoscopy subscore of the Mayo Score is modified in accordance with United States Food and Drug Administration guidance so that a value of 1 does not include friability.
4. The physician's global assessment acknowledged the three other criteria; the patient's daily record of abdominal discomfort and general sense of well-being, and other observations, such as physical findings and the patient's performance status.

Source: Schroeder et al. 1987

Total Mayo score is comprised of all components of MSS (stool frequency, rectal bleeding, endoscopic subscore and physician's global assessment) and partial Mayo score is comprised of 3 components excluding endoscopic subscore. If there is an incomplete component, total and partial Mayo score will not be calculated.

Endoscopic subscore by flexible proctosigmoidoscopy (or colonoscopy) will be evaluated at local and central level. The assessments using endoscopic subscore evaluated at central will be summarized and listed separately in all relative tables and listings as the scores evaluated at local. Centrally evaluated endoscopic subscore will be analysed only for the final report.

Descriptive statistics for actual and change from baseline of partial and total Mayo score at each scheduled visit will be calculated by treatment group for the Efficacy Population – UC.

The number and percentage of patients achieving clinical response will be summarized according to total Mayo score and partial Mayo score respectively at scheduled visits by treatment group for the Efficacy Population – UC.

A patient is defined as having a clinical response according to total Mayo score if the patient satisfies all of the followings;

- Decrease from baseline in total Mayo score at least 3 points, and at least 30%
- Decrease from baseline in subscore for rectal bleeding at least 1 point, or absolute subscore for rectal bleeding of 0 or 1

A patient is defined as having a clinical response according to partial Mayo score if the patient satisfies all of the followings;

- Decrease from baseline in partial Mayo score at least 2 points
- Decrease from baseline in subscore for rectal bleeding at least 1 point, or absolute subscore for rectal bleeding of 0 or 1

The number and percentage of patients achieving clinical remission will be summarized according to total Mayo score and partial Mayo score respectively at each scheduled visit by treatment group in Efficacy Population – UC.

A patient is defined as having a clinical remission according to total Mayo score if the total Mayo score is less than or equal to 2 points with no individual subscore exceeding 1 point.

A patient is defined as having a clinical remission according to partial Mayo score if the partial Mayo score is less than or equal to 1 point.

All MSS information will be listed by treatment group for the All-randomized Population – UC.

12.2.2. Mucosal Healing

Mucosal healing will be assessed by endoscopic subscore of the MSS. The number and percentage of patients achieving mucosal healing will be summarized at each scheduled visit by treatment group for the Efficacy Population – UC. Mucosal healing is defined as absolute endoscopic subscore of 0 or 1 from MSS.

Mucosal healing will be listed along with the listing of MSS assessment (Section 12.2.1) for the All-randomized Population – UC.

12.2.3. Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

The SIBDQ scores for patients with UC will be summarized for the Efficacy Population – UC in the same manner as the SIBDQ scores for patients with CD (as described in Section 12.1.3). All SIBDQ information will be listed by treatment group for the All-randomized Population.

13. SAFETY ANALYSIS

All safety analyses will be performed in the Safety Population by treatment group presenting data on AEs, clinical laboratory results (clinical chemistry, hematology and urinalysis), complement (C3, C4) and total hemolytic complement, vital sign measurements, weight, BMI, 12-lead electrocardiograms (ECGs), hypersensitivity monitoring via vital sign measurements (including blood pressure, heart and respiratory rates and body temperature), physical examination findings, signs and symptoms of tuberculosis (Interferon-γ Release Assay [IGRA] and chest X-ray), local site pain (Visual Analogue Scale [VAS]), pregnancy tests, and immunogenicity tests. All safety data will be listed for the ITT Population unless otherwise specified.

13.1. Adverse Events

An AE is defined as any untoward medical occurrence in a patient enrolled into this study by signing the 'Informed Consent' page of eCRF, regardless of its causal relationship to study drug.

A treatment-emergent adverse event (TEAE) is defined as any event not present before exposure to study drug or any event already present that worsen in either intensity or frequency after exposure to study drug.

The Medical Dictionary for Regulatory Activities (MedDRA) version 20.1 or higher version will be used to code all AEs. AEs will be graded for intensity according to the Common Terminology Criteria for Adverse Events (CTCAE) v4.03.

If the stop date of an AE is partial or missing the following rules will be applied.

- Missing day (e.g. XXOCT2018): Assume the last day of the month. (e.g. 31OCT2018)
- Missing day and month (e.g. XXXXX2018): Assume December 31st. (e.g. 31DEC2018)
- Missing day, month and year (e.g. XXXXXXXXX): Leave it as Missing.

If the start date of an AE is partial or missing the following rules will be applied. If the stop date of the AE is partial, imputed stop date will be used instead of reported stop date.

- If the day of an Adverse Event is missing (e.g. XXOCT2018), the month and year of the partial date will be compared to the date of the first exposure to study drug.

  - If the month and year are equal for both dates, the AE start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, and (ii) the end date of the AE.
  - If the month and year are not equal, the AE start date will be imputed as the first day of the month (e.g. 01OCT2018).

- If the day and month is missing (e.g. XXXXX2018), the year of the partial date will be compared to the date of the first exposure to study drug.
  - If the years of both dates are equal, start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, and (ii) the end date of the AE.
  - If the year is not equal, start date will be imputed as the 1st of January of the partial date year (e.g. 01JAN2018).

- If the AE start date is missing (e.g. XXXXXXXXX), start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, and (ii) the end date of the AE.

Listings for AEs will include the following information: SOC, PT and Verbatim term; start and stop date; TEAE flag, study period (Dose-loading Phase, Maintenance Phase); intensity (CTCAE Grade 1 to 5); frequency (continuous, intermittent, transient); outcome (recovered/resolved, recovering/resolving, recovered/resolved with sequelae, not recovered/not resolved, fatal, unknown); relationship to study drug (unrelated, possible, probable, definite); action taken with study drug (dose not changed, dose reduced, dose increased, drug interrupted, drug withdrawn); any treatment received (no, yes with specified treatment); whether the event was serious (Yes, No); whether the AE is Infusion related reaction (IRR), Systemic injection reaction (SIR), Delayed hypersensitivity or localized injection site reaction (ISR) and infection/malignancy; AE occurred on or after Week 30 flag. All AEs will be listed.

In summaries, adverse events will be considered to be related if the relationship is possible, probable, or definite. If relationship or intensity is missing, it will be summarized separately under a missing category.

13.1.1. Incidence of Treatment-Emergent Adverse Events

The TEAEs during the study will be summarized by treatment group and SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE using only the worst intensity recorded at each level of summarization. The total number of events and number of patients with at least one TEAE over all SOCs will also be displayed. The summaries will be repeated in separate tables for TEAEs occurred in Maintenance Phase. In addition, tables for TEAEs occurred on or after Week 30 will be repeated for the Week 54 and final report. TEAEs occurred in Maintenance Phase is defined as any event not present before study drug administration at Week 6 or any event already present that worsens in either intensity or frequency after study drug administration at Week 6. In addition, TEAEs with PT reported for at least 5% of incidence rate which is rounded to one decimal place in any treatment group will be summarized separately.

13.1.2. Deaths

All patients who have a Serious Adverse Event (SAE) with serious criteria of "Death" will be presented in a listing and the following variables will be included; date of first/last dose, date of last visit, date of death, time to death from first/last dose, days on study, TEAE flag, SOC/ PT/ cause of death, whether an autopsy was performed (yes, no), whether a death certificate was completed (yes, no), relationship to study drug and AE occurred on or after Week 30 flag. Time (days) to death from first/last dose will be calculated as (date of death – date of first/last dose + 1). In case of death during the study, days on study will be calculated as (date of death – date of first dose +1). Otherwise, days on study will be calculated as (date of last visit – date of first dose +1).

13.1.3. Serious Adverse Events

An SAE is defined as any event that is immediately life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or results in death. Important medical events that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Treatment-Emergent Serious Adverse Events (TESAEs) will be summarized by treatment group and SOC, PT, relationship and intensity/serious criteria, displaying the number and percentage of patients with at least one TESAE using only the most severe SAE recorded at each level of summarization. The total number of events and number of patients with at least one TESAE over all SOCs will also be displayed. The summaries will be repeated in a separate table for TESAEs occurred in Maintenance Phase. In addition, tables for TESAEs occurred on or after Week 30 will be repeated for the Week 54 and final report.

All SAEs will be listed including the variables detailed in Section 13.1. Serious criteria and SAE description will be presented in an additional information listing.

13.1.4. Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation

All patients who have a TEAE with an action taken with study drug of "Drug Withdrawn" will be summarized by treatment group and by SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE leading to study drug discontinuation, using only the most severe TEAE recorded at each level of summarization. The total number of events and number of patients with at least one TEAE which led to study drug discontinuation will also be displayed. The summaries will be repeated in a separate table for TEAEs leading to study discontinuation occurred in Maintenance Phase. In addition, tables for TEAEs leading to study discontinuation occurred on or after Week 30 will be repeated for the Week 54 and final report.

All TEAEs leading to study drug discontinuation will be listed including the variables detailed in Section 13.1.

13.1.5. Treatment-Emergent Adverse Events of Special Interest

The AEs of special interest are as following:

- Infusion related reaction (IRR), Systemic injection reaction (SIR) and Delayed hypersensitivity

  The AEs checked as 'infusion related/anaphylactic reaction/hypersensitivity (Administration related reaction (ARR))' in the eCRF will be classified as IRR, SIR or Delayed hypersensitivity based on the date/time of latest administration, as shown in the table below.

The latest administration before AE	AE Occurrence Time	Classification
IV infusion	Between IV infusion start and after 24 hours of IV infusion end	IRR
	After 24 hours of IV infusion end	Delayed hypersensitivity
SC injection	Between SC injection start and after 24 hours of SC injection start	SIR
	After 24 hours of SC injection start	Delayed hypersensitivity

  Note) if administration time or AE start time is unknown, AEs that occurred within 1 day after study drug administration will be classified as IRR or SIR. Otherwise, will be classified as Delayed hypersensitivity.

- Localized injection site reactions (ISR)

  AEs classified as ISR in the eCRF will be included.

- Infection

  AEs coded with a System Organ Class of 'Infections and Infestations' will be included.

- Malignancies

  AEs coded with a System Organ Class of 'Neoplasms benign, malignant and unspecified (incl cysts and polyps)' excluding terms which includes 'benign' in High Level Group Term (HLGT), High Level Term (HLT), PT and Lowest Level Term (LLT). Additional medical review will be applied to AEs in this SOC to determine whether events should be included in this category.

The IRR, SIR and delayed hypersensitivity will be summarized together in one table, and other TEAEs of special interest will be summarized in separate tables. These are displayed

by treatment group, SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE using only the most severe TEAE recorded at each levels of summarization. The total number of events and number of patients with at least one TEAE of special interest will also be displayed. In addition, tables for signs and symptoms regarding IRR, SIR and delayed hypersensitivity and localized ISR will be provided separately by SOC, PT (as coded by MedDRA version 20.1 or higher version) and intensity. All summaries will be repeated in separate tables for TEAEs of special interest that occurred in Maintenance Phase. In addition, tables for TEAEs of special interest occurred on or after Week 30 will be repeated for the Week 54 and final report.

All TEAEs of special interest will be flagged in listings for AEs. TEAEs classified as IRR, SIR, Delayed hypersensitivity and localized ISR will be presented in separate listings including the variables detailed in Section 13.1. Experienced Signs and symptoms will be presented in additional information listings for IRR, SIR and Delayed hypersensitivity and localized ISR, separately.

13.2. Clinical Laboratory Evaluations

Clinical laboratory (clinical chemistry, hematology and urinalysis) test samples will be analyzed at the central laboratory at each scheduled visit. Erythrocyte Sedimentation Rate (ESR) samples will be analyzed at the local laboratory using kits supplied centrally. Additional clinical laboratory test samples will be collected if a patient experiences delayed hypersensitivity after 24 hours of study drug administration. All summaries will be based on the SI (System International) units provided by the central laboratory, no unit conversion will be done. Result of clinical laboratory parameters listed in lab specification of the central laboratory and ESR will be tabulated by treatment group at each scheduled visit. All of the clinical laboratory results will be presented in listings.

Actual value and change from baseline of all numeric laboratory parameters including clinical chemistry, hematology and urinalysis (if applicable) will be summarized using descriptive statistics by laboratory category, test parameter and visit. For the purpose of summarization, any numeric values recorded below the lower limit or above the upper limit of quantification will be set to the respective limit for all related summaries. In listings, original results containing inequality signs will be displayed.

The central laboratory test results for parameters including clinical chemistry, hematology and urinalysis (if applicable) are categorized with ‘Normal’ and ‘Abnormal’ and then will be summarized in a shift table from baseline to each scheduled visits. The number and percentage of patients will be displayed for post-baseline visits by treatment group, test parameter and visit.

Some numeric parameters will be labeled with a CTCAE term, and grading will be applied to post-baseline values for numeric parameters where possible according to CTCAE v 4.03. Grades that require clinical input only will not be assigned to these parameters. Grades which are part numeric and part clinical input will be assigned based on the numeric portion only. If different grades share the same criteria due to exclusion of clinical input, lower grade will be used. The CTCAE terms and ranges for applicable parameters are

listed in Appendix 2. The CTCAE grades for this analysis will be Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe) and Grade 4 (Life-threatening). The CTCAE Grade 5 (Death) will not be applied in this analysis since death cannot be determined from a numeric laboratory result. If the post-baseline result for a patient does not satisfy any CTCAE grade, it will be classified as "No Grade".

The number and percentage of patients with a result for each grade will be summarized by laboratory category, treatment group, CTCAE term and visit. Additional tables will be generated using the most severe grade after administration at Week 0 and Week 6, respectively. The most severe grade will be selected including unscheduled visits.

Clinical chemistry, hematology and urinalysis data will be presented in separate listings along with high and low flags, if applicable, to show if a value was outside the normal range and CTCAE results for applicable parameters.

13.3. Complement (C3, C4) and Total Hemolytic Complement

Complement (C3, C4) and total hemolytic complement will be assessed at Week 0. Additional assessment for complement (C3, C4), total hemolytic complement will be assessed if delayed hypersensitivity occurs after 24 hours of study drug administration. All complement tests data will be presented in a listing by treatment group for the ITT Population.

13.4. Vital Signs and Weight

Vital signs (including systolic and diastolic blood pressure, heart rate, respiratory rate and body temperature), weight and BMI will be assessed at scheduled visits prior to beginning of the study drug administration. For hypersensitivity monitoring, vital signs will also be assessed at the following time points of scheduled visit:

- Prior to the beginning of the study drug administration
- 1 hour (±10 minutes) after the end of the study drug administration

All vital signs data and weight assessed will be summarized using descriptive statistics of actual value and change from baseline by treatment group, parameter at each scheduled visit for the Safety Population.

The number and percentage of patients who have clinically notable hypersensitivity result will be summarized in a table by treatment group, visit, time points and parameter for the Safety Population. The criteria for clinically notable results are defined as follows:

Table 9. Hypersensitivity Classification for Vital Signs

Parameter	Low	High
Systolic blood pressure (mmHg)	<= 90	>= 160
Diastolic blood pressure (mmHg)	<= 50	>= 90
Heart rate (beats per minute)	<= 50	>= 100
Respiratory rate (breaths per minute)	<= 12	>= 20
Body temperature (ºC)	<= 35.0	>= 38.0

All vital signs data including hypersensitivity monitoring results, weight and BMI will be listed for each patient by treatment group, visit, time points and parameter for the ITT Population. High and low flags will also be presented in the listing to show whether a value is outside of the normal range.

13.5. Electrocardiograms

Findings of 12-Lead ECG will be classified as either "Normal", "Abnormal, Not Clinically Significant", or "Abnormal, Clinically Significant". The number and percentage of patients will be summarized by treatment group and visit for the Safety Population, in the form of a shift table to detect changes from baseline. All 12-Lead ECG data will be listed for each patient by treatment group and visit for the ITT Population.

13.6. Physical Examination

Physical examinations will be performed on scheduled visit before the beginning of the study drug administration (on the same visit day as the study drug administration). The following body systems will be examined:

- General Appearance
- Head, Ears, Eyes, Nose, Throat
- Neck and Thyroid
- Skin
- Cardiovascular System
- Respiratory System
- Abdominal System
- Neurological System
- Musculoskeletal System
- Lymph Nodes
- Other

Findings of physical examination will be collected as either "Normal", "Abnormal, not clinically significant" or "Abnormal, clinically significant". The number and percentage of patients will be summarized in a table by treatment group, visit and body system for the Safety Population, in the form of a shift table to detect changes from baseline. All physical examination data will be listed for each patient by treatment group, visit and body system for the ITT Population.

13.7. Tuberculosis Assessment

TB will be assessed using IGRA, Chest X-ray and clinically monitored throughout the study.

Results for IGRA will be classified as either “Positive”, “Indeterminate” or “Negative”. If the IGRA result is indeterminate at screening, one retest will be possible during the screening period. If the IGRA result is again indeterminate or positive, the patient should be excluded from the study. If the repeated IGRA result is negative, the patient may be included in the study. The retest will be used for the summary. Both first and retest results will be listed. The number and percentage of patients with IGRA results will be summarized for baseline (as defined in Section 5.5) and Treatment Period for the Safety Population. All post-baseline results of IGRA will be reported in a Treatment Period category using the following methodology:

- If a patient has at least one result of “Positive” in the Treatment Period, they will be considered as “Positive".
- If a patient has no “Positive” results and at least one result of “Indeterminate” in the Treatment Period then they will be considered as “Indeterminate”
- If a patient has only “Negative” results in the Treatment Period then they will be considered as “Negative”

Results for Chest X-ray will be classified as either “Normal”, “Abnormal, Not Clinically Significant” or “Abnormal, Clinically Significant”. The patients will be monitored throughout the study to confirm the presence of any signs or symptoms indicative of tuberculosis.

Each patient’s IGRA, Chest X-ray and TB clinical monitoring results will be separately listed by treatment group and visit for the ITT Population.

13.8. Local Site Pain

Local site pain measurements using 100 mm Visual Analogue Scale (VAS) will be performed immediately (not exceeding 1 hour) after the end of the study drug administration on scheduled visits. Local site pain data (scale standardized) will be summarized using descriptive statistics by treatment group and visit for the Safety Population. All local site pain data will be listed by treatment group and visit for the ITT Population.

13.9. Pregnancy Test

Pregnancy tests will be conducted and summarized only for female patients of childbearing potential. Pregnancy tests consist of serum and urine pregnancy tests. Serum pregnancy tests will be performed by a central laboratory at Screening and EOS. Urine Pregnancy Tests will be performed locally at scheduled visits. Serum pregnancy test results will be classified as “Positive”, “Inconclusive” or “Negative”. Urine pregnancy test results will be classified as “Positive” or “Negative”. If a urine pregnancy test result is “Positive”, a

confirmatory serum pregnancy test should be performed at the central laboratory. The number and percentage of female patients who have urine pregnancy test results will be summarized by treatment group, visit and test for the Safety Population. All pregnancy test results will be listed for each patient tested by treatment group and visit for the ITT Population.

13.10. Immunogenicity

Serum sample for immunogenicity will be collected at Week 0, 6, 14, 22, 30, 38, 46, 54, and EOS. Additional serum samples for immunogenicity testing may be collected if a patient experiences any delayed hypersensitivity after 24 hours of study drug administration. Immunogenicity assessment consists of both anti-drug antibody (ADA) and neutralizing antibody (NAb) assays.

The ADA assay will follow a three tiered approach consisting of (i) screening assay, (ii) specificity/confirmatory assay, and (iii) titration. The test outcome for the screening assay will be: {"Potential Positive" or "Negative"}. Samples that are "Potential Positive" in the screening assay will be undergone further testing in the specificity/confirmatory assay to determine if patients are a true positive. The test outcome for the specificity/confirmatory assay will be: {"Reactive", "Negative", and "Not applicable (N/A)"}. "Reactive" indicates a true positive test outcome and will be labeled as "Positive" in outputs, "Negative" is considered negative and "N/A" indicates the assay was negative at the screening phase of the process. Patients with a "Negative" test outcome for either screening or specificity/confirmatory assays will be considered negative for the overall ADA assessment. For further characterization, the antibody level will be assessed by titration in confirmed positive samples.

Samples that are positive in the ADA specificity/confirmatory assay will be analyzed further to conduct a NAb assessment. The test outcome for the screening assay will be: {"Positive" or "Negative"}. For further characterization, the antibody level will be assessed by titration in samples that are "Positive" in the screening NAb assay.

The results of the final ADA and the screening NAb assay will be summarized. The number and percentage of patient will be presented by treatment group and test at each scheduled visit for the Safety Population.

In addition, the number of patients and percentages with positive ADA and NAb conversion will be summarized for the Safety Population. The rule of ADA and NAb conversion is following:

- ADA Conversion is defined as patients who reported at least one ADA positive result after Week 0 administration in patients who

    1) Have at least one immunogenicity result (including NRR) after Week 0 administration excluding EOS visit. And

    2) Have not any ADA positive result before Week 0 administration.

- NAb Conversion is defined as patients who reported at least one NAb positive result after Week 0 administration in patients who

    1) Have at least one immunogenicity result (including NRR) after Week 0 administration excluding EOS visit. And

    2) Have not any NAb positive result before Week 0 administration.

A listing showing immunogenicity test results for each patient will be provided by treatment group and visit for the ITT Population.

The ADA and NAb titer values of the CT-P13 tagged assay will be determined as the lowest concentration of the diluted sample that is detected at or above titer cut point and be reported as the reciprocal of that dilution. Descriptive statistics of actual ADA and NAb titer will be displayed by treatment group for the Safety Population. The actual results of ADA and NAb titer for each visit will also be presented in the listing of immunogenicity results for the ITT Population.

14. Overall Satisfaction

14.1. Patient Overall Satisfaction Assessment

Patient overall satisfaction of CT-P13 IV and CT-P13 SC as tertiary endpoint will be assessed on scheduled visits. Patient overall satisfaction will be measured by marking a line through the 100 mm line (0 mm equals “extremely unsatisfied” and 100 mm equals “extremely satisfied”). Patient overall satisfaction data (scale standardized) will be summarized using descriptive statistics by treatment group and visit for the Safety Population. All patient overall satisfaction data will be listed for each patient by treatment group and visit for the ITT Population.

15. Changes in the Planned Analysis

15.1. Changes in the Protocol

1. Section 7.1.4 of the protocol states that the following secondary PK parameters for the study drug will be considered in Part 2 (between Week 22 and Week 30):

   - **AUC_{τ}**: Area under the concentration-time curve at steady state between Week 22 and Week 30
   - **AUC_{ss8W}**: Total exposure over the 8 weeks interval from Week 22 to Week 30
   - **C_{max}**: Observed maximum serum concentration after study drug administration
   - **T_{max}**: Time of observed maximum serum concentration
   - **$T_{1/2}$**: Terminal half life
   - **MRT**: Mean residence time
   - **CL**: Clearance after IV dosing
   - **CL/F**: Apparent clearance after SC dosing
   - **BA**: Bioavailability (absolute and/or relative)
   - **AUC_{τ}/DN**: Dose normalized total exposure over dosing interval (= AUC_{τ}/total dose administered)
   - **C_{max}/DN**: Dose normalized peak exposure (= C_{max}/total dose administered)
   - **C_{trough}:** Trough concentration (concentration before the next study drug administration)

   The definition of the above secondary PK parameters was updated to clarify that the PK endpoints between Week 22 and Week 30 are model predicted values calculated by population PK model. In case of MRT, it will be obtained for only IV group. In addition, BA and AUC_{τ}/DN will not be considered as the secondary PK parameters in this analysis.

2. For the clarification of the systemic and localized reaction of the drug, the adverse event reported as “Administration Related Reaction” in eCRF and occurred within 1 day after study drug administration was classified as “Infusion Related Reaction” for IV infusion and “Systemic Injection Reaction” for SC injection. The AE reported as “Injection Site reaction” in eCRF was analysed as “Localized injection site reaction.”

16. Reference List

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17. APPENDICES

Appendix 1: Schedule of Events for Part 2

	Screening	Treatment Period										EOS[1]
Study Week		**0**	**2**	**6**	**14**	**22**	**PK Monitoring Visit[32]**	**30**	**38**	**46**	**54**	
Study Day	**–42~**	**0**	**14**	**42**	**98**	**154**		**210**	**266**	**322**	**378**	
Visit Window		**N/A**	**± 3 days**									
Arm 1[2] treatment		**IV**	**IV**	**IV**	**IV**	**IV**		**SC[3]**	**SC[3]**			
Arm 2[4] treatment				**SC[4]**	**SC[4]**							
Informed consent	X											
Demography[5]	X											
Medical history[6]	X											
Hepatitis B and HBV-DNA[7]	X					(X[8])				(X[8])		(X)
Hepatitis C and HIV-1 & -2[9]	X											
Inclusion and exclusion criteria	X	X[8]										
Randomization				X[8]								
Serum pregnancy test[10]	X											X
Urine pregnancy test[11]		X[8]	X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	
Clinical laboratory tests [12]	X	X[8]	X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X
ESR[13]	X	X[8]	X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X
Chest X-ray[14]	X											
Interferon-γ release assay[15]	X							X[8]			X[8]	X[26]
Physical examinations	X	X[8]	X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X
Vital signs and Weight[16]	X	X[8]	X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X
12-lead ECG[17]	X			X	X			X			X	X
Fecal calprotectin[18]	X	X[8]	X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X[26]
SIBDQ		X[8]	X[8]	X[8]	X[8]	X[8]		X[8]			X[8]	X[26]
Patients with Crohn's disease												
Colonoscopy (SES-CD)[19]	X[20]					X[8]					X[8]	X[26]
CDAI score[21]	X[22]		X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X[26]
Patients with Ulcerative Colitis												
Flexible proctosigmoidoscopy (Endoscopic subscore of MSS)[23]	X					X[8]					X[8]	X[26]
MSS assessment[24]	X[25]		X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X[26]
VAS Local site pain[27]		X	X	X	X	X		X	X	X	X	
VAS Patient overall satisfaction[28]		X	X	X	X	X		X	X	X	X	

	Screening	Treatment Period										EOS[1]
Study Week		**0**	**2**	**6**	**14**	**22**	**PK Monitoring Visit[32]**	**30**	**38**	**46**	**54**	
Study Day	**–42~**	**0**	**14**	**42**	**98**	**154**		**210**	**266**	**322**	**378**	
Visit Window		**N/A**	**± 3 days**									
Immunogenicity[29]		X[8]		X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X
Hypersensitivity monitoring[30]		X	X	X	X	X		X	X	X	X	
C3, C4 and Total Hemolytic Complement[31]		X[8]										
Pharmacokinetic blood sampling		X[8]	X[8]	X[8]	X[8]	X[8]	X[32]	X[8]	X[8]	X[8]	X[8]	
Pharmacodynamic blood sampling (CRP)[33]	X	X[8]	X[8]	X[8]	X[8]	X[8]		X[8]	X[8]	X[8]	X[8]	X
Biomarkers (genotype, optional)[34]		X[8]										
Biomarkers (amino acids)[35]		X		X		X					X	
Prior, Concomitant medications[36]	X											
TB clinical monitoring[37]	X											
AEs monitoring[38]	X											

Abbreviations: AE, adverse event; CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; ECG, Electrocardiogram; EOS, End-of-Study; ESR, Erythrocyte sedimentation rate; HIV, human immunodeficiency virus; IV, intravenous; MSS, Mayo Scoring System; N/A, not applicable; SC, subcutaneous; SES-CD, Simplified Endoscopic Activity Score for Crohn's Disease; SIBDQ, Simplified Inflammatory Bowel Disease Questionnaire; TB, tuberculosis; VAS, Visual Analogue Scale.

1. All EOS assessments will be completed 2 weeks after the last study drug administration. For patients with early discontinuation before switching to CT-P13 SC at Week 30 in Arm 1 or before randomization at Week 6 in Arm 2, the EOS Visit will occur 8 weeks after the last dose of CT-P13 IV is received.
2. CT-P13 IV will be administered at Weeks 0, 2, 6, 14 and 22. CT-P13 IV will be then switched to CT-P13 SC at Week 30 with CT-P13 SC dose based on body weight at Week 30. Further doses of study treatment with CT-P13 SC will be given every 2 weeks up to Week 54.
3. A dosing window of ±3 days is allowed, including self-injection.
4. CT-P13 SC dose based on body weight at Week 6 will be administered by PFS at Week 6 and further SC injections will be given every 2 weeks up to Week 54. A dosing window of ±3 days is allowed including self-injection.
5. Age, gender, ethnicity and race.
6. At Screening, patients will be assessed for the history of Crohn's disease or ulcerative colitis, respiratory disease, diabetes mellitus and congestive heart failure etc.
7. At Screening, hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and hepatitis B core antibody (HBcAb) must be assessed in all patients (mandatory). If the HBsAg test result is positive, the patient must be excluded from the study. If a patient has HBsAg (negative), HBsAb (negative or positive) and HBcAb (positive), a HBV-DNA test will be further assessed at Screening. If the HBV-DNA test result is positive, the patient should be excluded from the study and if the HBV-DNA test result is negative, the patient can be included. For patients enrolled based on the HBV-DNA test, the test of HBsAg, HBsAb and HBV-DNA will be additionally performed at Weeks 22, 46 and EOS visits. Aspartate aminotransferase, alanine aminotransferase and total bilirubin results will be monitored as well.
8. Assessed prior to study drug administration.
9. If hepatitis C antibody, HIV-1 or -2 test result is positive, the patient must be excluded from the study.
10. A serum pregnancy test for women of childbearing potential should be conducted at Screening and at the EOS Visit.
11. A urine pregnancy test for women of childbearing potential will be used to confirm patients are not pregnant before study drug administration on each visit day or more frequently if required by country-specific legislation. A urine pregnancy test will be performed locally. If a urine pregnancy test result is positive, a confirmatory serum pregnancy test will be performed at the central laboratory.
12. Clinical laboratory (clinical chemistry, hematology, and urinalysis [urine microscopy]) test samples will be analyzed at the central laboratory. Additional clinical laboratory test samples will be collected if a patient experiences delayed hypersensitivity after 24 hours of study drug administration to determine serum sickness. CRP samples for PD

assessments should be drawn at the same time as the clinical laboratory blood samples.

13. ESR samples will be analyzed at the local laboratory using kits supplied centrally.
14. A chest x-ray (both posterior-anterior and lateral views) is not required at Screening if a chest x-ray from within the 42 days prior to the first administration of the study drug (Day 0) is available.
15. The IGRA will be performed at the central laboratory.
16. Vital signs (including blood pressure, heart and respiratory rates, and body temperature) and weight will be measured after 5 minutes of rest (sitting). In addition, measurement of height will be documented once at Screening.
17. All scheduled 12-lead ECGs must be performed locally after the patient has rested quietly for at least 5 minutes in the supine position. Regardless of the 12-lead ECG result, further cardiological evaluation can be done by the investigator's discretion.
18. Sampling and handling for calprotectin testing will be conducted only at the qualified or feasible sites.
19. Colonoscopy will be repeated in patients who have any confirmed mucosal abnormalities from previous assessment. Colonoscopy will be evaluated centrally by independent reviewer blinded to treatment allocation for reporting purposes, and evaluated at local level to confirm eligibility and for treatment practice. For colonoscopy after Screening, assessment window of -14 days is allowed.
20. Colonoscopy will be performed in all patients at Screening. However, colonoscopy at Screening would not be required if there is documented colonoscopy report of no colonic involvement within 3 years or endoscopic evidence of inflammation consistent with Crohn's disease within 3 months prior to the first administration of the study drug (Day 0).
21. Patients will complete CDAI diary at least 7 consecutive days immediately prior to CDAI assessment date, except when CDAI assessment is performed at the same date of colonoscopy procedure. If patient is planned to have bowel preparation for colonoscopy procedure, patient should not complete CDAI diary during the day before and up to the next day of colonoscopy procedure.
22. To determine eligibility, the components of the CDAI must be completed within 7 days prior to the first administration of the study drug (Day 0) and CDAI score will be calculated at Day 0.
23. If colonoscopy has been performed, it can replace flexible proctosigmoidoscopy for evaluation of endoscopic subscore. Endoscopic subscore by flexible proctosigmoidoscopy (or colonoscopy) will be evaluated centrally by independent reviewer blinded to treatment allocation for reporting purposes, and evaluated at local level to confirm eligibility or loss of response for treatment practice. Flexible proctosigmoidoscopy for endoscopic subscore assessment after Screening, assessment window of -14 days is allowed.
24. Patients will complete MSS diary at least 3 consecutive days immediately prior to assessment date, except when MSS assessment is performed at the same date of flexible proctosigmoidoscopy (or colonoscopy) procedure. If patient is planned to have bowel preparation for flexible proctosigmoidoscopy (or colonoscopy) procedure, patient should not complete MSS diary during the day before and up to the next day of procedure.
25. To determine eligibility, total Mayo score will be calculated at Day 0 using endoscopic subscore during Screening period and other 3 components completed within 3 days prior to the first administration of the study drug (Day 0).
26. End-of-study assessment will only be performed if the assessment was not done at Week 54, or in patient with discontinuation before Week 54.
27. All patients will assess local site pain using 100 mm Visual Analogue Scale (VAS) immediately (not exceeding 1 hour) after the end of administration of study drug.
28. All patients will assess overall satisfaction of CT-P13 IV or CT-P13 SC by using 100 mm VAS immediately (not exceeding 1 hour) after the end of administration of study drug.
29. Serum samples for immunogenicity testing will be drawn at the same time as the clinical laboratory tests before dosing, where applicable. Additional serum samples for immunogenicity testing may be collected if a patient experiences any delayed hypersensitivity after 24hours of study drug administration to determine serum sickness. Analysis will be performed at the central laboratory.
30. Additional vital signs including blood pressure, heart and respiratory rates, and body temperature (prior to the beginning of the study treatment administration and 1 hour (±10 minutes) after the end of the study drug administration) to monitor for possible hypersensitivity reactions. In addition, hypersensitivity will be monitored by routine continuous clinical monitoring, including patient-reported signs and symptoms. In case of hypersensitivity, emergency equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy, oxygen, and artificial ventilation must be available and any types of ECG can be performed. In addition, delayed hypersensitivity will be monitored after 24 hours of study drug administration, including serum sickness-like reaction (myalgia with fever or rash, arthralgia, lymphadenopathy, skin eruption or edema).
31. Additional serum samples for complement (C3, C4) and total hemolytic complement will be assessed if delayed hypersensitivity occurs after 24 hours of study drug administration

to determine serum sickness. Analysis will be performed at the central laboratory.

32. If the investigator deems hospitalization necessary for the blood sample collection, patients should remain in the hospital until blood samples for pharmacokinetic analysis have been collected. If the investigator deems hospitalization unnecessary and sampling can be adequately obtained without hospitalization, the patient does not have to remain hospitalized. Blood samples for pharmacokinetic analysis will be obtained at following time point;

Visit (Day)	Arm 1	Arm 2			
		Group A	Group B	Group C	Group D
Week 22 (Day 154)	• Pre-dose* • After EOI (+15 min) • 1 hr (±15 min) after EOI • 8 hr (±15 min) after SOI • 24 hr (±15 min) after SOI • 48±2 hr after SOI • 168±6 hr after SOI	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection	• Pre-dose**	• Pre-dose**	• Pre-dose**
Week 24 (Day 168)	• 14 days (±12 hr) after SOI at Week 22	• Pre-dose**	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection	• N/A	• N/A
Week 26 (Day 182)	• 28±1 days after SOI at Week 22	• N/A	• Pre-dose**	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection	• N/A

Visit (Day)	Arm 1	Arm 2			
		Group A	Group B	Group C	Group D
Week 28 (Day 196)	• 42±1 days after SOI at Week 22	• N/A	• N/A	• Pre-dose**	• Pre-dose** • 24±2 hr after injection • 48±2 hr after injection • 72±2 hr after injection • 96±4 hr after injection • 120±4 hr after injection • 144±4 hr after injection • 168±6 hr after injection • 216±4 hr after injection • 264±4 hr after injection
Week 30 (Day 210)	• Pre-dose*	• Pre-dose**	• Pre-dose**	• Pre-dose**	• Pre-dose**

EOI, End of the infusion; hr, hours; min; minutes; N/A, not applicable; SOI, Start of the infusion.

*prior to the beginning of study treatment administration on dosing day (or 56 days after previous dosing day only if patient has not received study treatment on each relevant dosing day)

**prior to the beginning of study treatment administration on dosing day (or 14 days after previous dosing day only if patient has not received study treatment on each relevant dosing day)

Note: If a patient in Arm 2 is not able to attend any of the sampling visits, it should be discussed with the Sponsor in advance.

33. CRP samples should be drawn at the same time as the clinical laboratory blood samples.
34. Blood samples of patients who sign a separate informed consent form will be collected.
35. Blood samples and consumption time of foods or drinks containing protein will be collected.
36. Use of all prior and concomitant medications for the treatment of Crohn's disease or Ulcerative colitis, from the diagnosis of disease until the last assessment date or EOS Visit, will be recorded in the patient's eCRF. Use of all concomitant medications for other purposes, from within 30 days prior to the first administration of the study drug (Day 0) patient enrolment until the last assessment date or EOS Visit, will be recorded. All concomitant medications will also be recorded when any serious adverse drug reactions occur after the EOS Visit.
37. Throughout the study, patients will be monitored for the clinical signs and symptoms of TB, and interferon-γ release assay or chest x-ray can be performed at the investigator's discretion based on the judgment on the signs and symptoms of TB monitoring. The investigator will confirm the absence of active TB prior to the subsequent dose administration.
38. Adverse events will be assessed from the date the ICF is signed until the last assessment date or EOS Visit. Where AEs are ongoing at the EOS Visit, the patient should be followed up for a further 30 days regardless of the relationship to study drug. The related AEs will be followed until resolution or improvement to baseline, relationship reassessed as unrelated, confirmed by the investigator that no further improvement could be expected, no more collection of clinical or safety data, or final database closure. Serious adverse drug reactions occurring up to 8 weeks after last dose of study drug will be reported and followed up until 8 weeks after last dose of study drug. In addition, if it is ongoing until 8 weeks after last dose of study drug, it should be followed up for a further 30 days. Adverse events of special interest (i.e. administration-related reaction, injection site reaction, delayed hypersensitivity, infection and malignancy) should be closely monitored

Appendix 2: Table of CTCAE Terms and Grades

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
Anemia	Hemoglobin	Low	<LLN - 10.0 g/dL; <LLN – 6.2 mmol/L <LLN - 100 g/L	<10.0 - 8.0 g/dL; <6.2 – 4.9 mmol/L <100 - 80g/L	<8.0 g/dL; <4.9 mmol/L <80 g/L;	-
Alanine aminotransferase increased	Alanine Aminotransferase (ALT)	High	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Alkaline phosphatase increased	Alkaline phosphatase	High	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Aspartate aminotransferase increased	Aspartate Aminotransferase (AST)	High	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Blood bilirubin increased	Total Bilirubin	High	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN
Cholesterol high	Total Cholesterol	High	>ULN - 300 mg/dL; >ULN - 7.75 mmol/L	>300 - 400 mg/dL; >7.75 - 10.34 mmol/L	>400 - 500 mg/dL; >10.34 - 12.92 mmol/L	>500 mg/dL; >12.92 mmol/L
CPK increased	Creatine Phosphokinase (CPK)	High	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
Creatinine increased	Creatinine	High	>1 - 1.5 x baseline; >ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 baseline; >3.0 - 6.0 x ULN	>6.0 x ULN
GGT increased	Gamma Glutamyl Transferase	High	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Hemoglobin increased	Hemoglobin	High	>0 - 2 gm/dL above ULN or above baseline if baseline is above ULN	>2 - 4 gm/dL above ULN or above baseline if baseline is above ULN	>4 gm/dL above ULN or above baseline if baseline is above ULN	-
Hyperkalemia	Potassium	High	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L	>6.0 - 7.0 mmol/L	>7.0 mmol/L
Hypernatremia	Sodium	High	>ULN - 150 mmol/L	>150 - 155 mmol/L	>155 - 160 mmol/L;	>160 mmol/L
Hypertriglyceridemia	Triglyceride	High	150 - 300 mg/dL; 1.71 - 3.42mmol/L	>300 - 500 mg/dL; >3.42 - 5.7 mmol/L	>500 - 1000 mg/dL; >5.7 - 11.4 mmol/L	>1000 mg/dL; >11.4 mmol/L;
Hypoalbuminemia	Albumin	Low	<LLN - 3 g/dL; <LLN - 30 g/L	<3 - 2 g/dL; <30 - 20 g/L	<2 g/dL; <20 g/L	-
Hypokalemia	Potassium		<LLN - 3.0 mmol/L	<LLN - 3.0 mmol/L #	<3.0 - 2.5 mmol/L	<2.5 mmol/L

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
		Low				
Hyponatremia	Sodium	Low	<LLN - 130 mmol/L	-	<130 - 120 mmol/L	<120 mmol/L
Lymphocyte count decreased	Lymphocytes	Low	<LLN - 800/mm^3; <LLN - 0.8 x $10e^9$/L	<800 - 500/mm^3; <0.8 - 0.5 x $10e^9$ /L	<500 - 200/mm^3; <0.5 - 0.2 x $10e^9$ /L	<200/mm^3; <0.2 x $10e^9$ /L
Lymphocyte count increased	Lymphocytes	High	-	>4000/mm^3 - 20,000/mm^3	>20,000/mm^3	-
Neutrophil count decreased	Total Neutrophils	Low	<LLN - 1500/mm^3; <LLN - 1.5 x $10e^9$ /L	<1500 - 1000/mm^3; <1.5 - 1.0 x $10e^9$ /L	<1000 - 500/mm^3; <1.0 - 0.5 x $10e^9$ /L	<500/mm^3; <0.5 x $10e^9$ /L
Platelet count decreased	Platelet count	Low	<LLN - 75,000/mm^3; <LLN - 75.0 x $10e^9$ /L	<75,000 - 50,000/mm^3; <75.0 - 50.0 x $10e^9$ /L	<50,000 - 25,000/mm^3; <50.0 - 25.0 x $10e^9$ /L	<25,000/mm^3; <25.0 x $10e^9$ /L
White blood cell decreased	White Blood Cells	Low	<LLN - 3000/mm^3; <LLN - 3.0 x $10e^9$ /L	<3000 - 2000/mm^3; <3.0 - 2.0 x $10e^9$ /L	<2000 - 1000/mm3; <2.0 - 1.0 x $10e^9$ /L	<1000/mm^3; <1.0 x $10e^9$ /L

Note: The LLN and ULN values will be the normal ranges as provided by the central laboratory. # indicates that this grade will not be used because this grade shares the same criteria due to exclusion of clinical input.