Statistical Analysis Plan

Study Title: A Randomized, Double-blind, Placebo-controlled, Phase 2a Study to Evaluate the Efficacy and Safety of BBT-401-1S in Patients with Active Ulcerative Colitis

Sponsor: Bridge Biotherapeutics, Inc.
C's Tower #303
58, Pangyo-ro 255 beon-gil, Bundang-gu
Seongnam-si, Gyeonggi-do, Republic of Korea

US Representative: KCRN Research, LLC.
20251 Century Boulevard Suite 325
Germantown, MD 20874

Protocol Number: BBT401-UC-US02

Project Code: BBT401P2A

Version: 2.1 Final

Date: 22 Jul 2020

Statistical Analysis Plan

Study Title: A Randomized, Double-blind, Placebo-controlled, Phase 2a Study to Evaluate the Efficacy and Safety of BBT-401-1S in Patients with Active Ulcerative Colitis

Sponsor: Bridge Biotherapeutics, Inc.
C's Tower #303
58, Pangyo-ro 255 beon-gil, Bundang-gu
Seongnam-si, Gyeonggi-do, Republic of Korea

US Representative: KCRN Research, LLC.
20251 Century Boulevard Suite 325
Germantown, MD 20874

Protocol Number: BBT401-UC-US02

Project Code: BBT401P2A

Version: 2.1 Final

Date: 22 Jul 2020

SIGNATURE PAGE

Reviewed and Approved by:

Michelle Secic
Statistician, KCRN Research
31 Jul 2020
Date (DD MMM YYYY)

Hugh Lee
Project Manager, KCRN Research
31 Jul 2020
Date (DD MMM YYYY)

Christine Lee
Data Manager, KCRN Research
31 Jul 2020
Date (DD MMM YYYY)

Sponsor Review and Approval:

Jeong-Min Chun
Project Manager, Bridge Biotherapeutics
31Jul2020
Date (DD MMM YYYY)

Jeong-Hyun Ryou
Medical Director, Bridge Biotherapeutics
31Jul2020
Date (DD MMM YYYY)

TABLE OF CONTENTS

Glossary and Abbreviations

AE	Adverse Event
ALT	Alanine Transaminase
API	Active Pharmaceutical Ingredient
AST	Aspartate Transaminase
BLQ	Below the Lower level of Quantification
CFR	Code of Federal Regulations
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CRP	C-Reactive Protein
DP	Drug Product
ECG	Electrocardiogram
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HBsAg	Hepatitis B Surface Antigen
HIV	Human Immunodeficiency Virus
HRQoL	Health-related Quality of Life
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
IND	Investigational New Drug Application
ICF	Informed Consent Form
IRB	Institutional Review Board
ITT	Intent-To-Treat
MAD	Multiple Ascending Dose
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-To-Treat
PD	Pharmacodynamics
PI	Principal Investigator
PK	Pharmacokinetics
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SFU	Safety Follow-Up
SIBDQ	Short Inflammatory Bowel Disease Questionnaire
SMC	Safety Monitoring Committee
SOC	System Organ Class
SOP	Standard Operating Procedure
TEAE	Treatment-Emergent Adverse Event
UC	Ulcerative Colitis
UCEIS	Ulcerative Colitis Endoscopic Index of Severity
ULN	Upper Limit of Normal

1 REVISION HISTORY

SAP Version 1.0 was created and approved prior to any unblinding to the study team.

SAP Version 2.0 was planned to update a statistician of KCRN Research and Section 6 List of Tables and Figures. TFL shells were created for the 1st cohort and attached.

2 STUDY OBJECTIVES AND ENDPOINTS

2.1 Study Objectives

2.1.1 Primary Objective

The primary objective is to assess the efficacy and safety of multiple oral doses of BBT-401-1S in patients with active UC.

2.1.2 Secondary Objectives

The secondary objectives are to assess the plasma and tissue concentration of multiple oral doses of BBT-401-1S in patients with active UC and to evaluate the effects of BBT-401-1S on biomarkers.

2.2 Study Endpoints

2.2.1 Primary Endpoints

- Change from baseline in Total Mayo Score at Week 8

2.2.2 Secondary Endpoints

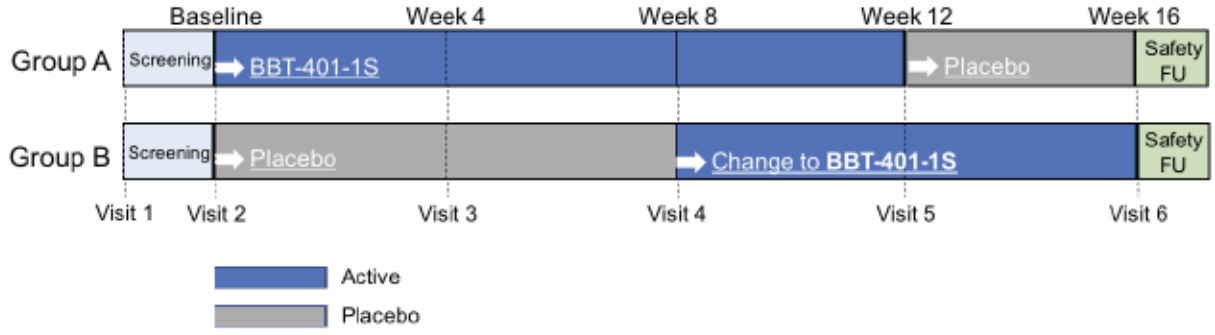
- Change from Baseline in Partial Mayo Score at Week 8
- Change from Baseline in Histologic Assessment of Endoscopic Biopsy at Week 8
- Change from Baseline in Ulcerative Colitis Endoscopic Index of Severity (UCEIS) Score at Week 8
- Change from Baseline in Short Inflammatory Bowel Disease Questionnaire (SIBDQ) at Week 8
- Number and Severity of Treatment Emergent Adverse Events (TEAEs) up to Week 8
- Change from Baseline in Concentration of Biomarkers (C-reactive protein [CRP], fecal calprotectin, and fecal lactoferrin) at Week 8
- Plasma and Tissue Concentration of BBT-401-1S in Patients with Active UC

3 STUDY DESIGN

3.1 Summary of Study Design

This randomized, placebo-controlled, dose-escalation, multicenter, Phase 2 study consists of three cohorts with 16-week treatment period per cohort that will be conducted sequentially. The first cohort will receive 400 mg of BBT-401-1S (starting dose). Efficacy, safety, and PK data of the first cohort will be used to select the dose of the subsequent cohort. For the 1st or 2nd cohort, if the 12th patient (75%) completes Visit 4 (Week 8), unblinding of 12 patients will be performed within 2 weeks after Visit 4 (Week 8) and the unblinding information will be only provided to the Sponsor for the analysis to determine the dose of the next cohort. A dose level may be repeated or added based on the results of the previous cohort(s).

Patients will receive a daily oral dose of BBT 401-1S or placebo for the 16 weeks. While patients who are assigned to Active Group will receive BBT-401-1S for the first 12 weeks and then placebo for the last 4 weeks, patients who are assigned to Placebo Group will receive placebo for the first 8 weeks and then BBT-401-1S for last 8 weeks.



The schedule of assessments is illustrated in Table 1.

Table 1. Schedule of Assessments

	Screening	Treatment Period						SFU
Visit Number	V1	V2	V3	V4	V5	V6	ET	
Visit Period	Up to W-4	Baseline	W4	W8	W12	W16	N/A	W2 from LD
Visit Window	N/A	Within 28 days from V1	±3 days	±3 days	±3 days	±3 days	N/A	+ 7 days from LD
Informed Consent	X							
Demographic Information	X							
Medical/medication History	X	X						
Inclusion/exclusion Criteria	X	X						
Vital Signs	X	X	X	X	X	X	X	X
Physical Examination	X	X[a]	X	X	X	X	X	
12-lead ECG	X	X[1]	X	X	X	X	X	
Clinical Lab Tests and Serum Biomarker[2]	X	X[a]	X	X	X	X	X	X
Endoscopy (biopsy)	X			X			X[3]	
Randomization		X						
Mayo Score	X	X	X	X	X	X	X	
Ulcerative Colitis Endoscopic Index of Severity	X			X			X[c]	
Short Inflammatory Bowel Disease Questionnaire		X	X	X	X	X	X	
Fecal Biomarker[4]		X	X	X	X	X	X	
Plasma Pharmacokinetics[5]		X	X	X				
Tissue Concentration[6]	X			X			X[c]	
Drug Dispensing (with subject diary)		X	X	X	X			
Drug Return and Compliance			X	X	X	X	X	
AE and Concomitant Medication		X	X	X	X	X[g]	X[g]	X

AE = adverse event; ECG = electrocardiogram; SFU = Safety Follow-Up; V = Visit; W = Week; ET = Early Termination; LD = Last Dose

1 Waived if the screening visit is conducted within 10 days prior to Visit 2 (Baseline).
2 Serum chemistry, hematology, coagulation test, HIV and hepatitis screens, serum hCG (women with childbearing potential only), and serum CRP (not measured at SFU).
3 Only if early termination occurs before Visit 4 (W8).
4 Fecal calprotectin and fecal lactoferrin. A collection container will be dispensed to patients on the previous visit.
5 Visit 2 (Baseline) and Visit 3 (W4): pre-dose and 3 and 6 hours post-dose; Visit 4 (W8): pre-dose only.
6 During the endoscopy (flexible proctosigmoidoscopy/colonoscopy) for biopsy.
9 Reviewing any changes in smoking habits of subject during the study period.

3.2 Determination of Sample Size

As this is an initial dose-escalation study, it is appropriately based on only a limited number of patients in each dose cohort. The size of the study is not based on any statistical power calculations and no formal sample size calculation has been done. Based on the experience from the previous studies and the use of a sequential dose-escalation design for this study, a total of 48 patients (16 patients per dose cohort) is considered appropriate for the study.

3.3 Treatments

Patients will receive a daily oral dose of BBT 401-1S or placebo for the 16 weeks. While patients who are assigned to Active Group will receive BBT-401-1S for the first 12 weeks and then placebo for the last 4 weeks, patients who are assigned to Placebo Group will receive placebo for the first 8 weeks and then BBT-401-1S for last 8 weeks.

3.4 Randomization and Blinding

A total of 16 subjects in each of the 3 dosing cohorts will be randomized to either active or placebo group in a 3:1 ratio (12 active and 4 placebo) using the electronic data capture (EDC) system in which the randomization code is integrated.

The randomization code will be generated by an unblinded statistician who is not involved with the study. The Sponsor, investigators, patients, and CRO and other relevant personnel involved with the conduct of the study, with the exception of clinical supply staff and the unblinded statistician, will be blinded to the identity of study medication.

For the 1st or 2nd cohort, if the 12th patient (75%) completes Visit 4 (Week 8), the CRO data management (DM) team confirm all clinical data of the 12 patients have no issue and then obtain the written consent from the Sponsor to breaking the code. Per the request of the CRO DM team, the randomization codes of the 12 patients will be opened via the unblinded statistician and notified to the Sponsor for the analysis to determine the next dose. After confirming all clinical data of remaining 4 patients for the 1st or 2nd cohort, the randomization codes will be subsequently opened to the sponsor through the same procedures stated above.

After the last patient of last cohort completes the SFU, the CRO DM team confirms the whole clinical database has no issue and then requests the database lock to the Sponsor. Per the Sponsor's approval on the database lock, the randomization code of all patients will be opened via the unblinded statistician and notified to the CRO for the statistical analysis.

Breaking of the randomization code without sponsor's permission is expressly forbidden except in the event of a medical emergency where the identity of the study medication must be known in order to properly treat the patient. In the event of a medical emergency, it is requested that the investigator make every effort to contact the study monitor or designee prior to breaking the code.

If the blind is broken due to the medical emergency, the subject must be early terminated; a written explanation must be prepared immediately.

4 STATISTICAL METHODS

4.1 General Considerations

This document describes the statistical analyses planned prior to final treatment assignment unblinding of the aggregate database. Any change to the data analysis methods described in the protocol will require an amendment ONLY if it changes a principal feature of the protocol. Any other change to the data analysis methods described in the protocol and the justification for making the change will be described in the clinical study report (CSR). Additional exploratory or ad-hoc analyses of the data will be conducted as deemed appropriate.

All tests of treatment effects will be conducted at a two-sided alpha level of 0.05 unless otherwise stated, and all confidence intervals (CI's) will be given at a two-sided 95% level, unless otherwise stated. Statistical analysis will be performed using SAS software (SAS, Version 9.1.2 or higher).

The following general terms will be used globally in the SAP:

- Unless otherwise specified, the statistical analyses will be reported using summary tables and data listings.
- Continuous variables will be summarized with n, mean, standard deviation, median, minimum, and maximum.
- Categorical variables will be summarized by counts and by percentages of subjects in corresponding categories.
- All summary tables will be presented by treatment and/or cohort.
- Individual subject data obtained from the case report form (CRFs) and any derived data will be presented by subject in data listings. Data listings will be sorted by subject, and visit date and time, if applicable.

4.2 Adjustments for Covariates

There will be no adjustment for covariates.

4.3 Analysis Sets

4.3.1 Modified Intent-to-Treat

A modified intent-to-treat (mITT) set will consist of all randomized patients who have received at least 1 dose of study medication and have at least 1 post-baseline efficacy measurement. The mITT set will be the primary set used for efficacy analyses.

4.3.2 Per-Protocol

The per-protocol set will consist of all subjects in the mITT who do not have pre-defined major protocol deviations that may affect the primary efficacy endpoint and have completed the study until Visit 4 (Week 8) .

4.3.3 Safety

The safety set will consist of all subjects who have received at least 1 dose of investigational product. The safety set will be the primary analysis dataset used for safety analyses.

4.3.4 Pharmacokinetics (PK)

The PK set will consist of all subjects who have received at least 1 dose of investigational product and there is at least 1 PK sampling. The PK set will be the primary analysis dataset used for PK analyses.

4.4 Baseline and Postbaseline Definition

Unless otherwise specified, the baseline value is defined as the last value obtained before the date and time of the first dose of study drug. Post-baseline values are defined as value obtained after the first dose of study drug. Change from baseline is defined as a post-baseline value minus the baseline value.

4.5 Handling of Dropouts or Missing Data

No adjustments for missing data and no imputation methods are planned for this study.

4.6 Treatment Group Comparability

4.6.1 Patient Disposition

Subject disposition information will be summarized for all subjects. Summaries will include: the number of subjects in each analysis set, the number of subjects completed the study, and the number of subjects discontinued study and its reason. All subjects randomized in the study will be included in the summary table. Patient allocation by investigator or site will be summarized. Patient allocation by investigator or site will also be listed as well. All subjects randomized to placebo from each cohort will be pooled in Placebo group and summarized as a placebo group.

4.6.2 Protocol Deviations

Summary and listings of subjects with significant protocol deviations or violations will be provided. The following list of significant protocol violations will be determined from the clinical database and from the study clinical/medical group:

- Lack of informed consent or late informed consent
- Violations of inclusion/exclusion criteria
- Significant violations of prohibited concomitant medication usage as determined by the clinical/medical group
- Other significant protocol violations as determined by the clinical/medical group

4.6.3 Patient Characteristics

The following patient characteristics at baseline will be summarized by treatment group for all mITT patients:

- Demographic (age, gender, ethnic origin, height, weight, BMI)
- Medical history and Pre-existing condition

Medical history and pre-existing conditions will be summarized by preferred term (PT) within system organ class (SOC). Medical history is defined as illness(es) that ended prior to the signing of informed consent. Pre-existing conditions and AEs at baseline are those AEs occurring during the baseline/screening visits that are Visits 1 and 2.

4.6.4 Prior and Concomitant Therapy

Verbatim terms on eCRFs will be mapped to Anatomical Therapeutic Chemical (ATC) class and Generic Drug Names using the World Health Organization (WHO) Drug Dictionary Enhanced (WHODDE) B2 format, March 1, 2015 release.

Prior medications are defined as medications started to be taken prior to the first administration of the study drug. Concomitant medications are defined as medications started on or after the day of the first administration of the study drug during the study.

Prior and concomitant medications will be tabulated for the mITT set by WHODDE ATC level 2 classifications, preferred term, and treatment. If a subject reports the same preferred term multiple times, then the frequency of that preferred term will only be incremented by one. As with the preferred term, if a subject reports multiple medications within the same ATC level 2 classification, then the frequency of that ATC level 2 classification will only be incremented by one. Percentages will be calculated using the total number of subjects in the safety analysis set. Each summary will be ordered by descending order of incidence of preferred term within each ATC class. Prior and concomitant medications will be included in a data listing.

4.7 Efficacy Analyses

Unless otherwise specified, all efficacy analyses will be based on the mITT and subjects will be analyzed according to their randomized treatment. However, additional

sensitivity/supplementary analyses will be conducted using the PP analysis set for all efficacy endpoints.

4.7.1 Primary Efficacy Analysis

Descriptive statistics will be presented including mean, standard deviation (SD), median, max, and min by treatment and cohort group for the change from baseline to Week 8 in Total Mayo score. Also, to better assess the differences between each dose and the placebo for the change from baseline to Week 8 in Total Mayo score, a mixed model repeated measures (MMRM) analysis will be performed. The MMRM model will include treatment (whether 1st dose, 2nd dose, or 3rd dose vs. Placebo) and the baseline score as fixed effects, and center as a random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix will be used for estimation in the MMRM analysis. If the fit of the model with the unstructured covariance structure does not converge, the following covariance structures will be tried in order until convergence is reached: Toeplitz with heterogeneity, autoregressive with heterogeneity, Toeplitz, and autoregressive. Each dose will be compared with placebo—model-based point estimates for the treatment effects and 95% confidence intervals (CIs) will be calculated.

4.7.2 Secondary Efficacy Analyses

The secondary efficacy analyses will be based on the mITT set on the following endpoints:

- Change from Baseline to Week 8 in Partial Mayo Score
- Change from Baseline to Week 8 in Histologic Assessment of Endoscopic Biopsy
- Change from Baseline to Week 8 in UCEIS Score
- Change from Baseline to Week 8 in SIBDQ

For each secondary efficacy endpoint described above, descriptive statistics will be presented by treatment and cohort group including mean, SD, median, max, and min. Similar to the primary efficacy analysis, mixed model repeated measures (MMRM) analyses will be performed for various secondary efficacy endpoints as noted above.

4.8 Safety Analyses

The safety and tolerability of treatment will be assessed by summarizing the following:

- AEs
- Treatment-emergent adverse events (TEAEs)
  - By PT
  - By SOC
  - By maximum severity
  - By considered to be related to investigational product by investigator
- Serious Adverse Events (SAEs)
- AE leading to discontinuation
- Vital signs and weight
- Laboratory measurements

- Electrocardiograms (ECGs)

All safety analyses will be based on the safety analysis set. AE rates will be summarized by treatment group and overall, and will be broken down by severity, seriousness and relation to study drug. Physical examinations, vital signs, ECG and standard laboratory results will be summarized with means, standard deviations, medians and ranges for continuous variables and with counts and percentages for categorical variables. Statistical tests are not planned for safety.

4.8.1 Adverse Events

An AE is defined as any untoward medical occurrence in a subject who is administered a medicinal product and that does not necessarily have a causal relationship to the treatment. All AEs will be included in the data listings. Verbatim terms on case report forms will be mapped to preferred terms and system organ classes (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA) (version 19.1).

A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug. TEAE summary will be displayed by cohort and treatment. Unless otherwise specified, summaries that are displayed by SOC and preferred terms will be ordered alphabetically by SOC, and within each SOC, preferred terms will also be ordered alphabetically. Summaries of the following types will be presented:

- Subject incidence of TEAEs by MedDRA SOC and preferred term.
- Subject incidence of TEAEs by MedDRA SOC, preferred term, and severity. Severity will be recorded as deemed by investigator. At each level of subject summarization, a subject is classified according to the highest severity if the subject reported one or more events.
- Subject incidence of study drug related TEAEs by MedDRA SOC and preferred term.
- Subject incidence of TEAEs by descending incidence of preferred terms.
- Subject incidence of serious TEAEs by MedDRA SOC and preferred term, if applicable.
- Subject incidence of TEAE leading to early termination by MedDRA SOC and preferred term, if applicable.

For each subject and for each adverse event, the duration of the event will be calculated as:

Duration of AE = AE stop date - AE start date + 1

The duration of AEs will be displayed in the data listing.

4.8.2 Serious Adverse Events

A serious adverse event (SAE) is any AE or suspected adverse reaction that in the view of either the investigator or Sponsor, results in any of the following outcomes:

- Death
- A life-threatening AE: it is defined as an AE or suspected adverse reaction that in the view of the investigator or Sponsor, its occurrence places the patient or subject at immediate

risk of death. It does not include an AE or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

- Inpatient hospitalization or prolongation of existing hospitalization.
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life function.
- A congenital anomaly/birth defect.
- Important medical events that may not result in death, life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of outcomes listed in the above definition.

Life threatening:
An adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Hospitalization:
Any adverse event leading to hospitalization or prolongation of hospitalization will be considered as 'serious', UNLESS at least one of the following exceptions is met:

- the admission results in a hospital stay of less than 24 hours OR
- the admission is pre-planned (i.e., elective or scheduled surgery arranged prior to the start of the study)

However, it should be noted that invasive treatment during any hospitalization may fulfill the criteria of 'medically important' and as such may be reportable as a SAE dependent on clinical judgment.

Disability means a substantial disruption of a person's ability to conduct normal life functions.

Important medical event:
As guidance for determination of important medical events see the 'WHO Adverse Reaction Terminology – Critical Terms List'. These terms either see or might be indicative of a serious disease state. Such reported events warrant special attention because of their possible association with a serious disease state and may lead to more decisive action than reports on other terms.

4.8.3 Clinical Laboratory Evaluation

Abnormal laboratory findings without clinical significance (based on the investigator's judgment) should not be recorded as adverse events; however, laboratory value changes requiring therapy or adjustment in prior therapy are considered as adverse events.
Adverse events will be reviewed continuously throughout the study.

Laboratory results (hematology, serum chemistry and urinalysis) will be presented in data listing. Abnormal values will be flagged as high or low relative to the local lab normal ranges, where applicable. Values that are deemed as abnormal, clinically significant will also be flagged.

Laboratory results will be summarized using descriptive statistics at baseline and post-dose. Changes from baseline will also be summarized. Only non-missing assessments at baseline and post-dose will be analyzed.

Any clinically significant lab abnormalities will be determined by the Principal Investigator and will be reported in the AE table summaries.

4.8.4 Vital Signs

Vital signs will be summarized using descriptive statistics at baseline and at each post-dose time point. Changes from baseline will also be summarized.

4.8.5 Electrocardiogram

ECG parameters (numeric) will be summarized using descriptive statistics at baseline and at each post-dose time point. Changes from baseline will also be summarized.

4.9 PD Analyses

No formal statistical analysis of PD endpoints (i.e. biomarkers) will be performed. PD data from each assay will be listed.

4.10 PK Analyses

4.10.1 Measurements and Collection Schedule

Plasma:
Blood samples for the determination of plasma BBT-401-1S concentrations will be collected at Visit 2 (Week 0) and Visit 3 (Week 4) at predose and at 3 and 6 hours postdose and Visit 4 (Week 8) at predose.

Tissue:
Tissue samples will be collected from descending colon and rectum during endoscopy procedures of Visit 1 (Screening) and Visit 4 (Week 8).

4.10.2 Bioanalytical Methods

Plasma and tissue concentrations of BBT-401-1S will be determined using high performance liquid chromatography-tandem mass spectrometry (HPLC MS/MS) methods. Plasma method was validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Celerion,

Lincoln, Nebraska. The analytical range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for plasma BBT-401-1S concentration is expected to be 1.00 – 1000 ng/mL. Tissue method will be qualified to detect the tissue concentrations of BBT-401-1S at 1.00 – 1000 ng/g range using biopsy samples of approximately 20 mg.

4.10.3 Plasma/Tissue Concentrations

Plasma and tissue BBT-401-1S concentrations as determined at the collection times and analyzed per the bioanalytical methods described in Section 4.10.1 and Section 4.10.2 will be summarized.

4.10.4 Parameter Calculation

Due to limited sampling time points to calculate PK parameters, there will be no PK parameter calculation such as T_{max}, C_{max}, AUC for plasma or tissue concentration.

4.10.5 Data Summarization and Presentation

Plasma and tissue concentrations of BBT-401-1S will be listed by time point and visit schedule (e.g., W0, W4 etc), respectively, for all subjects who receive a daily oral dose of BBT 401-1S. Plasma and tissue concentrations of BBT-401-1S will be presented with the same level of precision as received from the bioanalytical laboratory. All BLQ and missing values will be presented as "BLQ" or ".", respectively, in the concentration listings and footnoted accordingly.

BBT-401-1S plasma and tissue concentrations will be listed and summarized by treatment (dose group) for all subjects, if appropriate. Summary statistics, including sample size (n), arithmetic mean (mean), standard deviation (SD), coefficient of variation (CV%), minimum, median, and maximum will be calculated for BBT-401-1S plasma and tissue concentrations, if appropriate. The level of precision for each concentration statistic will be presented as follows: minimum/maximum, mean, median and SD in same precision as in bioanalytical data, n will be presented as an integer and CV% will be presented to 1 decimal place.

4.10.6 Statistical Analysis of Plasma/Tissue Concentrations

No formal statistical analysis will be performed for plasma/tissue concentrations.

4.11 Interim Analysis and Data Monitoring

There will be no formally planned interim analyses. However, in order to select the 2nd cohort dose, if 12th patient (75%) of 1st cohort completes Visit 4 (Week 8), unblinding of 12 patients will be performed within 2 weeks after Visit 4. The unblinding information will be only provided to the Sponsor for the analysis determining the dose of next cohort. Likewise, after 12th patient of 2nd Cohort completes Visit 4, similar unblinding of 2nd cohort will occur in order to select the dose for

the 3rd cohort. The analysis of the unblinded data of 1st and/or 2nd cohort will be analyzed by a third-party independent statistician. Including the study statistician, most of the key personnel of the study who directly participate in conducting of the study should be remained blinded.

4.12 Handling of Dropouts or Missing Data

No imputations will be made for missing values.

4.13 Subgroup Analysis

There are no planned subgroup efficacy analyses.

4.14 Multiple Comparison/Multiplicity

No adjustments for multiplicity or multiple testing will be made.

5 CHANGES TO PROTOCOL-SPECIFIED ANALYSES

No changes to protocol-specified analyses are planned.

6 LIST OF TABLES AND FIGURES

List of Tables

ICH Heading	Table Number	Table Description
14.1		**DEMOGRAPHIC**
	14.1.1	Summary of Patient Disposition (All Patients)
	14.1.2	Summary of Demographic and Baseline Characteristics (mITT Analysis set)
	14.1.3	Summary of Medical History (mITT Analysis set)
	14.1.4	Summary of Prior Medications (mITT Analysis set)
	14.1.5	Summary of Concomitant Medications (mITT Analysis set)
14.2		**EFFICACY**
14.2.1		**Primary Efficacy**
	14.2.1.1	Summary of Change of Total Mayo Score from Baseline to Week 8 (mITT Analysis set)
	14.2.1.2	Summary of Change of Total Mayo Score from Baseline to Week 8 (PP Analysis set)
14.2.2		**Secondary Efficacy**
	14.2.2.1.1	Summary of Change of Partial Mayo Score from Baseline to Week 8 (mITT Analysis set)
	14.2.2.1.2	Summary of Change of Partial Mayo Score from Baseline to Week 8 (PP Analysis set)

List of Data Listings

ICH Heading	Listing Number	Listing Description
16.2		**PATIENT DATA LISTINGS**
16.2.1		**Discontinued Patients**
	16.2.1.1	Patient Disposition
16.2.2		**Protocol Deviations**
	16.2.2.1	Inclusion/Exclusion Criteria Findings – Deviations
16.2.3		**Patients Excluded from the Efficacy Summary**
16.2.4		**Demographics and Baseline Characteristics**
	16.2.4.1	Demographics and Baseline Characteristics
	16.2.4.2	Medical History
	16.2.4.3	Prior and Concomitant Medications
16.2.5		**Compliance and/or Drug Administration Data**
	16.2.5.1.1	Study Drug Administration and Log
16.2.6		**Individual Efficacy Response Data**
	16.2.6.1	Total Mayo Score
	16.2.6.2	Partial Mayo Score
	16.2.6.3	Histologic Assessment of Endoscopic Biopsy
	16.2.6.4	Ulcerative Colitis Endoscopic Index of Severity
	16.2.6.5	Short Inflammatory Bowel Disease Questionnaire
	16.2.6.6	Biomarkers
16.2.7		**Adverse Events Listings**
	16.2.7.1	Adverse Events
	16.2.7.2	Serious Adverse Events
	16.2.7.3	Adverse Events Leading to Permanent Withdrawal of Study Treatment or Discontinuation from the Study
	16.2.7.4	Adverse Events Leading to Death
16.2.8		**Individual Lab Measures**
	16.2.8.1	Hematology
	16.2.8.2	Chemistry
	16.2.8.3	Vital Signs
	16.2.8.4	Electrocardiogram
	16.2.8.5	Physical Examination
16.2.9		**Pharmacokinetics**
	16.2.9.1	Individual Plasma Concentration Data
	16.2.9.2	Individual Tissue Concentration Data
16.2.10		**Other Miscellaneous Data**
	16.2.10.1	Randomization
	16.2.10.2	IP
	16.2.10.3	Investigator Signature

TABLES, FIGURES, AND LISTINGS SHELLS

Study Title: A Randomized, Double-blind, Placebo-controlled, Phase 2a Study to Evaluate the Efficacy and Safety of BBT-401-1S in Patients with Active Ulcerative Colitis

Sponsor: Bridge Biotherapeutics, Inc.

C's Tower #303
58, Pangyo-ro 255 beon-gil, Bundang-gu
Seongnam-si, Gyeonggi-do, Republic of Korea

US Representative: KCRN Research, LLC.

20251 Century Boulevard Suite 325
Germantown, MD 20874

Protocol Number: BBT401-UC-US02

Project Code: BBT401P2A

Version: 2.1 Final

Date: 22 Jul 2020

Tables and Listings to Be Generated

ICH Heading	Table Number	Table Description
14.1		**DEMOGRAPHIC**
	14.1.1	Summary of Patient Disposition (All Patients)
	14.1.2	Summary of Demographic and Baseline Characteristics (mITT Analysis set)
	14.1.3	Summary of Medical History (mITT Analysis set)
	14.1.4	Summary of Prior Medications (mITT Analysis set)
	14.1.5	Summary of Concomitant Medications (mITT Analysis set)
14.2		**EFFICACY**
14.2.1		**Primary Efficacy**
	14.2.1.1	Summary of Change of Total Mayo Score from Baseline to Week 8 (mITT Analysis set)
	14.2.1.2	Summary of Change of Total Mayo Score from Baseline to Week 8 (PP Analysis set)
14.2.2		**Secondary Efficacy**
	14.2.2.1.1	Summary of Change of Partial Mayo Score from Baseline to Week 8 (mITT Analysis set)
	14.2.2.1.2	Summary of Change of Partial Mayo Score from Baseline to Week 8 (PP Analysis set)
	14.2.2.2.1	Summary of Change of Histologic Assessment of Endoscopic Biopsy from Baseline to Week 8 (mITT Analysis set)
	14.2.2.2.2	Summary of Change of Histologic Assessment of Endoscopic Biopsy from Baseline to Week 8 (PP Analysis set)
	14.2.2.3.1	Summary of Change of Ulcerative Colitis Endoscopic Index of Severity (UCEIS) Score from Baseline to Week 8 (mITT Analysis set)
	14.2.2.3.2	Summary of Change of Ulcerative Colitis Endoscopic Index of Severity (UCEIS) Score from Baseline to Week 8 (PP Analysis set)
	14.2.2.4.1	Summary of Change of Short Inflammatory Bowel Disease Questionnaire (SIBDQ) from Baseline to Week 8 (mITT Analysis set)
	14.2.2.4.2	Summary of Change of Short Inflammatory Bowel Disease Questionnaire (SIBDQ) from Baseline to Week 8 (PP Analysis set)
14.2.3		**Exploratory Efficacy**
	14.2.3.1	Summary of Change of Concentration of Biomarkers from Baseline to Week 8 (mITT Analysis set)
	14.2.3.2	Summary of Change of Concentration of Biomarkers from Baseline to Week 8 (PP Analysis set)
14.3		**SAFETY**
14.3.1		**Display of Adverse Events**
	14.3.1.1	Overall Summary of Treatment-Emergent Adverse Events up to Week 8 (Safety Analysis set)
	14.3.1.2	Summary of Treatment-Emergent Adverse Events up to Week 8 by System Organ Class and Preferred Term (Safety Analysis set)
	14.3.1.3	Summary of Treatment-Emergent Adverse Events up to Week 8 by System Organ Class, Preferred Term, and Severity (Safety Analysis set)

ICH Heading	Listing Number	Listing Description
16.2		**PATIENT DATA LISTINGS**
16.2.1		**Discontinued Patients**
	16.2.1.1	Patient Disposition
16.2.2		**Protocol Deviations**
	16.2.2.1	Inclusion/Exclusion Criteria Findings – Deviations
16.2.3		**Patients Excluded from the Efficacy Summary**
16.2.4		**Demographics and Baseline Characteristics**
	16.2.4.1	Demographics and Baseline Characteristics
	16.2.4.2	Medical History
	16.2.4.3	Prior and Concomitant Medications
16.2.5		**Compliance and/or Drug Administration Data**
	16.2.5.1.1	Study Drug Administration and Log
16.2.6		**Individual Efficacy Response Data**
	16.2.6.1	Total Mayo Score
	16.2.6.2	Partial Mayo Score
	16.2.6.3	Histologic Assessment of Endoscopic Biopsy
	16.2.6.4	Ulcerative Colitis Endoscopic Index of Severity
	16.2.6.5	Short Inflammatory Bowel Disease Questionnaire
	16.2.6.6	Biomarkers
16.2.7		**Adverse Events Listings**
	16.2.7.1	Adverse Events
	16.2.7.2	Serious Adverse Events
	16.2.7.3	Adverse Events Leading to Permanent Withdrawal of Study Treatment or Discontinuation from the Study
	16.2.7.4	Adverse Events Leading to Death
16.2.8		**Individual Lab Measures**
	16.2.8.1	Hematology
	16.2.8.2	Chemistry
	16.2.8.3	Vital Signs
	16.2.8.4	Electrocardiogram
	16.2.8.5	Physical Examination
16.2.9		**Pharmacokinetics**
	16.2.9.1	Individual Plasma Concentration Data
	16.2.9.2	Individual Tissue Concentration Data
16.2.10		**Other Miscellaneous Data**
	16.2.10.1	Randomization
	16.2.10.2	IP
	16.2.10.3	Investigator Signature

Table 14.1.1
Summary of Patient Disposition
All Patients

	Placebo n %	BBT-401-1S n %	All Subjects n %
Screened	xx	xx	XX
Randomized	XX	XX	XX
Site Number 01	XX (XX.X)	XX (XX.X)	XX (XX.X)
Site Number 02	XX (XX.X)	XX (XX.X)	XX (XX.X)
…	XX (XX.X)	XX (XX.X)	XX (XX.X)
Modified Intent-to-Treat (mITT)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Per-Protocol	XX (XX.X)	XX (XX.X)	XX (XX.X)
Safety	XX (XX.X)	XX (XX.X)	XX (XX.X)
Pharmacokinetics (PK)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dosed [1]	XX (XX.X)	XX (XX.X)	XX (XX.X)
Completed Initial 8-Week Treatment			
Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)
No	XX (XX.X)	XX (XX.X)	XX (XX.X)
If No, Reason for Early Termination of Initial 8-Week Treatment			
Subject's request or request of legal representative	XX (XX.X)	XX (XX.X)	XX (XX.X)
Per Principal Investigator, continuation would be detrimental to subject's well-being	XX (XX.X)	XX (XX.X)	XX (XX.X)
Sponsor request	XX (XX.X)	XX (XX.X)	XX (XX.X)
Withdrawal of consent	XX (XX.X)	XX (XX.X)	XX (XX.X)
Significant Protocol Deviation	XX (XX.X)	XX (XX.X)	XX (XX.X)
Non-compliance with the protocol or study drug	XX (XX.X)	XX (XX.X)	XX (XX.X)
Clinical Progression	XX (XX.X)	XX (XX.X)	XX (XX.X)
Adverse Event	XX (XX.X)	XX (XX.X)	XX (XX.X)
Lost to follow-up	XX (XX.X)	XX (XX.X)	XX (XX.X)
Death	XX (XX.X)	XX (XX.X)	XX (XX.X)
Other	XX (XX.X)	XX (XX.X)	XX (XX.X)
Completed Visit 6 (Week 16)			
Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)
No	XX (XX.X)	XX (XX.X)	XX (XX.X)

[1] 'Dosed' is defined as all randomized patients who received at least one dose of study medication.

Note: Percentages are based on the number of subjects randomized.

Bridge Biotherapeutics, Inc.
PROTOCOL: BBT401-UC-US02
Draft Version (to mention only if not final)

Confidential
<DMC or Final Analysis>

Table 14.1.2
Summary of Demographic and Baseline Characteristics
mITT Analysis set

	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Age (Years)			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Gender, n (%)			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Male	XX (XX.X)	XX (XX.X)	XX (XX.X)
Female	XX (XX.X)	XX (XX.X)	XX (XX.X)
Ethnicity, n (%)			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Hispanic	XX (XX.X)	XX (XX.X)	XX (XX.X)
Non-Hispanic	XX (XX.X)	XX (XX.X)	XX (XX.X)
Race, n (%)			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Black or African American	XX (XX.X)	XX (XX.X)	XX (XX.X)
Native American Indian or Native Alaskan	XX (XX.X)	XX (XX.X)	XX (XX.X)
Native Hawaiian or Other Pacific Islander	XX (XX.X)	XX (XX.X)	XX (XX.X)
Asian	XX (XX.X)	XX (XX.X)	XX (XX.X)
White	XX (XX.X)	XX (XX.X)	XX (XX.X)
Other	XX (XX.X)	XX (XX.X)	XX (XX.X)
Height (cm)			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Weight (kg)			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X

Table 14.1.3
Summary of Medical History
mITT Analysis set

System Organ Class Preferred Term	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any reported Medical History and Pre-existing Conditions [1]	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 3	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
….			

[1] Medical history is defined as illness(es) that ended prior to the signing of informed consent. Pre-existing conditions and AEs at baseline are those AEs occurring during the baseline/screening visits that are Visits 1 and 2.
Note 1: Medical history and Pre-existing Conditions were coded using the MedDRA version 23.0.
Note 2: Subjects with one or more records within a level of MedDRA are counted only once in that level.

Table 14.1.4
Summary of Prior Medications
mITT Analysis set

Therapeutic Subclassification [ATC2] Preferred Medication Name	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any Prior Medication [1]	XX (XX.X)	XX (XX.X)	XX (XX.X)
Therapeutic Subclass 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
Therapeutic Subclass 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
Therapeutic Subclass 3	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
….			

[1] Prior medications are defined as medications started to be taken prior to the first administration of the study drug.
Note 1: WHO Drug Dictionary Enhanced (WHODDE) B3 format (01MAR2020 release) was used to code medication names.
Note 2: If a subject reports same prefer term multiple times, the frequency of that preferred term will only be incremented by one. Same as preferred term, if a subject reports multiple medications within the same ATC level 2 classification, then the frequency of that ATC level 2 classification will only be incremented by one.

Table 14.1.5
Summary of Concomitant Medications
mITT Analysis set

Therapeutic Subclassification [ATC2] Preferred Medication Name	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any Concomitant Medication [1]	XX (XX.X)	XX (XX.X)	XX (XX.X)
Therapeutic Subclass 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
Therapeutic Subclass 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
Therapeutic Subclass 3	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Medication Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)

….

[1] Concomitant medications are defined as medications started on or after the day of the first administration of the study drug during the study.
Note 1: WHO Drug Dictionary Enhanced (WHODDE) B3 format (01MAR2020 release) was used to code medication names.
Note 2: If a subject reports same prefer term multiple times, the frequency of that preferred term will only be incremented by one. Same as preferred term, if a subject reports multiple medications within the same ATC level 2 classification, then the frequency of that ATC level 2 classification will only be incremented by one.

Table 14.2.1.1.1
Summary of Change of Total Mayo Score from Baseline to Week 8
mITT Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Table 14.2.1.1.2
Summary of Change of Total Mayo Score from Baseline to Week 8
PP Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Table 14.2.2.1.1
Summary of Change of Partial Mayo Score from Baseline to Week 8
mITT Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Table 14.2.2.1.2
Summary of Change of Partial Mayo Score from Baseline to Week 8
PP Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Table 14.2.2.2.1
Summary of Change of Histologic Assessment of Endoscopic Biopsy from Baseline to Week 8
mITT Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Specimen Region of Origin :XXXXXXXX		
Laboratory Test: XXXXXXXXX		
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Programming Note: Start a new page for each laboratory test.

Table 14.2.2.2.2
Summary of Change of Histologic Assessment of Endoscopic Biopsy from Baseline to Week 8
PP Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Specimen Region of Origin :XXXXXXXX		
Laboratory Test: XXXXXXXXX		
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Programming Note: Start a new page for each laboratory test.

Table 14.2.2.3.1
Summary of Change of Ulcerative Colitis Endoscopic Index of Severity (UCEIS) Score from Baseline to Week 8
mITT Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Table 14.2.2.3.2
Summary of Change of Ulcerative Colitis Endoscopic Index of Severity (UCEIS) Score from Baseline to Week 8
PP Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Table 14.2.2.4.1
Summary of Change of Short Inflammatory Bowel Disease Questionnaire (SIBDQ) from Baseline to Week 8
mITT Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
SIBDQ Question #: xxxxxx		
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Programming Note: Start a new page for each question.

Table 14.2.2.4.2
Summary of Change of Short Inflammatory Bowel Disease Questionnaire (SIBDQ) from Baseline to Week 8
PP Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
SIBDQ Question #: xxxxxx		
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Programming Note: Start a new page for each question.

Table 14.2.3.1
Summary of Change of Concentration of Biomarkers from Baseline to Week 8
mITT Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Biomarker #1		
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)
Biomarker #2		
…		

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Programming Note: Start a new page for each biomarker.

Table 14.2.3.2
Summary of Change of Concentration of Biomarkers from Baseline to Week 8
PP Analysis set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Biomarker #1		
Baseline		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Change from Baseline to Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
LS Mean (SE)	XX.X (XX.XX)	XX.X (XX.XX)
P-Value, Active vs Placebo		0.XXX
LS Mean Difference (SE)		XX.X (XX.XX)
95% CI for Differences		(XX.X, XX.X)
Biomarker #2		
…		

Note: Least Squares means, p-values were from MMRM model with treatment and baseline score as fixed effects, and center as random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix is used for estimation in the MMRM analysis.

Programming Note: Start a new page for each biomarker. This should include C-reactive protein [CRP], fecal calprotectin, and fecal lactoferrin.

Table 14.3.1.1
Overall Summary of Treatment-Emergent Adverse Events up to Week 8
Safety Analysis Set

	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Number of Patients with at Least 1 TEAE up to Week 8	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Patients with at Least 1 Serious TEAE up to Week 8	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Patients with at Least 1 TEAE up to Week 8 Leading to Study Discontinuation	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Patients with TEAEs by Worst Severity			
Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Patients with TEAEs by Worst Relationship			
Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
Possibly Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
Probably Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
Related	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note 1: A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug.
Note 2: If a patient experienced more than 1 event in a category, then that patient is counted only once in that category
Note 3: MedDRA Dictionary (Version 23.0) was used for coding adverse events.
Output ID: <Unique Output id i.e. t-enrol> Draft-DDMMMYYY HH:MM:SS DATE OF DATABASE EXTRACTION: DDMMMYYYY
<Path/Program Name> Page 1 of X

Table 14.3.1.2
Summary of Treatment-Emergent Adverse Events up to Week 8 by System Organ Class and Preferred Term
Safety Analysis set

System Organ Class Preferred Term	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any TEAEs up to Week 8	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 3	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note 1: A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug.
Note 2: Subjects with one or more adverse events within a level of MedDRA term is counted only once in that level.
Note 3: System Organ Class (SOC) terms are sorted using alphabetical order. Within each SOC, preferred terms are sorted using alphabetical order.
Note 4: MedDRA Dictionary (Version 23.0) was used for coding adverse events.

Table 14.3.1.3
Summary of Treatment-Emergent Adverse Events up to Week 8 by System Organ Class, Preferred Term, and Severity
Safety Analysis Set

System Organ Class Preferred Term	Severity	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any TEAEs up to Week 8				
	Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 1				
	Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1				
	Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2				
	Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note 1: A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug.
Note 2: Subjects with one or more adverse events within a level of MedDRA term is counted only once in that level using the most severe incident.
Note 3: System Organ Class (SOC) terms are sorted using alphabetical order. Within each SOC, preferred terms are sorted using alphabetical order.
Note 4: MedDRA Dictionary (Version 23.0) was used for coding adverse events.

Table 14.3.1.4
Summary of Treatment-Emergent Adverse Events up to Week 8 by System Organ Class, Preferred Term, and Relationship to Study Drug
Safety Analysis Set

System Organ Class Preferred Term	Relationship	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any TEAEs up to Week 8				
	Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Overall	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 1				
	Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Overall	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1				
	Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Overall	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2				
	Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Overall	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note 1: A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug.
Note 2: Subjects with one or more adverse events within a level of MedDRA term is counted only once in that level using the most related incident.
Note 3: System Organ Class (SOC) terms are sorted using alphabetical order. Within each SOC, preferred terms are sorted using alphabetical order.
Note 4: MedDRA Dictionary (Version 23.0) was used for coding adverse events.

Table 14.3.1.5
Summary of Treatment-Emergent Serious Adverse Events up to Week 8 by System Organ Class and Preferred Term
Safety Analysis set

System Organ Class Preferred Term	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any Serious TEAEs up to Week 8	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 3	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note 1: A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug.
Note 2: Subjects with one or more adverse events within a level of MedDRA term is counted only once in that level.
Note 3: System Organ Class (SOC) terms are sorted using alphabetical order. Within each SOC, preferred terms are sorted using alphabetical order.
Note 4: MedDRA Dictionary (Version 23.0) was used for coding adverse events.

Table 14.3.1.6
Summary of Treatment-Emergent Adverse Events up to Week 8 Leading to Study Discontinuation by System Organ Class and Preferred Term
Safety Analysis set

System Organ Class Preferred Term	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Subjects with Any TEAEs up to Week 8 Leading to Study Discontinuation	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)
…			
System Organ Class 3	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note 1: A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug.
Note 2: Subjects with one or more adverse events within a level of MedDRA term is counted only once in that level.
Note 3: System Organ Class (SOC) terms are sorted using alphabetical order. Within each SOC, preferred terms are sorted using alphabetical order.
Note 4: MedDRA Dictionary (Version 23.0) was used for coding adverse events.

Table 14.3.2.1
Summary of Values and Changes of Hematology Parameters by Visit
Safety Analysis Set

Laboratory Group: XXXXXXXXX
Laboratory Test: XXXXXXXXX (Unit)

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Visit XX			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Visit XX - Change from Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
….			

Table 14.3.2.2
Summary of Values and Changes of Chemistry Parameters by Visit
Safety Analysis Set

Laboratory Group: XXXXXXXXX
Laboratory Test: XXXXXXXXX (Unit)

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Visit XX			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Visit XX - Change from Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
….			

Table 14.3.3.1
Summary of Vital Sign Parameters by Visit
Safety Analysis Set

Vital Signs Parameter: XXXXXXXXX (Unit)

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Visit XX			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Visit XX - Change from Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
….			
….			

Table 14.3.3.2
Summary of Electrocardiogram Parameters by Visit
Safety Analysis Set

Electrocardiogram Parameter: XXXXXXXXX (Unit)

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Visit XX			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Visit XX - Change from Baseline			
n (missing)	XX (XX)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)	XX.X(X.XX)
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
….			

Table 14.3.3.3
Summary of Physical Examination by Visit
Safety Analysis Set

Body Category: **xxxxxxxxxx**

Study Visit Body Category Status [1]	Placebo (N=XX)	BBT-401-1S (N=XX)	Overall (N=XX)
Baseline	XX (XX.X)	XX (XX.X)	XX (XX.X)
NCS	XX (XX.X)	XX (XX.X)	XX (XX.X)
CS			
Visit XX	XX (XX.X)	XX (XX.X)	XX (XX.X)
NCS	XX (XX.X)	XX (XX.X)	XX (XX.X)
CS			

….

Table 14.4.1.1
Plasma BBT-401-1S Concentrations (ng/mL) Following the Administration of BBT-401-1S or Placebo
PK Analysis Set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Baseline Pre-dose		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)
Coefficient of Variance (CV %)	XX.X	XX.X
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Baseline 3H Post dose		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)
Coefficient of Variance (CV %)	XX.X	XX.X
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Baseline 6H Post dose		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)
Coefficient of Variance (CV %)	XX.X	XX.X
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX

….

Table 14.4.2.1
Tissue BBT-401-1S Concentrations (ng/g) Following the Administration of BBT-401-1S or Placebo
PK Analysis Set

Study Visit	Placebo (N=XX)	BBT-401-1S (N=XX)
Colon Screening		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)
Coefficient of Variance (CV %)	XX.X	XX.X
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Rectum Screening		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)
Coefficient of Variance (CV %)	XX.X	XX.X
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Colon Week 8		
n (missing)	XX (XX)	XX (XX)
Mean (SD)	XX.X(X.XX)	XX.X(X.XX)
Coefficient of Variance (CV %)	XX.X	XX.X
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX

….

Listing 16.2.1.1
Patient Disposition

Subject ID	Randomized (Yes/No)	Cohort	Treatment	Dosed (Yes/No)	Analysis Population	Did the subject complete initial 8-week treatment? (Yes/No)	If No, what was the reason for early termination of initial 8-week treatment?	Did the subject complete Visit 6 (Week 16)? (Yes/No)
xx-yyy	Yes/No	xxx	xxx	Yes/No	mITT/PP/SAF/PK	Yes/No	xxxx	Yes/No

Listing 16.2.2.1
Inclusion/Exclusion Criteria Findings – Deviations

Subject ID	Criteria Type	Criteria Details	Value
xx-yyy	Inclusion/Exclusion	xxxxxxxxxxxxxxxxxxxxxxxxxx	Yes/No

Programming note:
1. Only include subjects who answer No to any inclusion Criteria or answer Yes to any Exclusion Criteria.
2. For each subject, only display inclusion Criteria with answer = No and Exclusion Criteria with answer = Yes.

Listing 16.2.4.1
Demographics and Baseline Characteristics

Subject ID	Cohort	Treatment	Age (Years)	Gender	Ethnicity	Race
xx-yyy	xxx	xxx	xx	M/F	xxxx	xxxx

Listing 16.2.4.2
Medical History

Subject ID	Cohort/ Treatment	Body System/ Category	Description of Medical History	Date of Onset	Date of Resolution
xx-yyy	xxx/xxxx	xxxxxx	xxxxxxxxxxxxx	DD-MMM-YYYY	DD-MMM-YYYY/Ongoing

Subject ID	Cohort/ Treatment	Does the subject have assessed Mayo Score previously? (Yes/No)	Mayo Score Type/Score/Date of Assessed	Does the subject have experienced any hospitalizations due to UC? (Yes/No)	Date of Hospitalization/ Treatments Received	Does the subject currently have any extraintestinal manifestations of UC? (Yes/No)	Sites	Extraintestinal Manifestations
xx-yyy	xxx/xxxx	Yes/No	xxxxx/xxx/DD-MMM-YY	Yes/No	DD-MMM-YY/xxxxxx	Yes/No	xxx/xxx/xxx	xxxxx

Subject ID	Cohort/ Treatment	History of Alcoholism and Drug Abuse? (yes/No)	If 'Yes, describe year	Smoking Status	If 'Current smoker', how many cigarettes smoked in a day	Weekly Alcohol Consumption	Has the subject taken any medications and/or UC therapies within 3 months prior to V1 (Screening)? (Yes/No)
xx-yyy	xxx/xxxx	Yes/No	xxxxxxx		xx	Type/amount/unit	Yes/No

Listing 16.2.4.3
Prior and Concomitant Medications

Subject ID	Cohort/ Treatment	Medication Name	Start Date	Stop Date	Dose	Dose Form	Unit	Route	Frequency	Indication
xx-yyy	xxx/xxx	xx	DD-MMM-YYYY	DD-MMM-YYYY/Ongoing	xxxx	xxxx	xxxx	xxxx	xxxx	xxxx

Listing 16.2.5.1
Study Drug Administration and Log

Subject ID	Cohort /Treatment	Visit	Date of IP Returned	Number of bottles returned	Number of days that IP dosing should be taken during previous treatment period (from last visit date to last dosing date)	Number of days that IP dosing was missed during previous treatment period	Patient Compliance (%)
xx-yyy	**xxx/xxx**	**xxxx**	DD-MMM-YYYY/Not Done	**xxx**	**xxxx**	**xxxx**	**xxxx**

Listing 16.2.6.1
Total Mayo Score

Subject ID	Cohort /Treatment	Visit	Date of Local Read Score Assessed	Local Read Score	Central Read Score	Evidence of UC extending proximal to the rectum?	Total Mayo Score
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done	xxxxx	xxxxx	xxxxx	xxxxx

Listing 16.2.6.2
Partial Mayo Score

Subject ID	Cohort /Treatment	Visit	Date of Assessment	Stool Frequency	Rectal Bleeding	Physician's Global Assessment	Partial Mayo Score
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done	xxxxxx	xxxxxx	xxxxxx	xxxx

Listing 16.2.6.3
Histologic Assessment of Endoscopic Biopsy

Subject ID	Cohort /Treatment	Visit	Date	Specimen Region of Origin	Laboratory Test	Results
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY		xxxx	xxxxx

Programming note:
For results, present both numerical and character values if available.

Listing 16.2.6.4
Ulcerative Colitis Endoscopic Index of Severity

Subject ID	Cohort /Treatment	Visit	Date of Assessment	Vascular Pattern	Bleeding	Erosions and Ulcers	Score
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done	xxxxxx	xxxxxx	xxxxxx	xxxx

Listing 16.2.6.5
Short Inflammatory Bowel Disease Questionnaire

Subject ID	Cohort /Treatment	Visit	Date and Time of Assessment	Q1: How often has the feeling of fatigue or being tired and worn out been a problem for you during the past 2 weeks?	Q2: How often during the last 2 weeks have you delayed or canceled a social engagement because of your bowel problem?	Q3: How much difficulty have you had, as a result of your bowel problems, doing leisure or sports activities you would have liked to have done during the past 2 weeks?	Q4: How often during the last 2 weeks have you been troubled by pain in the abdomen?	Q5: How often during the last 2 weeks have you felt depressed or discouraged?
xx-yyy	xxx/xxx	xxxx	xxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx

Subject ID	Cohort /Treatment	Visit	Date and Time of Assessment	Q6: Overall, in the last 2 weeks, how much of a problem have you had with passing large amounts of gas?	Q7: Overall, in the last 2 weeks, how much of a problem have you had maintaining or getting to, the weight you would like to be at?	Q8: How often during the last 2 weeks have you felt relaxed and free of tension?	Q9: How much of the time during the last 2 weeks have you been troubled by a feeling of having to go to the bathroom even though your bowels were empty?	Q10: How much of the time during the last 2 weeks have you felt angry as a result of your bowel problem?
xx-yyy	xxx/xxx	xxxx	xxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx

Programming note:
For each question, present both numerical and character responses if available.

Listing 16.2.6.6
Biomarker

Subject ID	Cohort /Treatment	Visit	Biomarker Parameter	Date of Sample	Results
xx-yyy	xxx/xxx	xxxx	xxxx	DD-MMM-YYYY/Not Done	xxxxx

Programming note: this should include C-reactive protein [CRP], fecal calprotectin, and fecal lactoferrin.

Listing 16.2.7.1
Adverse Events

Subject ID	Cohort /Treatment	AE Term	Description	Severity	Date of Onset/ Resolution	Outcome	Action taken with Study Drug	Relatedness	Is the adverse event serious? (Yes/No)	Seriousness Criteria	Date of Death
xx-yyy	xxx/xxx	xxxx	xxxxxxxx	xxxx	DD-MMM-YYYY/ DD-MMM-YYYY/ Ongoing	xxxxxxx	xxxxxxx	xxxxx	Yes/No	xxxxxx	DD-MMM-YYYY

Listing 16.2.7.2
Serious Adverse Events

Subject ID	Cohort /Treatment	AE Term	Description	Severity	Date of Onset/ Resolution	Outcome	Action taken with Study Drug	Relatedness	Is the adverse event serious? (Yes/No)	Seriousness Criteria	Date of Death
xx-yyy	xxx/xxx	xxxx	xxxxxxxx	xxxx	DD-MMM-YYYY/ DD-MMM-YYYY/ Ongoing	xxxxxxx	xxxxxxx	xxxxx	Yes/No	xxxxxx	DD-MMM-YYYY

Listing 16.2.7.3
Adverse Events Leading to Permanent Withdrawal of Study Treatment or Discontinuation from the Study

Subject ID	Cohort /Treatment	AE Term	Description	Severity	Date of Onset/ Resolution	Outcome	Action taken with Study Drug	Relatedness	Is the adverse event serious? (Yes/No)	Seriousness Criteria	Date of Death
xx-yyy	xxx/xxx	xxxx	xxxxxxxx	xxxx	DD-MMM-YYYY/ DD-MMM-YYYY/ Ongoing	xxxxxxx	xxxxxxx	xxxxx	Yes/No	xxxxxx	DD-MMM-YYYY

Listing 16.2.7.4
Adverse Events Leading to Death

Subject ID	Cohort /Treatment	AE Term	Description	Severity	Date of Onset/ Resolution	Outcome	Action taken with Study Drug	Relatedness	Is the adverse event serious? (Yes/No)	Seriousness Criteria	Date of Death	Primary Cause of Death
xx-yyy	xxx/xxx	xxxx	xxxxxxxx	xxxx	DD-MMM-YYYY/ DD-MMM-YYYY/ Ongoing	xxxxxxx	xxxxxxx	xxxxx	Yes/No	xxxxxx	DD-MMM-YYYY	xxxxx

Listing 16.2.8.1
Hematology

Subject ID	Cohort /Treatment	Visit	Date of Sample	Laboratory Parameter(Unit)	Results	Evaluation (NCS/CS)
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done	xxxx	xxxx	NCS/CS

Listing 16.2.8.2
Chemistry

Subject ID	Cohort /Treatment	Visit	Date of Sample	Laboratory Parameter(Unit)	Results	Evaluation (NCS/CS)
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done	xxxx	xxxx	NCS/CS

Listing 16.2.8.4
Vital Signs

Subject ID	Cohort /Treatment	Visit	Date of Assessment	Parameter (Unit)	Results
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done	xxxx	xxxx

Listing 16.2.8.5
Electrocardiogram

Subject ID	Cohort /Treatment	Visit	Date and Time of ECG	Parameter(Unit)	Results	Overall Interpretation	If 'NCS' or CS', then describe
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/HH:MM/Not Done/Waived per protocol	xxxx	xxxx	xxxxx	xxxxx

Listing 16.2.8.6
Physical Examination

Subject ID	Cohort /Treatment	Visit	Date of Physical Examination	Body Category	Status(NCS/CS)	Abnormal Finding
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done/Waived per protocol	xxxxxxx	NCS/CS	xxxxxxxxxxxxxxx

Listing 16.2.9.1
Individual Plasma Concentration Data

Subject ID	Cohort /Treatment	Visit	Date of Sampling	Time Point	Time of Sampling	Results
xx-yyy	xxx/xxx	xxxx	DD-MMM-YYYY/Not Done	Pre-dose/3H Post dose/6H Post dose	HH:MM/Not Done	xxxx

Listing 16.2.9.2
Individual Tissue Concentration Data

Subject ID	Cohort /Treatment	Visit	Date of Sampling	Results
xx-yyy	xxx/xxx	Colon Screening/Rectum Screening/Colon Week 8 /Rectum Week 8	DD-MMM-YYYY/Not Done	xxxx

Listing 16.2.10.1
Randomization

Subject ID	Which cohort is the subject in?	Is this subject eligible to participate in this study? (Yes/No)	If Yes, Randomization Code
xx-yyy	**xxx**	Yes/No	**xxxx**

Listing 16.2.10.2
IP

Subject ID	Cohort /Treatment	Visit	Dose(mg/day)	IP Code	Date and Time of IP Administration at Site	Date of IP Distributed	Re-distributed IP Codes
xx-yyy	xxx/xxx	xxxx	xxx	xxx	DD-MMM-YYYY/HH:MM/Not Done	DD-MMM-YYYY/Not Done	xxxx/None

Listing 16.2.10.3
Investigator Signature

Subject ID	Cohort /Treatment	Did you (Principal Investigator) review all the study information? (Yes/No)	Name	Date	Type
xx-yyy	xxx/xxx	Yes/No	xxxx	xxxx	xxxx

SIGNATURE PAGE

Reviewed and Approved by:

Michelle Secic
Statistician, KCRN Research
31 Jul 2020
Date (DD MMM YYYY)

Hugh Lee
Project Manager, KCRN Research
31 Jul 2020
Date (DD MMM YYYY)

Christine Lee
Data Manager, KCRN Research
31 Jul 2020
Date (DD MMM YYYY)

Sponsor Review and Approval:

Jeong-Min Chun
Project Manager, Bridge Biotherapeutics
31Jul2020
Date (DD MMM YYYY)

Jeong-Hyun Ryou
Medical Director, Bridge Biotherapeutics
31Jul2020
Date (DD MMM YYYY)

TABLE OF CONTENTS

Glossary and Abbreviations

AE	Adverse Event
ALT	Alanine Transaminase
API	Active Pharmaceutical Ingredient
AST	Aspartate Transaminase
BLQ	Below the Lower level of Quantification
CFR	Code of Federal Regulations
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CRP	C-Reactive Protein
DP	Drug Product
ECG	Electrocardiogram
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HBsAg	Hepatitis B Surface Antigen
HIV	Human Immunodeficiency Virus
HRQoL	Health-related Quality of Life
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
IND	Investigational New Drug Application
ICF	Informed Consent Form
IRB	Institutional Review Board
ITT	Intent-To-Treat
MAD	Multiple Ascending Dose
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-To-Treat
PD	Pharmacodynamics
PI	Principal Investigator
PK	Pharmacokinetics
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SFU	Safety Follow-Up
SIBDQ	Short Inflammatory Bowel Disease Questionnaire
SMC	Safety Monitoring Committee
SOC	System Organ Class
SOP	Standard Operating Procedure
TEAE	Treatment-Emergent Adverse Event
UC	Ulcerative Colitis
UCEIS	Ulcerative Colitis Endoscopic Index of Severity
ULN	Upper Limit of Normal

1 REVISION HISTORY

SAP Version 1.0 was created and approved prior to any unblinding to the study team.

SAP Version 2.0 was planned to update a statistician of KCRN Research and Section 6 List of Tables and Figures. TFL shells were created for the 1st cohort and attached.

2 STUDY OBJECTIVES AND ENDPOINTS

2.1 Study Objectives

2.1.1 Primary Objective

The primary objective is to assess the efficacy and safety of multiple oral doses of BBT-401-1S in patients with active UC.

2.1.2 Secondary Objectives

The secondary objectives are to assess the plasma and tissue concentration of multiple oral doses of BBT-401-1S in patients with active UC and to evaluate the effects of BBT-401-1S on biomarkers.

2.2 Study Endpoints

2.2.1 Primary Endpoints

- Change from baseline in Total Mayo Score at Week 8

2.2.2 Secondary Endpoints

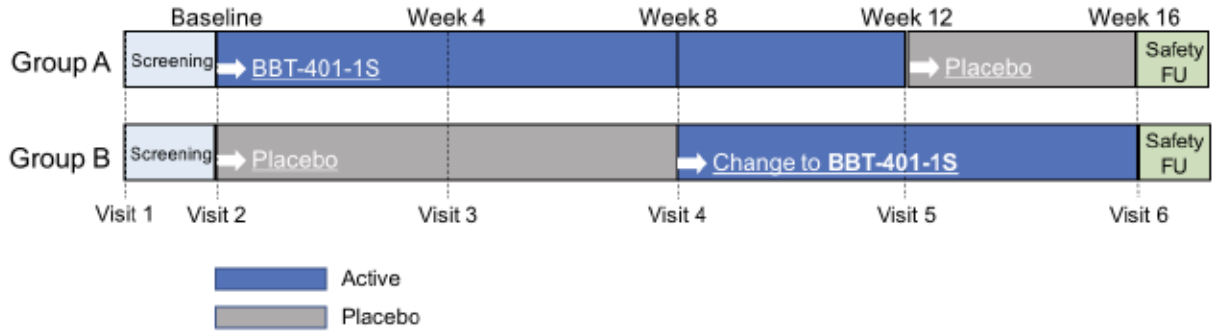
- Change from Baseline in Partial Mayo Score at Week 8
- Change from Baseline in Histologic Assessment of Endoscopic Biopsy at Week 8
- Change from Baseline in Ulcerative Colitis Endoscopic Index of Severity (UCEIS) Score at Week 8
- Change from Baseline in Short Inflammatory Bowel Disease Questionnaire (SIBDQ) at Week 8
- Number and Severity of Treatment Emergent Adverse Events (TEAEs) up to Week 8
- Change from Baseline in Concentration of Biomarkers (C-reactive protein [CRP], fecal calprotectin, and fecal lactoferrin) at Week 8
- Plasma and Tissue Concentration of BBT-401-1S in Patients with Active UC

3 STUDY DESIGN

3.1 Summary of Study Design

This randomized, placebo-controlled, dose-escalation, multicenter, Phase 2 study consists of three cohorts with 16-week treatment period per cohort that will be conducted sequentially. The first cohort will receive 400 mg of BBT-401-1S (starting dose). Efficacy, safety, and PK data of the first cohort will be used to select the dose of the subsequent cohort. For the 1st or 2nd cohort, if the 12th patient (75%) completes Visit 4 (Week 8), unblinding of 12 patients will be performed within 2 weeks after Visit 4 (Week 8) and the unblinding information will be only provided to the Sponsor for the analysis to determine the dose of the next cohort. A dose level may be repeated or added based on the results of the previous cohort(s).

Patients will receive a daily oral dose of BBT 401-1S or placebo for the 16 weeks. While patients who are assigned to Active Group will receive BBT-401-1S for the first 12 weeks and then placebo for the last 4 weeks, patients who are assigned to Placebo Group will receive placebo for the first 8 weeks and then BBT-401-1S for last 8 weeks.



The schedule of assessments is illustrated in Table 1.

Table 1. Schedule of Assessments

	Screening	Treatment Period						SFU
Visit Number	V1	V2	V3	V4	V5	V6	ET	
Visit Period	Up to W-4	Baseline	W4	W8	W12	W16	N/A	W2 from LD
Visit Window	N/A	Within 28 days from V1	±3 days	±3 days	±3 days	±3 days	N/A	+ 7 days from LD
Informed Consent	X							
Demographic Information	X							
Medical/medication History	X	X						
Inclusion/exclusion Criteria	X	X						
Vital Signs	X	X	X	X	X	X	X	X
Physical Examination	X	X[a]	X	X	X	X	X	
12-lead ECG	X	X[1]	X	X	X	X	X	
Clinical Lab Tests and Serum Biomarker[2]	X	X[a]	X	X	X	X	X	X
Endoscopy (biopsy)	X			X			X[3]	
Randomization		X						
Mayo Score	X	X	X	X	X	X	X	
Ulcerative Colitis Endoscopic Index of Severity	X			X			X[c]	
Short Inflammatory Bowel Disease Questionnaire		X	X	X	X	X	X	
Fecal Biomarker[4]		X	X	X	X	X	X	
Plasma Pharmacokinetics[5]		X	X	X				
Tissue Concentration[6]	X			X			X[c]	
Drug Dispensing (with subject diary)		X	X	X	X			
Drug Return and Compliance			X	X	X	X	X	
AE and Concomitant Medication		X	X	X	X	X[g]	X[g]	X

AE = adverse event; ECG = electrocardiogram; SFU = Safety Follow-Up; V = Visit; W = Week; ET = Early Termination; LD = Last Dose

1 Waived if the screening visit is conducted within 10 days prior to Visit 2 (Baseline).
2 Serum chemistry, hematology, coagulation test, HIV and hepatitis screens, serum hCG (women with childbearing potential only), and serum CRP (not measured at SFU).
3 Only if early termination occurs before Visit 4 (W8).
4 Fecal calprotectin and fecal lactoferrin. A collection container will be dispensed to patients on the previous visit.
5 Visit 2 (Baseline) and Visit 3 (W4): pre-dose and 3 and 6 hours post-dose; Visit 4 (W8): pre-dose only.
6 During the endoscopy (flexible proctosigmoidoscopy/colonoscopy) for biopsy.
9 Reviewing any changes in smoking habits of subject during the study period.

3.2 Determination of Sample Size

As this is an initial dose-escalation study, it is appropriately based on only a limited number of patients in each dose cohort. The size of the study is not based on any statistical power calculations and no formal sample size calculation has been done. Based on the experience from the previous studies and the use of a sequential dose-escalation design for this study, a total of 48 patients (16 patients per dose cohort) is considered appropriate for the study.

3.3 Treatments

Patients will receive a daily oral dose of BBT 401-1S or placebo for the 16 weeks. While patients who are assigned to Active Group will receive BBT-401-1S for the first 12 weeks and then placebo for the last 4 weeks, patients who are assigned to Placebo Group will receive placebo for the first 8 weeks and then BBT-401-1S for last 8 weeks.

3.4 Randomization and Blinding

A total of 16 subjects in each of the 3 dosing cohorts will be randomized to either active or placebo group in a 3:1 ratio (12 active and 4 placebo) using the electronic data capture (EDC) system in which the randomization code is integrated.

The randomization code will be generated by an unblinded statistician who is not involved with the study. The Sponsor, investigators, patients, and CRO and other relevant personnel involved with the conduct of the study, with the exception of clinical supply staff and the unblinded statistician, will be blinded to the identity of study medication.

For the 1st or 2nd cohort, if the 12th patient (75%) completes Visit 4 (Week 8), the CRO data management (DM) team confirm all clinical data of the 12 patients have no issue and then obtain the written consent from the Sponsor to breaking the code. Per the request of the CRO DM team, the randomization codes of the 12 patients will be opened via the unblinded statistician and notified to the Sponsor for the analysis to determine the next dose. After confirming all clinical data of remaining 4 patients for the 1st or 2nd cohort, the randomization codes will be subsequently opened to the sponsor through the same procedures stated above.

After the last patient of last cohort completes the SFU, the CRO DM team confirms the whole clinical database has no issue and then requests the database lock to the Sponsor. Per the Sponsor's approval on the database lock, the randomization code of all patients will be opened via the unblinded statistician and notified to the CRO for the statistical analysis.

Breaking of the randomization code without sponsor's permission is expressly forbidden except in the event of a medical emergency where the identity of the study medication must be known in order to properly treat the patient. In the event of a medical emergency, it is requested that the investigator make every effort to contact the study monitor or designee prior to breaking the code.

If the blind is broken due to the medical emergency, the subject must be early terminated; a written explanation must be prepared immediately.

4 STATISTICAL METHODS

4.1 General Considerations

This document describes the statistical analyses planned prior to final treatment assignment unblinding of the aggregate database. Any change to the data analysis methods described in the protocol will require an amendment ONLY if it changes a principal feature of the protocol. Any other change to the data analysis methods described in the protocol and the justification for making the change will be described in the clinical study report (CSR). Additional exploratory or ad-hoc analyses of the data will be conducted as deemed appropriate.

All tests of treatment effects will be conducted at a two-sided alpha level of 0.05 unless otherwise stated, and all confidence intervals (CI's) will be given at a two-sided 95% level, unless otherwise stated. Statistical analysis will be performed using SAS software (SAS, Version 9.1.2 or higher).

The following general terms will be used globally in the SAP:

- Unless otherwise specified, the statistical analyses will be reported using summary tables and data listings.
- Continuous variables will be summarized with n, mean, standard deviation, median, minimum, and maximum.
- Categorical variables will be summarized by counts and by percentages of subjects in corresponding categories.
- All summary tables will be presented by treatment and/or cohort.
- Individual subject data obtained from the case report form (CRFs) and any derived data will be presented by subject in data listings. Data listings will be sorted by subject, and visit date and time, if applicable.

4.2 Adjustments for Covariates

There will be no adjustment for covariates.

4.3 Analysis Sets

4.3.1 Modified Intent-to-Treat

A modified intent-to-treat (mITT) set will consist of all randomized patients who have received at least 1 dose of study medication and have at least 1 post-baseline efficacy measurement. The mITT set will be the primary set used for efficacy analyses.

4.3.2 Per-Protocol

The per-protocol set will consist of all subjects in the mITT who do not have pre-defined major protocol deviations that may affect the primary efficacy endpoint and have completed the study until Visit 4 (Week 8) .

4.3.3 Safety

The safety set will consist of all subjects who have received at least 1 dose of investigational product. The safety set will be the primary analysis dataset used for safety analyses.

4.3.4 Pharmacokinetics (PK)

The PK set will consist of all subjects who have received at least 1 dose of investigational product and there is at least 1 PK sampling. The PK set will be the primary analysis dataset used for PK analyses.

4.4 Baseline and Postbaseline Definition

Unless otherwise specified, the baseline value is defined as the last value obtained before the date and time of the first dose of study drug. Post-baseline values are defined as value obtained after the first dose of study drug. Change from baseline is defined as a post-baseline value minus the baseline value.

4.5 Handling of Dropouts or Missing Data

No adjustments for missing data and no imputation methods are planned for this study.

4.6 Treatment Group Comparability

4.6.1 Patient Disposition

Subject disposition information will be summarized for all subjects. Summaries will include: the number of subjects in each analysis set, the number of subjects completed the study, and the number of subjects discontinued study and its reason. All subjects randomized in the study will be included in the summary table. Patient allocation by investigator or site will be summarized. Patient allocation by investigator or site will also be listed as well. All subjects randomized to placebo from each cohort will be pooled in Placebo group and summarized as a placebo group.

4.6.2 Protocol Deviations

Summary and listings of subjects with significant protocol deviations or violations will be provided. The following list of significant protocol violations will be determined from the clinical database and from the study clinical/medical group:

- Lack of informed consent or late informed consent
- Violations of inclusion/exclusion criteria
- Significant violations of prohibited concomitant medication usage as determined by the clinical/medical group
- Other significant protocol violations as determined by the clinical/medical group

4.6.3 Patient Characteristics

The following patient characteristics at baseline will be summarized by treatment group for all mITT patients:

- Demographic (age, gender, ethnic origin, height, weight, BMI)
- Medical history and Pre-existing condition

Medical history and pre-existing conditions will be summarized by preferred term (PT) within system organ class (SOC). Medical history is defined as illness(es) that ended prior to the signing of informed consent. Pre-existing conditions and AEs at baseline are those AEs occurring during the baseline/screening visits that are Visits 1 and 2.

4.6.4 Prior and Concomitant Therapy

Verbatim terms on eCRFs will be mapped to Anatomical Therapeutic Chemical (ATC) class and Generic Drug Names using the World Health Organization (WHO) Drug Dictionary Enhanced (WHODDE) B2 format, March 1, 2015 release.

Prior medications are defined as medications started to be taken prior to the first administration of the study drug. Concomitant medications are defined as medications started on or after the day of the first administration of the study drug during the study.

Prior and concomitant medications will be tabulated for the mITT set by WHODDE ATC level 2 classifications, preferred term, and treatment. If a subject reports the same preferred term multiple times, then the frequency of that preferred term will only be incremented by one. As with the preferred term, if a subject reports multiple medications within the same ATC level 2 classification, then the frequency of that ATC level 2 classification will only be incremented by one. Percentages will be calculated using the total number of subjects in the safety analysis set. Each summary will be ordered by descending order of incidence of preferred term within each ATC class. Prior and concomitant medications will be included in a data listing.

4.7 Efficacy Analyses

Unless otherwise specified, all efficacy analyses will be based on the mITT and subjects will be analyzed according to their randomized treatment. However, additional

sensitivity/supplementary analyses will be conducted using the PP analysis set for all efficacy endpoints.

4.7.1 Primary Efficacy Analysis

Descriptive statistics will be presented including mean, standard deviation (SD), median, max, and min by treatment and cohort group for the change from baseline to Week 8 in Total Mayo score. Also, to better assess the differences between each dose and the placebo for the change from baseline to Week 8 in Total Mayo score, a mixed model repeated measures (MMRM) analysis will be performed. The MMRM model will include treatment (whether 1st dose, 2nd dose, or 3rd dose vs. Placebo) and the baseline score as fixed effects, and center as a random effect. Restricted Maximum Likelihood (REML) with an unstructured variance-covariance matrix will be used for estimation in the MMRM analysis. If the fit of the model with the unstructured covariance structure does not converge, the following covariance structures will be tried in order until convergence is reached: Toeplitz with heterogeneity, autoregressive with heterogeneity, Toeplitz, and autoregressive. Each dose will be compared with placebo—model-based point estimates for the treatment effects and 95% confidence intervals (CIs) will be calculated.

4.7.2 Secondary Efficacy Analyses

The secondary efficacy analyses will be based on the mITT set on the following endpoints:

- Change from Baseline to Week 8 in Partial Mayo Score
- Change from Baseline to Week 8 in Histologic Assessment of Endoscopic Biopsy
- Change from Baseline to Week 8 in UCEIS Score
- Change from Baseline to Week 8 in SIBDQ

For each secondary efficacy endpoint described above, descriptive statistics will be presented by treatment and cohort group including mean, SD, median, max, and min. Similar to the primary efficacy analysis, mixed model repeated measures (MMRM) analyses will be performed for various secondary efficacy endpoints as noted above.

4.8 Safety Analyses

The safety and tolerability of treatment will be assessed by summarizing the following:

- AEs
- Treatment-emergent adverse events (TEAEs)
  - By PT
  - By SOC
  - By maximum severity
  - By considered to be related to investigational product by investigator
- Serious Adverse Events (SAEs)
- AE leading to discontinuation
- Vital signs and weight
- Laboratory measurements

- Electrocardiograms (ECGs)

All safety analyses will be based on the safety analysis set. AE rates will be summarized by treatment group and overall, and will be broken down by severity, seriousness and relation to study drug. Physical examinations, vital signs, ECG and standard laboratory results will be summarized with means, standard deviations, medians and ranges for continuous variables and with counts and percentages for categorical variables. Statistical tests are not planned for safety.

4.8.1 Adverse Events

An AE is defined as any untoward medical occurrence in a subject who is administered a medicinal product and that does not necessarily have a causal relationship to the treatment. All AEs will be included in the data listings. Verbatim terms on case report forms will be mapped to preferred terms and system organ classes (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA) (version 19.1).

A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs or worsens on or after the first dose of study drug. TEAE summary will be displayed by cohort and treatment. Unless otherwise specified, summaries that are displayed by SOC and preferred terms will be ordered alphabetically by SOC, and within each SOC, preferred terms will also be ordered alphabetically. Summaries of the following types will be presented:

- Subject incidence of TEAEs by MedDRA SOC and preferred term.
- Subject incidence of TEAEs by MedDRA SOC, preferred term, and severity. Severity will be recorded as deemed by investigator. At each level of subject summarization, a subject is classified according to the highest severity if the subject reported one or more events.
- Subject incidence of study drug related TEAEs by MedDRA SOC and preferred term.
- Subject incidence of TEAEs by descending incidence of preferred terms.
- Subject incidence of serious TEAEs by MedDRA SOC and preferred term, if applicable.
- Subject incidence of TEAE leading to early termination by MedDRA SOC and preferred term, if applicable.

For each subject and for each adverse event, the duration of the event will be calculated as:

Duration of AE = AE stop date - AE start date + 1

The duration of AEs will be displayed in the data listing.

4.8.2 Serious Adverse Events

A serious adverse event (SAE) is any AE or suspected adverse reaction that in the view of either the investigator or Sponsor, results in any of the following outcomes:

- Death
- A life-threatening AE: it is defined as an AE or suspected adverse reaction that in the view of the investigator or Sponsor, its occurrence places the patient or subject at immediate

risk of death. It does not include an AE or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

- Inpatient hospitalization or prolongation of existing hospitalization.
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life function.
- A congenital anomaly/birth defect.
- Important medical events that may not result in death, life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of outcomes listed in the above definition.

Life threatening:
An adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Hospitalization:
Any adverse event leading to hospitalization or prolongation of hospitalization will be considered as 'serious', UNLESS at least one of the following exceptions is met:

- the admission results in a hospital stay of less than 24 hours OR
- the admission is pre-planned (i.e., elective or scheduled surgery arranged prior to the start of the study)

However, it should be noted that invasive treatment during any hospitalization may fulfill the criteria of 'medically important' and as such may be reportable as a SAE dependent on clinical judgment.

Disability means a substantial disruption of a person's ability to conduct normal life functions.

Important medical event:
As guidance for determination of important medical events see the 'WHO Adverse Reaction Terminology – Critical Terms List'. These terms either see or might be indicative of a serious disease state. Such reported events warrant special attention because of their possible association with a serious disease state and may lead to more decisive action than reports on other terms.

4.8.3 Clinical Laboratory Evaluation

Abnormal laboratory findings without clinical significance (based on the investigator's judgment) should not be recorded as adverse events; however, laboratory value changes requiring therapy or adjustment in prior therapy are considered as adverse events.
Adverse events will be reviewed continuously throughout the study.

Laboratory results (hematology, serum chemistry and urinalysis) will be presented in data listing. Abnormal values will be flagged as high or low relative to the local lab normal ranges, where applicable. Values that are deemed as abnormal, clinically significant will also be flagged.

Laboratory results will be summarized using descriptive statistics at baseline and post-dose. Changes from baseline will also be summarized. Only non-missing assessments at baseline and post-dose will be analyzed.

Any clinically significant lab abnormalities will be determined by the Principal Investigator and will be reported in the AE table summaries.

4.8.4 Vital Signs

Vital signs will be summarized using descriptive statistics at baseline and at each post-dose time point. Changes from baseline will also be summarized.

4.8.5 Electrocardiogram

ECG parameters (numeric) will be summarized using descriptive statistics at baseline and at each post-dose time point. Changes from baseline will also be summarized.

4.9 PD Analyses

No formal statistical analysis of PD endpoints (i.e. biomarkers) will be performed. PD data from each assay will be listed.

4.10 PK Analyses

4.10.1 Measurements and Collection Schedule

Plasma:
Blood samples for the determination of plasma BBT-401-1S concentrations will be collected at Visit 2 (Week 0) and Visit 3 (Week 4) at predose and at 3 and 6 hours postdose and Visit 4 (Week 8) at predose.

Tissue:
Tissue samples will be collected from descending colon and rectum during endoscopy procedures of Visit 1 (Screening) and Visit 4 (Week 8).

4.10.2 Bioanalytical Methods

Plasma and tissue concentrations of BBT-401-1S will be determined using high performance liquid chromatography-tandem mass spectrometry (HPLC MS/MS) methods. Plasma method was validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Celerion,

Lincoln, Nebraska. The analytical range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for plasma BBT-401-1S concentration is expected to be 1.00 – 1000 ng/mL. Tissue method will be qualified to detect the tissue concentrations of BBT-401-1S at 1.00 – 1000 ng/g range using biopsy samples of approximately 20 mg.

4.10.3 Plasma/Tissue Concentrations

Plasma and tissue BBT-401-1S concentrations as determined at the collection times and analyzed per the bioanalytical methods described in Section 4.10.1 and Section 4.10.2 will be summarized.

4.10.4 Parameter Calculation

Due to limited sampling time points to calculate PK parameters, there will be no PK parameter calculation such as T_{max}, C_{max}, AUC for plasma or tissue concentration.

4.10.5 Data Summarization and Presentation

Plasma and tissue concentrations of BBT-401-1S will be listed by time point and visit schedule (e.g., W0, W4 etc), respectively, for all subjects who receive a daily oral dose of BBT 401-1S. Plasma and tissue concentrations of BBT-401-1S will be presented with the same level of precision as received from the bioanalytical laboratory. All BLQ and missing values will be presented as "BLQ" or ".", respectively, in the concentration listings and footnoted accordingly.

BBT-401-1S plasma and tissue concentrations will be listed and summarized by treatment (dose group) for all subjects, if appropriate. Summary statistics, including sample size (n), arithmetic mean (mean), standard deviation (SD), coefficient of variation (CV%), minimum, median, and maximum will be calculated for BBT-401-1S plasma and tissue concentrations, if appropriate. The level of precision for each concentration statistic will be presented as follows: minimum/maximum, mean, median and SD in same precision as in bioanalytical data, n will be presented as an integer and CV% will be presented to 1 decimal place.

4.10.6 Statistical Analysis of Plasma/Tissue Concentrations

No formal statistical analysis will be performed for plasma/tissue concentrations.

4.11 Interim Analysis and Data Monitoring

There will be no formally planned interim analyses. However, in order to select the 2nd cohort dose, if 12th patient (75%) of 1st cohort completes Visit 4 (Week 8), unblinding of 12 patients will be performed within 2 weeks after Visit 4. The unblinding information will be only provided to the Sponsor for the analysis determining the dose of next cohort. Likewise, after 12th patient of 2nd Cohort completes Visit 4, similar unblinding of 2nd cohort will occur in order to select the dose for

the 3rd cohort. The analysis of the unblinded data of 1st and/or 2nd cohort will be analyzed by a third-party independent statistician. Including the study statistician, most of the key personnel of the study who directly participate in conducting of the study should be remained blinded.

4.12 Handling of Dropouts or Missing Data

No imputations will be made for missing values.

4.13 Subgroup Analysis

There are no planned subgroup efficacy analyses.

4.14 Multiple Comparison/Multiplicity

No adjustments for multiplicity or multiple testing will be made.

5 CHANGES TO PROTOCOL-SPECIFIED ANALYSES

No changes to protocol-specified analyses are planned.

6 LIST OF TABLES AND FIGURES

List of Tables

ICH Heading	Table Number	Table Description
14.1		**DEMOGRAPHIC**
	14.1.1	Summary of Patient Disposition (All Patients)
	14.1.2	Summary of Demographic and Baseline Characteristics (mITT Analysis set)
	14.1.3	Summary of Medical History (mITT Analysis set)
	14.1.4	Summary of Prior Medications (mITT Analysis set)
	14.1.5	Summary of Concomitant Medications (mITT Analysis set)
14.2		**EFFICACY**
14.2.1		**Primary Efficacy**
	14.2.1.1	Summary of Change of Total Mayo Score from Baseline to Week 8 (mITT Analysis set)
	14.2.1.2	Summary of Change of Total Mayo Score from Baseline to Week 8 (PP Analysis set)
14.2.2		**Secondary Efficacy**
	14.2.2.1.1	Summary of Change of Partial Mayo Score from Baseline to Week 8 (mITT Analysis set)
	14.2.2.1.2	Summary of Change of Partial Mayo Score from Baseline to Week 8 (PP Analysis set)

List of Data Listings

ICH Heading	Listing Number	Listing Description
16.2		**PATIENT DATA LISTINGS**
16.2.1		**Discontinued Patients**
	16.2.1.1	Patient Disposition
16.2.2		**Protocol Deviations**
	16.2.2.1	Inclusion/Exclusion Criteria Findings – Deviations
16.2.3		**Patients Excluded from the Efficacy Summary**
16.2.4		**Demographics and Baseline Characteristics**
	16.2.4.1	Demographics and Baseline Characteristics
	16.2.4.2	Medical History
	16.2.4.3	Prior and Concomitant Medications
16.2.5		**Compliance and/or Drug Administration Data**
	16.2.5.1.1	Study Drug Administration and Log
16.2.6		**Individual Efficacy Response Data**
	16.2.6.1	Total Mayo Score
	16.2.6.2	Partial Mayo Score
	16.2.6.3	Histologic Assessment of Endoscopic Biopsy
	16.2.6.4	Ulcerative Colitis Endoscopic Index of Severity
	16.2.6.5	Short Inflammatory Bowel Disease Questionnaire
	16.2.6.6	Biomarkers
16.2.7		**Adverse Events Listings**
	16.2.7.1	Adverse Events
	16.2.7.2	Serious Adverse Events
	16.2.7.3	Adverse Events Leading to Permanent Withdrawal of Study Treatment or Discontinuation from the Study
	16.2.7.4	Adverse Events Leading to Death
16.2.8		**Individual Lab Measures**
	16.2.8.1	Hematology
	16.2.8.2	Chemistry
	16.2.8.3	Vital Signs
	16.2.8.4	Electrocardiogram
	16.2.8.5	Physical Examination
16.2.9		**Pharmacokinetics**
	16.2.9.1	Individual Plasma Concentration Data
	16.2.9.2	Individual Tissue Concentration Data
16.2.10		**Other Miscellaneous Data**
	16.2.10.1	Randomization
	16.2.10.2	IP
	16.2.10.3	Investigator Signature