Janssen Research & Development *

Clinical Protocol

A Phase 3 Randomized, Open-label Study to Assess the Efficacy, Safety, and Pharmacokinetics of Golimumab Treatment, a Human anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Pediatric Participants with Moderately to Severely Active Ulcerative Colitis

PURSUIT 2

Short Title

A Study of the Efficacy and Safety of Golimumab in Pediatric Participants with Moderately to Severely Active Ulcerative Colitis

Protocol CNTO148UCO3003; Phase 3
AMENDMENT 6

SIMPONI® (golimumab)

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US sites of this study will be conducted under US Food & Drug Administration IND regulations (21 CFR Part 312).

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GCP Compliance: This study will be conducted in compliance with Good Clinical Practice, and applicable regulatory requirements.

PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

DOCUMENT HISTORY	
Document	**Date**
Amendment 6	11 November 2023
Amendment 5	14 October 2022
Amendment 4	16 March 2021
Amendment 3	8 Jul 2019
Amendment 2	13 May 2019
Amendment 1	27 Jun 2018
Original Protocol	17 May 2018

Amendment 6 (11 November 2023)

Overall Rationale for the Amendment: Upon implementation of this amendment, laboratory assessments will be streamlined and PUCAI will be eliminated after Week 90 to reduce subject burden while maintaining collection of meaningful safety data during the study extension.

The changes made to the clinical protocol CNTO148UCO3003 as part of Protocol Amendment 6 are listed below, including the rationale of each change and a list of all applicable sections. Changes made in previous protocol amendments are listed in Section 10.20 Appendix 20: Protocol Amendment History.

Section Number and Name	Description of Change	Brief Rationale
Section 1.1. Synopsys Statistical Methods Statistical Hypothesis Section 9.1. Statistical Hypothesis	Primary hypothesis was revised as follows: The primary hypothesis is that golimumab is an effective therapy in pediatric UC relative to a historical placebo control as assessed by clinical remission **at Week 6** based on the Mayo score. The historical placebo **clinical remission rate** ~~control~~ is based on meta-analysis of 7 adult UC studies including infliximab Phase 3 (C0168T37 and C0168T46), golimumab Phase 2/3 (C0524T16 and C0524T17), adalimumab Phase 3 (ULTRA 1 and ULTRA 2), and vedolizumab Phase 3 (GEMINI 1).	Specified the timing when clinical remission is assessed.
1.1 Synopsis Statistical Methods Sample size calculations	"Mayo clinical" added throughout the text.	Added to clarify planned analyses.
Section 1.1. Synopsis Endpoints Section 3.1. Endpoints Major Secondary Endpoints Section 9.4.1.2. Major Secondary Endpoints Section 9.4.1.3.	Sentence moved or added: For endpoints beyond Week 6, analyses will be performed on participants who are in clinical response at Week 6 as assessed by the Mayo score.	Clarified definition of several secondary endpoints.

Section Number and Name	Description of Change	Brief Rationale
Other Endpoints		
Section 1.3. Schedule of Activities Table 2	Title of column 3 was revised: Every 6 months starting Week 66 **through and including Week 90** for all participants. Addition of new column 4: **Every year after Week 90 (starting at Week 114) for all participants** with Xs added for Clinical Laboratory Assessments and PK/Immunogenicity. Footnote o was revised: Samples should be collected every 6 months during Year 1 of the study extension and, starting at Week ~~108~~ **114**, annually thereafter. New footnote p was added: **PUCAI will be collected until each participant completes a Week 90 visit.**	Sufficient information will be collected up to and including Week 90 to assess safety and efficacy. After Week 90, safety laboratory assessments will be collected annually to reduce participant burden. PUCAI was removed after each participant completes Week 90 since sufficient information for this endpoint will have been collected in the study prior to this point.
Section 4.1. Overall Design Study extension (Week 54 to end of study)	Text for Group 1 was revised: ~~**Group 1 (Golimumab):** After the Week 54 evaluations, at the discretion of the investigator, if participants receiving golimumab are able to benefit from continued SC golimumab, the participants will continue to receive SC golimumab q4w starting at Week 54 under this protocol's study extension until marketing authorization is obtained for golimumab for the treatment of pediatric participants with UC, the participant turns 18 and has access to commercially available golimumab or until a decision is made not to pursue an indication in this pediatric UC population, whichever occurs first. Participants who continue golimumab treatment as part of the study extension will be intermittently evaluated per the protocol for efficacy, PK, and safety.~~ **Group 1 (Golimumab):** Following the Week 54 evaluations (end of the main pivotal study), participants who are receiving benefit from golimumab, at the discretion of the investigator, may continue to receive SC golimumab q4w in an extension period until one of the following conditions below is met, whichever occurs first: 1. marketing authorization is obtained for golimumab for the treatment of pediatric participants with UC and golimumab is either commercially available or 2 years have lapsed since marketing authorization, or 2. the participant turns 18 years of age and has access to commercially available golimumab, or 3. until a decision is made by the sponsor not to pursue an indication in this pediatric UC population.	Further defined end of study language.

Section Number and Name	Description of Change	Brief Rationale
Section 4.4.1. Study Completion Study extension	The text for the section was revised as follows: ~~At Week 54, participants who may benefit will continue to receive SC golimumab q4w under this protocol until marketing authorization is obtained for golimumab for the treatment of pediatric participants with UC, the participant turns 18 and has access to commercially available golimumab, or until a decision is made not to pursue an indication in this pediatric UC population, whichever occurs first. Participants who prematurely discontinue study interventions for any reason before this time point will not be considered to have completed the study extension phase.~~ Following the Week 54 evaluations (end of the main pivotal study), participants who are receiving benefit from golimumab, at the discretion of the investigator, may continue to receive SC golimumab q4w in an extension period until one of the following conditions below is met, whichever occurs first: 1. marketing authorization is obtained for golimumab for the treatment of pediatric participants with UC and golimumab is either commercially available or 2 years have lapsed since marketing authorization, or 2. the participant turns 18 years of age and has access to commercially available golimumab, or 3. until a decision is made by the sponsor not to pursue an indication in this pediatric UC population.	Further defined end of study language.
Section 6.4. Study Intervention Compliance	The text for the section was revised as follows: **Visit window:** From Week 0 through Week 54, it is expected that all visits will occur within a range of ±7 days of the scheduled visit. Any visits outside of these ranges should be discussed with the sponsor. ~~If a study visit occurs outside the specified visit window, the participant should then resume his or her normal dose schedule relative to the baseline visit (Week 0) as soon as possible.~~ After Week 54 the follow-up study visits should occur within ±14 days of the scheduled study visit. Any out-of-range visit**s after Week 54** should be documented in the participant's source notes. **Dosing window: From Week 0 through the end of the trial, any doses that are planned to occur outside of ±7 day dosing window should be discussed with the sponsor.** **Golimumab should be administered as close as possible to the q4w dosing schedule.**	Doses outside of ±7 days range requires discussion with the sponsor to determinate appropriate dose schedule to ensure adequate time between doses.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted.

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1. PROTOCOL SUMMARY

1.1. Synopsis

A Phase 3 Randomized, Open-Label Study to Assess the Efficacy, Safety, and Pharmacokinetics of Golimumab Treatment, a Human anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Pediatric Participants with Moderately to Severely Active Ulcerative Colitis

Protocol number: CNTO148UCO3003

EudraCT Number: 2017-004496-31

STUDY INTERVENTION

SIMPONI® (golimumab) is a fully human monoclonal antibody with an immunoglobulin G1 heavy chain isotype (G1m[z] allotype) and a kappa light chain isotype. The molecular weight of golimumab ranges from 149,802 to 151,064 daltons. Golimumab binds to human tumor necrosis factor alpha (TNFα) with high affinity and specificity and neutralizes TNFα bioactivity.

OBJECTIVES

Primary Objectives

- To evaluate the efficacy of golimumab in inducing clinical remission as assessed by the Mayo score, in pediatric participants with moderately to severely active ulcerative colitis (UC).
- To evaluate the safety profile of golimumab, in pediatric participants with moderately to severely active UC.

Secondary Objectives

- To evaluate the efficacy of golimumab in inducing clinical response as assessed by the Mayo Score and clinical remission as measured by the Pediatric Ulcerative Colitis Activity Index Score (PUCAI) Score.
- To evaluate the efficacy of golimumab on endoscopic healing.
- To evaluate the efficacy of golimumab during the long-term phase.
- To evaluate the effect of golimumab on additional efficacy and quality of life measures.
- To evaluate the pharmacokinetic (PK) and exposure-response of golimumab during short- and long-term phases.

Additional Objective (Usability Assessment Substudy)

- To evaluate the potential for at home use of golimumab in the participant population during the Usability Assessment Substudy.

OVERALL DESIGN

This is a multicenter, randomized, open-label golimumab study in pediatric participants aged 2 to 17 years with moderately to severely active UC, defined as a baseline Mayo score of 6 through 12, inclusive, with an endoscopy subscore of ≥2. Prior to Amendment 4, central randomization was implemented in this study. Participants ≥30 kg were randomized in a 3:1 ratio across intervention groups, golimumab and infliximab, respectively. Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.

In this study, the remission rate of golimumab in pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints.

This study will also include an infliximab arm. No formal comparisons between golimumab and infliximab will be performed.

Endoscopies performed for this study are to be performed using study software and submitted for central review. Scoring for disease activity based on endoscopic appearance is to be performed both by the local endoscopist and the central reviewer. All decisions to initiate (Week 0) or continue therapy (Week 6) will be based on local reads. Analyses of the primary and major secondary endpoints will be based on locally read endoscopy measures. Analyses of these endpoints will also be performed using the centrally read endoscopy measures.

This 54-week study will consist of a 6-week short-term phase and a 48-week long-term phase followed by a study extension (for eligible golimumab-treated participants).

Beginning at Week 58, participants who are eligible to continue receiving golimumab in the study extension will be offered the option for self-administration (at least 12 years old) or caregiver administration (any age). At home administration (AHA) is optional; if a pediatric participant or caregiver elects against self- or caregiver administration, the health care professional will continue to administer injections in this study.

At select sites, participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in a Usability Assessment Substudy. An attempt will be made to enroll approximately 10-20 participants in the Usability Assessment Substudy at Week 58. The objective of the Substudy is to provide supportive data that the Prefilled Syringe with UltraSafe (PFS-U) and Prefilled Pen-Varioject (PFP-V) as designed, together with the appropriate training and written Instructions for Use, are suitable for AHA by pediatric participants or their caregivers.

An internal Data Monitoring Committee (consisting of Sponsor members [a gastroenterologist, a clinician and a statistician at a minimum] outside of the study team), will be established to monitor safety data (for both golimumab and infliximab treatments arms) on an ongoing basis until all participants reach the Week 54 visit or terminate the study prior to the Week 54 visit.

STUDY POPULATION

The study population will include pediatric participants aged 2 to 17 years with moderately to severely active UC, defined as a baseline Mayo score of 6 through 12, inclusive, with an endoscopy subscore of ≥2.

All study participants must have:

- Demonstrated an inadequate response to, have failed to tolerate, or have a medical contraindication to conventional therapies (ie, intravenous or oral corticosteroids or the immunomodulators methotrexate, azathioprine or 6-mercaptopurine);

  OR

- Demonstrated corticosteroid dependence;

  OR

- Require repeated (>3 per year) courses of corticosteroids.

Participants with prior exposure to biologic anti-TNFα agents will be ineligible for participation.

NUMBER OF PARTICIPANTS

Prior to Amendment 4, approximately 125 participants who satisfy inclusion/exclusion criteria were to be included in the study at sites located globally, including in North and South America, Asia, and Europe. At least 24 golimumab participants with body weight <45 kg, and at least 5 golimumab participants with body weight <30 kg will be included.

In order to ensure at least 5 participants with body weight <30 kg receive golimumab, participants who weigh <30 kg were to only be allocated to the golimumab treatment arm. The remaining 120 participants were to be randomized in a 3:1 ratio to golimumab or infliximab, respectively.

Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.

Upon implementation of Amendment 5, no new participants will be enrolled. Approximately 70 participants will participate in this study (at least 60 participants will receive golimumab, at least 10 participants will receive infliximab). Of the 60 golimumab participants, at least 15 will have a body weight <45 kg and at least 5 will have a body weight <30 kg.

INTERVENTION GROUPS AND DURATION

Golimumab

During the short-term phase, pediatric participants will receive dose regimens of subcutaneous (SC) golimumab at Week 0 and Week 2 based on body weight as shown in Table I below. Participants must weigh ≥10 kg and be >70 cm tall. This is the lower range of weight and height that the prefilled pen has been validated for to deliver SC golimumab. This limit accommodates >97% of all 2-year old girls based on published growth charts (www.cdc.gov/growthcharts). Participants' golimumab doses for all administrations through Week 10 (inclusive) will be based on the participants' weight and height at Week 0 or, if not available, the most recent height and weight from screening. The same weight and height should be used through Week 10. Golimumab doses from Week 14 through Week 54 will be based on the participants' weight and height obtained with that week's visit or the height and weight measured at the previous site visit. In the study extension, golimumab doses will be based on the participants' most current weight and height or the last recorded height and weight.

Table I: Dosage by body weight

Pediatric participants with ulcerative colitis (2 to 17 years of age)	**Short-term phase**	**Long-term phase**[†]
With body weight <45 kg	120 mg/m^2 at Week 0* 60 mg/m^2 at Week 2*	60 mg/m^2 every 4 weeks from Week 6*
With body weight ≥45 kg	200 mg at Week 0 100 mg at Week 2	100 mg every 4 weeks from Week 6

[†] Participants in clinical response to golimumab at Week 6.
*BSA doses are capped at 200 mg and 100 mg for the 120 mg/m^2 and 60 mg/m^2 doses, respectively.

At Week 6, all participants will be evaluated for clinical response; participants in clinical response will continue receiving open-label golimumab during the long-term phase.

Participants not in clinical response (as evaluated by the Mayo score) at Week 6 may have study intervention discontinued (and complete a safety follow-up at least 16 weeks after the last administration of golimumab) OR may continue receiving golimumab for up to 2 additional doses at Weeks 6 and 10 as specified in Table I at the discretion of the investigator. At Week 14, these participants who received the 2 additional doses will need to demonstrate a partial Mayo response to continue on in the study; participants in partial Mayo response will continue receiving open-label golimumab once every 4 weeks (q4w) during

the long-term phase (Table I). Participants who received the 2 additional doses and are not partial Mayo responders at Week 14 will have study intervention discontinued and should complete a final safety follow-up at least 16 weeks following the last administration of study intervention.

Infliximab

All participants in the infliximab treatment arm will be administered infliximab 5 mg/kg at Weeks 0 and 2. Starting at Week 6, infliximab administrations of 5 mg/kg will continue q8w through Week 46 for those participants in clinical response at Week 6. Infliximab doses for all administrations through Week 8 (inclusive) will be based on the participants' weight at Week 0 or, if not available, the most recent weight from screening. The same weight should be used through Week 8. Infliximab doses from Week 14 through Week 46 will be based on the participants' weight obtained with that week's visit or the weight measured at the previous site visit.

For those participants not in clinical response at Week 6 (as defined by the Mayo score), or participants who were in response at Week 6 but have a clinical flare in their UC (defined in Section 6.5.3) an additional step-wise dose escalation approach may be taken at the investigator's discretion. The first step is a dose increase at Week 6 to 10 mg/kg [capped at 1 gm] q8w or 5 mg/kg at Weeks 6 and 8, and 10 mg/kg (capped at 1 gm) at Week 14 and q8w thereafter, respectively). At Week 14, if the participant has demonstrated a partial Mayo response, they will continue to receive infliximab 10mg/kg q8w. Additionally, if the participant has not achieved a partial Mayo response by Week 14, starting at the Week 14 visit, the investigators can also shorten the interval between doses to q4w.

At Week 22, those participants who had received an escalation in their infliximab dosing to 10 mg/kg q4w will need to demonstrate a partial Mayo response to continue in the study. Participants in partial Mayo response will continue receiving open-label infliximab 10 mg/kg q4w through Week 46. Participants who have not achieved a partial Mayo response at Week 22 will have study intervention discontinued and should complete a final safety follow-up at least 8 weeks following the last administration of infliximab.

Participants who dose-escalate in response to a UC flare after Week 6 will be reassessed after 2 administrations at the new higher dose. Participants in partial Mayo response will continue receiving open-label infliximab through Week 46 at the new higher dose. Participants who have not achieved a partial Mayo response will have study intervention discontinued and should complete a final safety visit at least 8 weeks following the last administration of infliximab.

After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have the Week 54 or Early Termination visit.

Finally, while dose escalation should be based on clinical criteria as described above, investigators at their discretion may utilize infliximab serum levels to assist their decision making. This approach was chosen as it most closely mimics clinical practice in treatment of pediatric UC, allowing investigators some flexibility in dosing to treat their patients. Also, if an investigator wants to dose-escalate using a different regimen than listed above, discuss the plan with the medical monitor. After the Week 54 evaluations, participants receiving infliximab will be transitioned off the study to standard medical care.

EFFICACY EVALUATIONS

Efficacy evaluations will include the following:

- Mayo score
- Partial Mayo score
- PUCAI score
- C-reactive protein

- Fecal calprotectin
- IMPACT III
- TUMMY-UC and Observer TUMMY-UC

Endpoints

Primary Endpoint

The primary endpoint is clinical remission at Week 6 as assessed by the Mayo score.

Clinical remission as measured by the Mayo score is defined as a Mayo score ≤2 points, with no individual subscore >1 (based on Mayo endoscopy subscore assigned by the local endoscopist).

Major Secondary Endpoints

For endpoints beyond Week 6, analyses will be performed on participants who are in clinical response at Week 6 as assessed by the Mayo score.

- Symptomatic remission at Week 54.
- Clinical remission at Week 54 as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).
- Clinical remission at Week 54 as assessed by the PUCAI score.
- Clinical remission at Week 6 as assessed by the PUCAI score.
- Clinical response at Week 6 as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).
- Endoscopic healing at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).
- Endoscopic healing at Week 54 (based on Mayo endoscopy subscore assigned by the local endoscopist).
- Clinical remission at Week 54, as assessed by the Mayo score, for participants who are in clinical remission at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).
- Participants who were not receiving corticosteroids for at least 12 Weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).

The definitions of the major secondary endpoints are provided below:

- **Symptomatic remission**: Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0.
- **Clinical response**: a decrease from baseline in the Mayo score of ≥30% and ≥3 points, with either a decrease from baseline in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1.
- **Clinical remission as measured by the PUCAI score**: a PUCAI score <10.
- **Endoscopic healing**: an endoscopy subscore of the Mayo score of 0 or 1.

PHARMACOKINETIC EVALUATIONS

Serum samples will be used to evaluate the pharmacokinetics of golimumab and infliximab. Samples collected for the analyses of serum concentrations of golimumab or infliximab may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period, or for the

evaluation of relevant biomarkers. Genetic analyses will not be performed on these serum samples. Participant confidentiality will be maintained.

IMMUNOGENICITY EVALUATIONS

Serum samples will be screened for antibodies binding to golimumab or infliximab and the titer of confirmed positive samples will be reported as applicable. Other analyses may be performed to further characterize the immunogenicity of golimumab or infliximab.

PHARMACODYNAMIC AND BIOMARKER EVALUATIONS

Inflammatory pharmacodynamics (PD) markers (C-reactive protein and fecal calprotectin) will be evaluated. Exploratory biomarker assessments will be performed to identify ribonucleic acid (RNA; mRNA or microRNA) expression patterns and microbial activities that are relevant to golimumab and/or infliximab treatment and/or pediatric UC, to correlate histologic and immunohistochemical assessments of disease and healing, and to evaluate whether biomarkers can be developed to predict a golimumab response and/or UC disease activity.

SAFETY EVALUATIONS

Safety evaluations conducted at each study visit will include the assessment of adverse events (AEs; at the visit and those occurring between evaluation visits), a tuberculosis evaluation and other infection assessment, clinical laboratory blood tests (complete blood count and serum chemistries), vital signs, concomitant medication review, and observations for injection-site reactions, reactions temporally associated with an infusion, and/or allergic reactions.

STATISTICAL METHODS

Statistical Hypothesis

The primary hypothesis is that golimumab is an effective therapy in pediatric UC relative to a historical placebo control as assessed by clinical remission at Week 6 based on the Mayo score. The historical placebo clinical remission rate is based on a meta-analysis of 7 adult UC studies including infliximab Phase 3 (C0168T37 and C0168T46), golimumab Phase 2/3 (C0524T16 and C0524T17), adalimumab Phase 3 (ULTRA 1 and ULTRA 2), and vedolizumab Phase 3 (GEMINI 1).

Criteria for Success

The success of the study will ultimately be based on the totality of evidence. The primary analysis will be based on the proportion of golimumab pediatric participants in clinical remission at Week 6 based on the Mayo score and its associated 90% confidence interval (CI). The criteria for the primary analysis will have been met if the lower limit of the two-sided 90% CI for the proportion of golimumab participants in clinical remission at Week 6 is >10.0% (ie, the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 derived from a meta-analysis of 7 adult UC studies including 2 adult Phase 2/3 studies of golimumab and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints).

Sample Size Calculation

Sample size calculations were based on the need to have a sufficient number of participants assigned to the golimumab treatment arm to achieve the criteria defined in the Criteria for Success. In addition, collecting sufficient PK data to adequately characterize the PK of golimumab in participants with UC is also considered.

A sample size of 60 participants in the golimumab arm will ensure that the lower bound of the 90% CI for the pediatric golimumab Mayo clinical remission rate is above 10.0% (ie, the upper bound of the 95% CI for the historical placebo control) as long as the observed remission rate is at least 18.3%. The probability of observing a Mayo clinical remission rate of ≥18.3%, given different assumptions for the true rate of Mayo clinical remission is shown in Table II below.

With 60 golimumab-treated participants, the probability of observing a Mayo clinical remission rate of ≥18.3% ranges from 50% (if the golimumab adult UC remission rate of 17.8% is assumed) to greater than 99% (if the remission rate of 42.9% from the first golimumab study in pediatric UC is assumed). It is reasonable to assume that the true Mayo clinical remission rate in pediatric UC participants is greater than the remission rate observed in the adult UC study, as the remission rate in the first golimumab pediatric UC study was at least twice that observed in the adult UC study. Therefore, if we assume the remission rate to be 22.5%, then the probability of observing a remission rate of ≥18.3% is at least 80% (Table II).

Table II: Probability of Observing a Clinical Remission Rate of ≥18.3% With Differing Assumptions for the True Remission Rate

Clinical Remission as Assessed by the Mayo Score	Probability of Observing ≥18.3% N=60
17.8% (observed adult remission rate; C0524T17)	50%
20.0%	68%
22.5%	82%
25.0%	91%
42.9% (observed pediatric remission rate; CNTO148UCO1001)	>99.9%

The precision (ie, half width of the CI) based on this sample size of 60 golimumab participants is 8.1% (assuming a Mayo clinical remission rate of 17.8% at Week 6) and 10.5% (assuming a clinical remission rate at Week 6 of 42.9%).

Furthermore, the Fisher Information Matrix-based optimal design analysis indicates that PK data from a total of 60 participants (including 45 participants in the ≥45 kg subgroup and 15 participants in the <45 kg subgroup) would be sufficient to adequately characterize the PK of golimumab in pediatric participants with UC.

Primary Efficacy Analysis

The primary analysis population includes all participants (including the youngest weight cohort [<30 kg]) who were treated with golimumab. The primary analysis will be based on the proportion of pediatric participants who received golimumab and who were in clinical remission at Week 6 based on the Mayo score (endoscopy subscore assigned by local endoscopist) and its associated 90% CI. The criteria for the primary analysis will have been met if the lower limit of the two-sided 90% CI for the proportion of pediatric golimumab participants in clinical remission at Week 6 is greater than the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 (ie, >10.0%) derived from a meta-analysis of 7 adult UC studies including 2 Phase 2/3 studies of golimumab and 5 Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints.

Treatment failure rules will override the clinical remission status based on the Mayo score. Participants who meet any of the following criteria for treatment failure through Week 6 will be considered to not have achieved clinical remission at Week 6:

- Had a colectomy (partial or full) or ostomy,

OR

- Discontinued study intervention due to lack of efficacy or an AE of worsening of UC,

OR

- Had a protocol prohibited medication change (to be detailed in the Statistical Analysis Plan).

In addition, participants who do not return for evaluation or have insufficient data to calculate their Mayo Score at Week 6 (ie, all 4 Mayo subscores are missing) will be considered to not have achieved clinical remission (based on the Mayo Score) at Week 6.

Major Secondary Efficacy Analyses

Summary statistics will be provided for all efficacy endpoints. In particular, counts and percentages will be used to summarize major secondary endpoints. Unless otherwise specified, all endpoints that involve the Mayo endoscopy subscore will be based on the subscore assigned by the local endoscopist. For endpoints beyond Week 6, analyses will be performed on participants who are in clinical response at Week 6 as assessed by the Mayo score.

Pharmacokinetic Analyses

Serum golimumab and infliximab concentrations will be summarized for each golimumab/infliximab treatment group over time using descriptive statistics for all participants who receive at least 1 administration of golimumab/infliximab and had at least 1 postdose sample.

Immunogenicity Analyses

The incidence of anti-golimumab and anti-infliximab antibodies will be summarized for all participants who receive at least 1 dose of golimumab or infliximab and have appropriate samples for detection of antibodies to golimumab or infliximab (ie, participants with at least 1 sample obtained after their first dose of golimumab or infliximab).

Other immunogenicity

Other immunogenicity analyses may be performed to further characterize the immune responses that are generated.

Biomarker Analyses

Changes in serum/RNA or other biomarkers over time will be summarized by intervention group. Associations between baseline levels and changes from baseline in select markers and clinical response at screening and Weeks 0, 2, 6, and 54 will be explored.

Pharmacodynamic Analyses

Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information. Any pharmacodynamic (PD) samples received by the contract vendor or Sponsor after the cut-off date will not be analyzed, and therefore, excluded from the PD analysis.

Safety Analyses

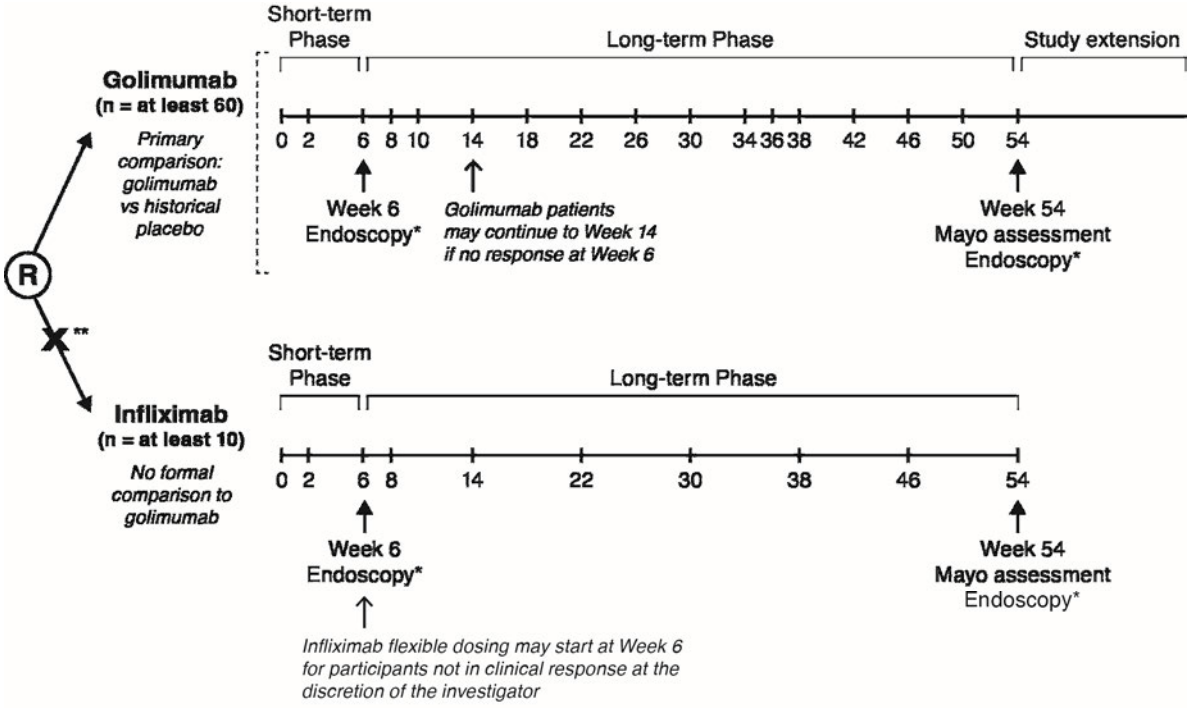
The following analyses will be used to assess the safety of participants in the study: frequency and type of AEs, frequency and type of serious adverse events, frequency and type of reasonably related AEs as assessed by the investigator, frequency and type of AEs leading to discontinuation of study intervention, frequency and type of infections (including serious infections, and infections requiring oral or parenteral antimicrobial treatment), frequency and type of AEs temporally associated with infusion, and frequency and type of injection-site reactions.

Laboratory parameters and change from baseline in selected laboratory parameters (hematology and chemistry), and maximum Common Terminology Criteria for Adverse Events (CTCAE) toxicity grade for postbaseline laboratory parameters will be summarized by treatment group. In addition, a listing of participants with any abnormal postbaseline laboratory values of CTCAE Grade ≥2 will also be provided.

All safety analyses will be based on the population of participants who received at least 1 administration of study intervention. Participants will be summarized by the treatment they actually received (golimumab versus infliximab).

1.2. Schema

Figure 1: Study Schema for CNTO148UCO3003 (Modified in Amendment 5)



Golimumab at Week 0 and Week 2:
≥ 45 kg: 200 → 100 mg
< 45 kg: 120 → 60 mg/m^2 (max 200 → 100 mg)

Golimumab every 4 weeks (Weeks 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50):
≥ 45 kg: 100 mg
< 45 kg: 60 mg/m^2 (max 100 mg)

Infliximab at Week 0 and Week 2:
5 mg/kg infliximab

Infliximab every 8 weeks (Weeks 6, 14, 22, 30, 38, 46):
5 mg/kg infliximab

Infliximab flexible dosing may start at Week 6 for participants not in clinical response at the discretion of the investigator; the first step is increase to 10 mg/kg and next step (if needed) is shorten dosing interval to every 4 weeks. Interval change should not occur before Week 14.

* Endoscopy will include central and local readings.
** Upon implementation of Amendment 4, no new participants will be randomized to the infliximab arm.

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1.3. Schedule of Activities (SoA)

Table 1: Study Schedule of Activities from Screening Through Week 54

Visit	Screening	Week 0	Week 2	Week 6	Week 8	Week 10[cc]	Week 14	Week 18[cc]	Week 22	Week 26[cc]	Week 30	Week 34[cc]	Week 36[cc]	Week 38	Week 42[cc]	Week 46	Week 50[cc]	Week 54	Early Term[d,f]	Final Safety Visit[e]
Study Procedures[a,b,c,d]																				
Screening/ Administrative																				
Informed consent/assent	X																			
Inclusion/exclusion criteria	X	X																		
Medical history and demographics	X																			
Sigmoidoscopy[g]	X																			
Confirmation of prestudy diagnostic UC biopsy results[h]	X																			
QuantiFERON® TB or T Spot® test[i]	X																			
Chest radiograph[j]	X																			
Primary tuberculosis screening[i]	X	X																		
Stool study including *Clostridium difficile* toxin[k]	X																			
Screening for up to date immunizations per local guidelines[l]	X																			
Hepatitis B testing[m]	X																			
HCV testing	X																			
HIV testing[n]	X																			
Serum pregnancy test	X																			

Table 1: Study Schedule of Activities from Screening Through Week 54

Visit	Screening	Week 0	Week 2	Week 6	Week 8	Week 10[cc]	Week 14	Week 18[cc]	Week 22	Week 26[cc]	Week 30	Week 34[cc]	Week 36[cc]	Week 38	Week 42[cc]	Week 46	Week 50[cc]	Week 54	Early Term[d,f]	Final Safety Visit[e]
Study Procedures[a,b,c,d]																				
Study intervention administration[o]																				
Administer SC golimumab[p,q]		X	X	X		X	X	X	X	X	X	X		X	X	X	X	X[p]		
Administer IV infliximab[q,bb,cc]		X	X	X	X[r]		X		X		X			X		X				
Safety Assessments																				
Physical examination	X						X							X				X	X	X
Vital signs[s]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X	X					X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight	X	X					X	X	X	X	X	X	X	X	X	X	X	X	X	X
Study intervention injection site evaluation		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X		
Tuberculosis evaluation[i]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X
Urine pregnancy test[t]		X	X	X	X[t]	X[t]	X	X[t]	X	X[t]	X	X[t]		X	X[t]	X	X[t]	X	X	
Concomitant medication review	X[u]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE review	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Efficacy Assessments																				
Sigmoidoscopy[g]				X														X	X	
Mayo Patient Diary Completed[v]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Mayo score calculation		X		X														X	X	
Partial Mayo score calculation			X		X	X	X	X	X	X	X	X	X	X	X	X	X			
PUCAI score	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
IMPACT III[w]		X		X			X				X							X	X	

Table 1: Study Schedule of Activities from Screening Through Week 54

Visit	Screening	Week 0	Week 2	Week 6	Week 8	Week 10[cc]	Week 14	Week 18[cc]	Week 22	Week 26[cc]	Week 30	Week 34[cc]	Week 36[cc]	Week 38	Week 42[cc]	Week 46	Week 50[cc]	Week 54	Early Term[d,f]	Final Safety Visit[e]
Study Procedures[a,b,c,d]																				
TUMMY UC/Observer TUMMY UC[x]		X		X			X				X							X	X	
CRP		X		X			X						X					X	X	
Fecal calprotectin		X		X			X						X					X	X	
Clinical Laboratory Assessments																				
Hematology, Chemistry	X			X			X			X[dd]				X				X	X	X
ANA and anti dsDNA antibodies		X		X						X[dd]			X					X	X	X
Pharmacokinetics/ Immunogenicity																				
Golimumab concentration[y]		X	X	X		X	X	X		X		X	X		X		X	X	X	X
Infliximab concentration[y]		X	X	X	X		X		X		X			X		X		X	X	X
Antibodies to golimumab[y]		X		X			X						X					X	X	X
Antibodies to infliximab[y]		X		X			X											X	X	X
Biomarkers																				
Colonic biopsy (RNA, histology)[z]	X			X														X	X	
Blood RNA[aa]	X		X	X														X	X	
Fecal biomarkers		X		X														X	X	

a. Screening for eligible participants will be performed within 6 weeks before administration of the study intervention.
b. All participants should return for a final visit, 16 weeks after the last administration of golimumab or 8 weeks after last infliximab administration.
c. All assessments are to be completed prior to study intervention administration, unless otherwise specified. Visit window should be ±7 days for each visit up to and including the Week 54 visit.
d. If there is an early discontinuation of study intervention (before Week 54) these study assessments should be collected. In the case of study termination refer to Section 7.
e. Participants who discontinue study intervention prior to Week 14 but do not terminate study participation should return for protocol specified procedures and evaluations up to and including the Week 14 visit. These participants should also return for the final safety visit 16 weeks after the last administration of golimumab or 8 weeks after the last administration of infliximab.
f. Prior to withdrawal of consent, participants who terminate study participation prior to Week 14 should complete assessments indicated at Week 14.
g. Should be performed within 2 weeks prior to the administration of study intervention at Week 0, within 2 weeks prior to Week 54, and within 7 days prior to study intervention for Week 6. All study endoscopies (sigmoidoscopy preferred unless colonoscopy clinically indicated) must be performed with study software to permit central reads and scoring in addition to local site study scoring. A colonoscopy will replace a sigmoidoscopy if screening for dysplasia is required. The Sponsor suggests that at least 48 hours must elapse between a colonoscopy with polypectomy or multiple biopsies and the study intervention administration (Week 0) visit.
h. Previous assessment must be consistent with a diagnosis of UC (eg, crypt distortion, crypt abscess, goblet cell depletion, and continuous distribution).
i. A tuberculin skin test is required if the QuantiFERON TB or T Spot test is not approved/registered in that country, OR the tuberculin skin test is mandated by local health authorities.
j. Chest radiograph should be obtained during the screening period unless one was obtained within 6 months before screening and the findings recorded in the study source documents. Chest radiographs should be reviewed to assess for potential undiagnosed pulmonary pathologies that may include manifestations of IBD, malignancies, and prior or current infection (eg, latent TB). Chest radiographs must be obtained in all cases when the QuantiFERON TB or T Spot test and/or the tuberculin skin test for TB is positive or repeatedly indeterminate.
k. Stool studies for enteric pathogens, including a stool culture and *Clostridium difficile* toxin assay, that have been performed at a local laboratory during the current episode of disease exacerbation and within 4 months prior to Week 0 may be used for screening. Additional testing such as ova and parasite or *E. coli* 0157:H7 assessments may be performed at the investigator's clinical discretion by the central laboratory. If previous results are unavailable, the central laboratory should be used to perform the tests at screening.
l. Refer to local immunization guidelines for immunosuppressed participants prior to Week 0.
m. For additional details, refer to Appendix 15 (Section 10.15).
n. HIV testing in study participants who are less than 6 years of age is not universally required. It is required in those study participants who are less than 6 years of age and the birth history is unknown (ie, adopted) or has exposure risks (parents with HIV or with risk factors) or at the discretion of the study investigator. In subjects who are less than 6 years of age where testing would be required, if there is a record of a negative HIV test at birth this is acceptable at the discretion of the study physician as long as it is entered into the study record.
o. Participants' golimumab or infliximab doses for Weeks 0 through 10, inclusive, will be based on the participants' height and weight at Week 0 or, if not available, the most recent height and weight from screening. The same height and weight should be used through Week 10 for golimumab administrations, and the same weight should be used through Week 8 for infliximab administrations. For all dose administrations after Week 10, weight and height at the current visit or the last recorded data will be used to determine study intervention dosage. For AHA of golimumab administrations after Week 54, dosages will be based on the most recent recorded height and weight obtained by the investigator during scheduled office visits.
p. Golimumab is to be administered only if the participant is eligible and will be participating in the study extension (see Table 2).
q. Participants should be evaluated for vital signs (including temperature, pulse/heart rate, respiratory rate, and blood pressure) before and approximately 30 minutes after every SC golimumab administration. Vital signs will be obtained before, approximately every 30 minutes during, and twice (at approximately 30 minute intervals) after completion of the IV infusion(s) of infliximab.
r. Only if decision is made to escalate the dose of infliximab to 10 mg/kg q8w, and only if participant was given 5 mg/kg Week 6, may the participant receive a dose at Week 8 of infliximab at 5 mg/kg, with subsequent doses of 10 mg/kg starting at Week 14. Infliximab infusions are capped at 1 gm maximum per administration. Additional details are available in Section 4, Study Design. If participant receives infliximab infusion at Week 8, they will need a urine pregnancy test in addition to the other assessments collected from all study participants.
s. Temperature, pulse/heart rate, respiratory rate, and blood pressure.

t. All girls of childbearing potential must have a negative urine pregnancy test prior to all study site administration of study intervention. If the visit does not include study intervention administration, a urine pregnancy test is not required unless it is the Week 54 or early discontinuation visit.
u. Concomitant medications administered up to 30 days before first dose of study intervention must be recorded at screening.
v. Mayo Patient Diary is completed for 7 continuous days within the 14 days prior to the screening visit. For the screening visit, the Mayo diary will be provided at screening and collected at the Week 0 visit.
w. Required only if participant is ≥10 years of age at Week 0.
x. Participants will record TUMMY UC questionnaire data daily for 5 days before the study site visit in a participant diary. For participants less than 8 years old, their caregiver will complete the Observer TUMMY UC questionnaire. The version used at the Week 0 assessment will be used at all subsequent assessments regardless of participant age.
y. At drug administration visits, blood samples should be collected prior to study intervention administration (for both golimumab and infliximab) and 1 hour postinfusion (only for infliximab at Weeks 0, 2, 6, and 46). The same blood draw can be used to collect serum samples for measuring study intervention concentration and antibodies to study intervention. Blood sampling in participants with a body weight of 10 kg to 24 kg must be divided between visits during the screening period. Contact Sponsor for details of recommended sampling sequence.
z. Should be performed within 2 weeks prior to the administration of study intervention at Week 0 and Week 54, and within 7 days for Week 6.
aa. The RNA blood sample should not be collected at any time point for any participant who at screening has a body weight of 10 kg to <12.3 kg, even if the weight increases to above 12.3 kg during the study. For participants who weighed more at screening but whose body weight falls to between 10 kg to <12.3 kg, the RNA blood sample should not be collected, and blood draws are not to exceed 8.0 mL at any one visit for this weight group.
bb. At visits during which the participant does not receive an administration of infliximab, the following evaluations do not need to be performed: urine pregnancy and injection site evaluation.
cc. For infliximab patients only: Visits at Week 10, 18, 26, 34, 36, 42, 50 and associated study procedures are optional, and only required if investigator implements flexible dosing and is administering infliximab at these time points.
dd. Infliximab participants who do not have a dosing visit at Week 26 should have hematology, chemistry, ANA, and anti dsDNA antibodies performed at Week 22 visit.

Table 2: Study Schedule of Activities for the Study Extension for Participants Who May Benefit from Continued Treatment: Golimumab Arm					
	Every 4 Weeks starting Week 54 for participants who receive study intervention administrations at site	**Every 12 weeks starting Week 66 for those participants who will perform AHA[n]**	**Every 6 months starting Week 66 through and including Week 90 for all participants**	**Every year after Week 90 (starting at Week 114) for all participants**	**Final Safety Visit for the Study[a]**
Study Procedures[b,c,d]					
Study intervention administration					
Administer study intervention[e,j,l]	X	X[m]			
Safety Assessments					
Physical examination (including skin examination)			X		X
Vital signs[f]	X	X			X
Height	X	X			X
Weight	X	X			X
Study intervention injection-site evaluation[f,j]	X				
Tuberculosis evaluation[g,j]	X	X			X
Urine pregnancy test[h]	X	X			
Concomitant medication review[j,k]	X	X			X
AE review[j]	X	X			X
Efficacy Assessments					
PUCAI score[p]			X		
Clinical Laboratory Assessments					
Hematology, Chemistry			X[o]	X[o]	X
ANA and anti-dsDNA antibodies			X[o]		X

Table 2: Study Schedule of Activities for the Study Extension for Participants Who May Benefit from Continued Treatment: Golimumab Arm

	Every 4 Weeks starting Week 54 for participants who receive study intervention administrations at site	Every 12 weeks starting Week 66 for those participants who will perform AHA[n]	Every 6 months starting Week 66 through and including Week 90 for all participants	Every year after Week 90 (starting at Week 114) for all participants	Final Safety Visit for the Study[a]
Pharmacokinetics/Immunogenicity					
Golimumab concentration[i]			X[o]	X[o]	X
Antibodies to golimumab[i]			X[o]	X[o]	X

a. Participants who discontinue the study and are not continuing-golimumab treatment after exiting the study must return for final safety visit (ie, 16 weeks after last administration) for this study. Participants who are planning to continue golimumab treatment after exiting the study should have all final safety visit assessments done during the last study visit while on study golimumab.
b. All assessments are to be completed prior to study intervention administration, unless otherwise specified. Visit window should be ±14 days for each visit up to and including the final visit
c. Participants who discontinue study intervention but do not terminate study participation should return for the final safety visit.
d. Prior to withdrawal of consent, participants who terminate study participation should complete assessments indicated at final safety visit.
e. Participants' study intervention administrations will be based on the participants' weight and height at the current visit or the last recorded data for those performing AHA and for those at the study site. Weight and height need to be checked at least every 12 weeks during the study extension phase of the study.
f. Participants should be evaluated for vital signs (including temperature, pulse/heart rate, respiratory rate, and blood pressure) before and approximately 30 minutes following study intervention administration by qualified site personnel.
g. See Section 8.3.6 for TB evaluations. If TB is suspected at any time, a chest x ray and QuantiFERON TB or T Spot test, or tuberculin skin test should be performed.
h. Girls of childbearing potential.
i. Blood samples should be collected prior to study intervention administration. The same blood draw can be used to collect serum samples for measuring study intervention concentration and antibodies to study intervention.
j. All participants electing AHA of study interventions, will document the details of the study intervention, dosing day, time, anatomic site and if there were any complications of the injection, as well as adverse event (including injection site reaction), concomitant medications and TB exposure information in an AHA diary, that is to be returned to the site at the upcoming visit, reviewed by the site staff (approximately every 12 weeks), and entered by site staff into the eCRF.
k. After Week 54, only include concomitant medications in eCRF that are associated with AE and SAEs (ie, used to treat event or suspected in causing event) and/or with the treatment of UC.
l. At Week 58, all participants are eligible for AHA of study intervention. Participants who are <12 years of age are eligible for AHA of study intervention by parent(s)/caregivers; participants >12 years of age are eligible for AHA by self or parent(s)/caregivers.
m. Every 12 weeks (within the visit window), the participants must come to the study site for collection of the indicated efficacy assessments, to return AHA diary, and to obtain golimumab supplies for self or caregiver administration. If the visit is 7 days or less from their regular q4w dosing schedule, participants should self or caregiver administer at home after the study site visit. If outside of 7 days participants should self or caregiver administer on their q4w schedule at home. All other q4w administration should be performed at home.
n. A diary will be provided for the participant to record AEs, TB evaluation, and concomitant medication review.
o. Samples should be collected every 6 months during Year 1 of the study extension and, starting at Week 114, annually thereafter.
p. PUCAI will be collected until each participant completes a Week 90 visit.

Table 3: Schedule of Activities for AHA and the Usability Assessment Substudy

Events	AHA and Usability Assessment Substudy Activities			
	First Training/self or caregiver administration visit[b]	**Second self or caregiver administration visit[b]**	**Third self or caregiver administration visit[b]**	**Subsequent study interventions to end of study**
Informed consent/assent for Substudy[a]	X			
Inclusion/exclusion criteria	X			
Training session conducted by site personnel	X			
Observation of self or caregiver training/administration by site personnel and completion of observer checklist (Appendix 10 [Section 10.10])	X			
Administration of golimumab by self or caregiver; or continued administration at the site, if desired	X	X	X	X
Completion of the Injection Device Assessment Questionnaire after completion of the second and third self- or caregiver administration visits by Substudy participants (Appendix 11 [Section 10.11])		X	X	
AHA diary	X	X	X	X
Device complaints/device-related AEs captured/investigated	X	X	X	X

a. Approximately 10 20 participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in an Usability Assessment Substudy at Week 58.
b. The training and self or caregiver administration visits will occur at Weeks 58, 62, and 66 visits for those participating in the Usability Assessment Substudy

2. INTRODUCTION

SIMPONI® (golimumab) is a fully human monoclonal antibody (mAb) with an immunoglobulin G1 heavy chain isotype (G1m[z] allotype) and a kappa light chain isotype. The molecular weight of golimumab ranges from 149,802 to 151,064 daltons. Golimumab binds to human tumor necrosis factor alpha (TNFα) with high affinity and specificity and neutralizes TNFα bioactivity.

Golimumab (subcutaneous [SC]) has been approved for both induction and maintenance therapy in adults with moderately to severely active ulcerative colitis (UC) disease in 88 countries globally including the United States (US) (15 May 2013), European Union (EU) (19 September 2013), and Canada (19 September 2013). Additionally, golimumab is approved for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis (AS), and non-radiographic axial spondyloarthritis. The first of these approvals in rheumatologic indications was in 2009. Golimumab for SC administration is also approved for use in children with polyarticular juvenile idiopathic arthritis (pJIA) in 46 countries, including the EU. Golimumab for intravenous (IV) administration is approved for the treatment of rheumatoid arthritis, psoriatic arthritis, and AS in several countries, with additional marketing authorizations pending for these indications worldwide.

This Phase 3 study (CNTO148UCO3003) will be a multicenter, randomized, open-label golimumab study in pediatric participants aged 2 to 17 years with moderately to severely active UC. This study will assess the efficacy, safety, and pharmacokinetics (PK) of SC golimumab in pediatric participants. The remission rate of golimumab in these pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved for this indication utilizing similar populations and endpoints. Additionally, the study will include an infliximab arm. Upon implementation of Amendment 4, no additional participants will be randomized to the infliximab arm; all newly enrolled participants will receive golimumab.

For the most comprehensive nonclinical and clinical information regarding the efficacy and safety of golimumab and infliximab, refer to the latest versions of the Investigator's Brochure (IB) for golimumab and infliximab, respectively.

The term "Sponsor" used throughout this document refers to the entities listed in the Contact Information page(s), which will be provided as a separate document.

2.1. Study Rationale

Golimumab was studied in a Phase 3 program of adults with moderately to severely active UC. This program demonstrated that golimumab is an effective anti-TNFα therapy in adults and was generally well tolerated, with a safety profile consistent with that observed for golimumab in other indications. Studies C0524T17 and C0524T18 were the basis for the approval of golimumab in adults with moderately to severely active UC in both the US (15 May 2013) and the European Union (EU [19 September 2013]).

Golimumab has the potential to offer pediatric participants with moderately to severely active UC a safe and effective therapy with a convenient SC injection option given every 4 weeks (q4w).

Accordingly, golimumab is being studied in pediatric participants from the ages of 2 to 17 years with moderately to severely active UC.

The clinical development program for golimumab in pediatric UC includes 2 studies.

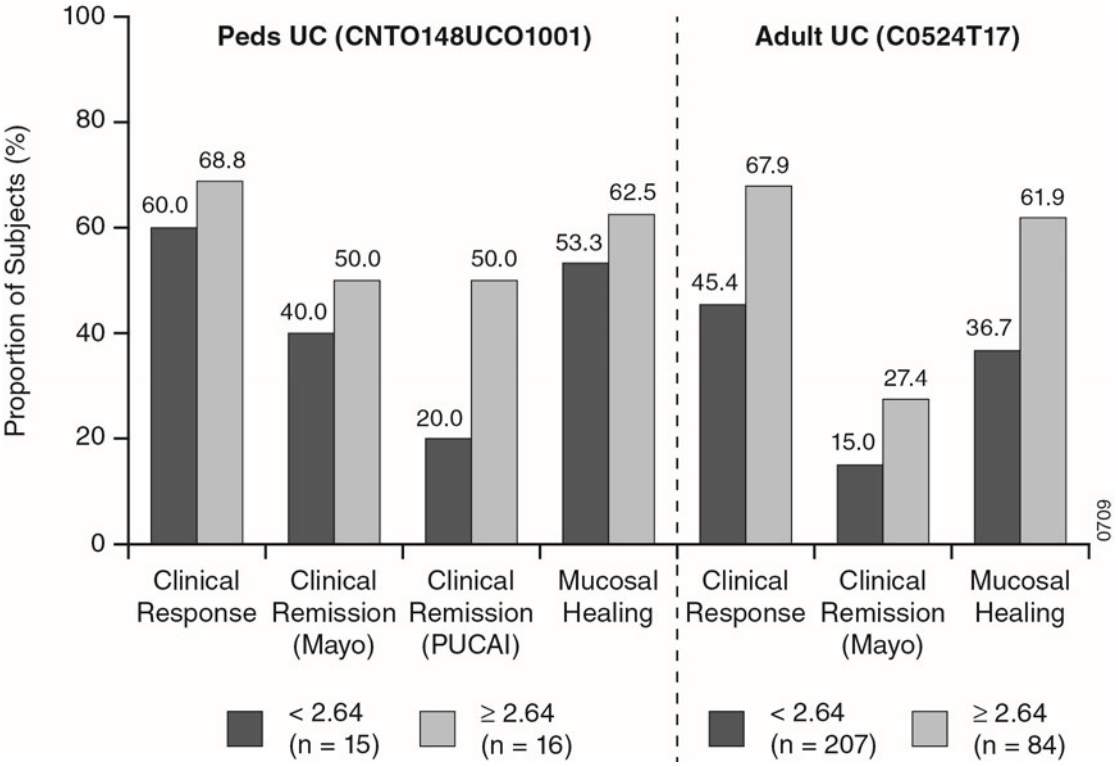
The first study is:

- CNTO148UCO1001 (ongoing): A multicenter, open-label study to assess the PK and safety of golimumab treatment in pediatric participants from 2 to 17 years of age with moderately to severely active UC. This study was divided into 2 parts: the main part of the study was the PK portion through Week 14, and the second part was the study extension. At Week 6, participants in clinical response were eligible to continue receiving open-label maintenance therapy with golimumab and to enter the study extension at Week 14. The study extension through the Week 126 database lock (DBL) is complete. The study extension after Week 126 is still ongoing.

  During the PK portion of the study, at Week 6, Mayo clinical response was induced in 21 of 35 (60.0%) participants, Mayo clinical remission in 15 of 35 (43%) participants, Pediatric Ulcerative Colitis Activity Index Score (PUCAI) clinical remission in 12 of 35 (34%) participants, and mucosal healing (Mayo subscore 0/1) in 19 of 35 (54%) participants.

  Results at Week 14 also demonstrated similarity of PK and a similar exposure-response (E-R) relationship between pediatric UC and adult UC. Figure 2 shows the descriptive E-R analysis of key efficacy endpoints by median serum golimumab concentrations at Week 6 from evaluable participants. Both the pediatric UC and the adult UC studies were each categorized into 2 groups based on the median serum concentration observed in the pediatric UC study: <2.64 µg/mL and ≥2.64 µg/mL.

Figure 2: Descriptive Exposure-response Analysis of Key Efficacy Endpoints by Median Serum Golimumab Concentrations at Week 6



Adapted from: [TEFEP06GAH.rtf] [CNTO148\CNTO148UCO1001\DBR W14\RE W14\tefep06gah.sas] 15JUL2015, 09:33.

Table 4 provides the safety data during the PK portion of the study. The safety profile did not differ from that observed in adults with moderately to severely active UC.

Table 4: Summary of Selected Safety Findings Through Week 14; Treated Subjects (Study CNTO148UCO1001)

	Golimumab
Treated Subjects	35
Average duration of follow up (weeks)	13.1
Average exposure (number of administrations)	3.2
Subjects who died	0
Subjects who discontinued study intervention because of 1 or more adverse events	3 (8.6%)
Subjects with 1 or more:	
Adverse events	33 (94.3%)
Serious adverse events	11 (31.4%)
Infections [a]	13 (37.1%)
Serious infections [a]	0
Neoplasms (malignant)	0
Injection site reactions	6 (17.1%)

[a] Infection as assessed by the investigator.

Adapted from: [TSFAE23.rtf] [CNTO148\CNTO148UCO1001\DBR_W14\RE_W14\tsfae23.sas] 29APR2015, 19:38

Key findings through the Week 126 DBL are summarized as follows:

- Overall, 11 of 20 participants starting the study extension at Week 14 completed the Week 126 visit. Ten of 20 participants (50%) starting the study extension at Week 14 were in clinical remission (PUCAI<10) at Week 110.[21] Safety data from this study extension appear to be consistent with other studies conducted in UC with golimumab.

The second study is:

- CNTO148UCO3003 (this study): A multicenter, randomized, open-label study to assess the efficacy, safety, and PK of golimumab treatment in pediatric participants from 2 to 17 years of age with moderately to severely active UC. In this study, the remission rate on golimumab in these pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints. A study extension is included for eligible golimumab-treated participants. In this study extension, participants will be eligible for at home administration (AHA). Participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in a Usability Assessment Substudy (Appendix 18 [Section 10.18]).

2.2. Background

Ulcerative colitis is a chronic gastrointestinal inflammatory disorder which involves the surface mucosa, the crypt epithelium, and submucosa of the colon.[43] Clinically, participants with UC suffer from diarrhea, rectal bleeding, weight loss, abdominal pain, fever, and may also display prominent extraintestinal manifestations, commonly colitic arthritis and AS.[20,43] Ulcerative colitis is characterized by a life-long chronic course of remissions and exacerbations, with most participants having an acute attack requiring hospitalization at some time during their illness.

Approximately 20% of participants with UC present before the age of 20 years, with disease being extensive in approximately 50% to 80% of these participants.[2,52] While the peak occurrence of pediatric UC is in late adolescence, all ages can be affected, and 4% of pediatric inflammatory bowel disease (IBD) participants are diagnosed in early (age <5 years) childhood.[25] Children aged 2 to 6 years account for approximately 10% of pediatric UC.[16,28] The disease affects equal proportions of males and females.

The overall clinical features, clinical course of the disease, and response to treatment are generally comparable in pediatric and adult populations with UC. However, pediatric-onset UC is often more extensive and severe with a greater prevalence of pancolitis (ie, up to 80% to 90% in pediatric participants compared with approximately 25% in adult participants).[19,39,52]

Overall, the cumulative frequency of colectomy is similar in pediatric- and adult-onset participants with UC.[52] However, the time from diagnosis to first surgery in UC has been reported to be significantly shorter in children compared with adults with UC. Within 10 years of diagnosis, 40.9% of children and 19.9% of adults with UC had undergone colectomy.[52] Colorectal carcinoma rarely occurs during childhood or adolescence.[24] However, the cumulative probability of developing colorectal cancer among adult participants with pediatric-onset UC is slightly higher than that observed among participants with adult-onset UC.[11] Pediatric participants with UC may also experience growth failure and delayed sexual development.[2,20,22]

Although there are multiple therapies in several distinct drug classes approved to treat adult UC, approved pharmacologic treatment options are limited for pediatric participants with UC, especially for those children who have failed to respond to or tolerate conventional therapy (5-aminosalicylate [5-ASA], corticosteroids, or immunomodulators [ie, 6-mercaptopurine (6-MP), azathioprine (AZA), and methotrexate (MTX)]). REMICADE® (infliximab) has been shown to be a safe and effective treatment for pediatric UC.[18] With the approval of infliximab for UC participants 6 years of age and older, pediatric participants with moderately to severely active UC have the treatment option of IV infusions of infliximab administered at Weeks 0, 2, and 6 and every 8 weeks thereafter.

When pharmacologic treatment is no longer effective in managing UC, the only alternative is colectomy. However, colectomy is associated with notable morbidity, particularly in children, along with detrimental impacts on their quality of life (QoL), their probability of conception later in life, and their physical and emotional development at a critical age of personality development.[49,50] As such, there is a need for additional safe and efficacious treatment options for pediatric participants with moderately to severely active UC.

2.3. Benefit/Risk Assessment

Detailed information about the known and expected benefits and risks of golimumab and infliximab may be found in their respective IB.

2.3.1. Known and Potential Benefits

2.3.1.1. Known Benefits

The clinical benefit of golimumab, an anti-TNFα agent approved for the treatment of UC in adults, has not yet been established in moderately to severely active UC in pediatric participants as the clinical development program is ongoing.

While it is possible that the participants in this study may not benefit from the study treatment, a Phase 1 study with golimumab that enrolled children between 2 to 17 years of age with moderate to severely active UC showed that continued clinical benefit was observed in children with UC who received golimumab q4w maintenance therapy through Week 110 as assessed by PUCAI scores.

The clinical benefit of infliximab is known, as infliximab has been demonstrated to be safe and efficacious for the treatment of moderately to severely active UC in pediatric patients (aged 6 to 17 years) and has been approved for this indication in multiple jurisdictions globally.

2.3.1.2. Potential Benefits

Participants in this study will be children 2 to 17 years of age with moderately to severely active UC. As golimumab has already been established as safe and efficacious for adults with moderately to severely active UC, the Sponsor anticipates that pediatric participants with UC are likely to benefit from treatment with golimumab as well, at least commensurate with that demonstrated in the adult studies of golimumab in UC. This is supported by our observations in CNTO148UCO1001, a Phase 1b multicenter, open-label study of golimumab in pediatric participants with moderately to severely active UC. This study, though of limited size, demonstrates that pediatric and adult golimumab pharmacokinetics are similar. Moreover, clinical benefit was suggested in these biologically naive pediatric participants with UC.[21] Participants may also have some benefit from the participation in a clinical trial irrespective of receiving study treatment, due to regular visits and assessments monitoring their overall health. Lastly, while not directly benefitting the participant, results from this clinical study will support a new indication for golimumab in treating moderately to severely active UC in pediatric participants aged 2 to 17 years, which would benefit other pediatric UC participants.

2.3.2. Known and Potential Risks

2.3.2.1. Known Risks

All therapies have the potential to cause adverse experiences. The anti-TNFα class of agents has been extensively studied in adults and pediatric participants and has a well-defined safety profile. Known risks for anti-TNFα agents such as golimumab and infliximab include infections, serious infections, tuberculosis (TB), and opportunistic infections. Other known risks include but are not limited to lymphoma, leukemia, lupus-like syndrome, and demyelinating disorders.

2.3.2.2. Potential Risks

A potential risk for the development of other malignancies and exposure during pregnancy are common to both golimumab and infliximab. In addition, for participants treated with golimumab, serious depression (including suicidality), and serum sickness are additional potential risks which cannot be excluded.

Detailed information about the safety profile and risks for golimumab, including a table of adverse drug reactions, may be found in the golimumab IB.

Detailed information about the safety profile and risks for infliximab, including a table of adverse drug reactions, may be found in the infliximab IB.

2.3.3. Overall Benefit: Risk Assessment

Based on the available data and proposed safety measures, the overall benefit: risk assessment for using golimumab in this clinical study is deemed acceptable based on the following considerations.

Disease morbidity: Pediatric UC is a debilitating disease that inflicts significant morbidity in participants and for which available treatments still impose a substantial burden on both participants and caregivers. Approved pharmacologic treatment options are limited for pediatric UC participants, especially for those children who have failed to respond to conventional therapy (5-ASAs, immunomodulators [6-MP, AZA, or MTX], or corticosteroids). Often, when medical therapies fail, the only alternative is colectomy, which is itself associated with notable morbidity, particularly in children. Colectomy can impact the child's QoL, can contribute to fertility issues later in life, and can be detrimental to the child's physical and emotional development.

UC Disease Similarity in Adults and Children: The basic pathogenesis and etiology of UC is likely the same in the pediatric and adult populations. Adult and pediatric genome-wide association scans have yet to identify risk variants that are specific to pediatric or adult UC,[34] although several risk variants have recently been identified in UC.[31] Ulcerative colitis is characterized by an abnormal and exacerbated immune response against mucosal constituents and components of the luminal flora in individuals with a genetic predisposition. Early preclinical and clinical data suggested that TNFα plays an important role in the pathogenesis of UC. In rodent models of chronic colitis, anti-TNFα antibodies downregulate production or activity of inflammatory cytokines and reduce the severity of intestinal inflammation.[27,29] In participants with UC, serum concentrations of TNFα and interleukin -6 have been shown to be elevated during active disease and to decrease during disease remission.[24,26,35] Braegger et al[6] demonstrated that elevated TNFα in the stool of participants with UC was a marker of disease activity.

These data led to the initiation of clinical studies to assess the efficacy and safety of the anti-TNFα agent infliximab. Subsequently, the positive outcomes of the randomized, placebo controlled clinical trials of the anti-TNFα infliximab, in the treatment of adults with moderate to severely active UC (ACT 1 and ACT 2[10,30,33]) provided further support for the role of TNFα in the pathogenesis of UC.

Benefit: Risk of Golimumab

Golimumab is the third anti-TNFα agent approved for the treatment of UC in adults, and its efficacy and safety have been demonstrated in adequate and well-controlled studies in adults with UC. Currently, the only approved anti-TNFα treatment option for pediatric participants with moderately to severely active UC is infliximab. Although infliximab is an effective treatment, it is administered IV by healthcare professionals in a clinic or hospital setting and may be inconvenient for pediatric participants and their caregivers. Moreover, infliximab is approved only for participants 6 years and above, which means pediatric UC participants between 2 and 6 have no approved anti-TNFα biologic therapies available to them.

Based upon their overall positive benefit: risk profile, TNFα-blockers such as etanercept, infliximab, adalimumab, and golimumab, have been studied in a number of pediatric autoimmune conditions such as pJIA, psoriasis, Crohn's disease, and UC and have been registered for pediatric indications globally. Golimumab was studied for pJIA in 173 children 2 years old and above.

For pediatric UC, there have been several supportive studies as well. Infliximab was approved in children 6 years old and above with Crohn's disease and UC. Moreover, as described in Section 2.1, the efficacy and safety of golimumab in pediatric UC has been tested in a small study of 35 children, ages 6 to 17 years (CNTO148UCO1001), which is presently in its study extension. Median serum golimumab concentrations in this group were comparable with a historical reference adult UC population at Weeks 2, 4, and 6. At Week 6, 60%, 34%, and 54%, of participants achieved Mayo clinical response, PUCAI clinical remission, and mucosal healing (Mayo subscore 0/1). A planned DBL of the study extension was conducted at Week 126. Overall, 11 of 20 participants starting the study extension at Week 14 completed the Week 126 visit. Ten of 20 participants (50%) starting the study extension at Week 14 were in clinical remission (PUCAI<10) at Week 110.[21]

Thus far, pediatric use of golimumab has been well tolerated in studies (CNTO148DML2001 [to arrest β-cell loss in Type 1 Diabetes], CNTO148JIA3003 [treatment of pJIA], CNTO148UCO1001 [treatment of UC], and CNTO148JIA3001 [treatment of pJIA]) with pediatric participants of 2 to 17 years of age. In general, the safety profile of golimumab in the pJIA and pediatric UC studies, including the type and frequency of the adverse reactions seen, is consistent with the known safety profile for the adult populations studied and consistent with other TNFα inhibitors. No new safety signals have been observed in pediatric populations using golimumab.

Benefit: Risk of Infliximab

The efficacy and safety of infliximab has been evaluated in adult subjects with moderately to severely active UC in 3 completed clinical studies: C0168T12, C0168T37 (ACT 1), and C0168T46 (ACT 2). Both ACT 1 and ACT 2 achieved the primary endpoint of clinical response at Week 8 (ACT 1: infliximab 5 mg/kg and 10 mg/kg [69.4% and 61.5%, respectively, versus placebo 37.2%; both p <0.001]; ACT 2: infliximab 5 mg/kg and 10 mg/kg [64.5% and 69.2%, respectively, versus placebo; 29.3%; both p <0.001]).

Approximately 500 adult subjects with UC have been treated with infliximab during clinical studies. The percentage of subjects who died or experienced malignancies during the clinical studies was <1%. Although serious infections did occur in ACT 1 and ACT 2, the overall occurrence was low: 3.9% in the combined infliximab group versus 2.5% in the placebo group.

The C0168T72 study was a Phase 3, randomized, open-label, parallel-group, multicenter study to assess the safety and efficacy of induction and maintenance infliximab treatment in pediatric subjects aged 6 through 17 years who had moderately to severely active UC (defined as a Mayo score of 6 to 12, inclusive, at baseline, including an endoscopic subscore ≥2). The study showed that infliximab 5 mg/kg administered at Weeks 0, 2, and 6 was efficacious in pediatric subjects with UC, with efficacy consistent with that seen in adults with UC in the infliximab 5 mg/kg group from the pooled ACT studies (73.3% and 66.9%, respectively, for the proportion of subjects in clinical response).

Infliximab was generally well tolerated in the pediatric UC population, with a safety profile consistent with that reported in other studies. There were no reports of deaths, malignancies, opportunistic infections, serious neurologic events, or TB and the safety profiles observed in the every 8 weeks (q8w) and every 12 weeks (q12w) maintenance treatment groups were similar. No new safety signals have been observed in pediatric populations using infliximab.

The conventional posology, however, is thought to be inadequate for certain groups of patients. In order to better mimic current clinical practice, this protocol permits step-wise dose escalation of infliximab (to a maximum of 10 mg/kg [capped at 1gm] q4w). This approach has been discussed and deemed appropriate by US Food and Drug Administration (FDA) and Pediatric Committee of the European Medicines Association, as well as experts in pediatric IBD in the US and EU. Real world experience has demonstrated that there is a need for more intensive dosing in patients in the setting of acute severe colitis or in patients with a flare in their UC due to a secondary loss of response.

Trough levels of infliximab tend to be lower in patients with acute severe colitis.[37,51] Higher rates of remission and lower rates of colectomy have been reported in UC patients treated with escalated dosing of infliximab in adults[13] and pediatric patients,[1,17] and these observations and clinical practice are being reflected in new guidelines for the management of acute severe colitis in pediatric patients.[48] Similarly, secondary loss of response (LOR) to infliximab after an initial response occurs in 20-40% of all IBD patients after 1 year of therapy.[4,5] Several studies in IBD broadly[14] and UC more specifically[41,38] have found significant clinical benefit in escalating infliximab dosing, with response rates generally between 25-45% and avoidance of the need for colectomy.[44] Small retrospective studies in psoriasis[45] and IBD[8,15] have found that dose escalation is generally well tolerated and not associated with new safety signals. These benefits in clinical response and avoidance of colectomy have offset concerns about the risks of infection and other side effects from the escalated infliximab dosing.

Additional Measures for Study Safety: Use of golimumab and other TNFα-blockers for both adults and children includes routine evaluation of safety. Participants in this study will be extensively evaluated during screening and excluded from participation if they have any relevant risk factors for TNFα-blockers or golimumab use, to limit the chance of untoward and adverse effects in this study.

Study sites are selected based on proven experience and qualification to run pediatric UC studies.

An internal Data Monitoring Committee (DMC) comprised of experienced medical personnel not involved in the conduct of this study, will be in place prior to the start of the study and will perform unblinded review of individual participant and cumulative safety data. The DMC will monitor data until all participants reach the Week 54 visit or terminate the study prior to the Week 54 visit (for additional details, see Section 9.5).

Criteria are established for discontinuation of treatment in individual participants, and study termination (Section 7).

More detailed information about the known and expected benefits and risks of golimumab and infliximab may be found in the respective IBs.

3. OBJECTIVES AND ENDPOINTS

Primary Objectives

- To evaluate the efficacy of golimumab in inducing clinical remission as assessed by the Mayo score, in pediatric participants with moderately to severely active UC.
- To evaluate the safety profile of golimumab, in pediatric participants with moderately to severely active UC.

Secondary Objectives

- To evaluate the efficacy of golimumab in inducing clinical response as assessed by the Mayo Score and clinical remission as measured by the PUCAI Score.
- To evaluate the efficacy of golimumab on endoscopic healing.
- To evaluate the efficacy of golimumab during the long-term phase.
- To evaluate the effect of golimumab on additional efficacy and QoL measures.
- To evaluate the PK and exposure-response of golimumab during short- and long-term phases.

Additional Objective (Usability Assessment Substudy)

- To evaluate the potential for at home use of golimumab in the participant population during the Usability Assessment Substudy.

3.1. ENDPOINTS

Primary Endpoint

The primary endpoint is clinical remission at Week 6 as assessed by the Mayo score.

Clinical remission as measured by the Mayo score is defined as a Mayo score ≤2 points, with no individual subscore >1 (based on Mayo endoscopy subscore assigned by the local endoscopist).

Major Secondary Endpoints

For endpoints beyond Week 6, analyses will be performed on participants who are in clinical response at Week 6 as assessed by the Mayo score.

1. Symptomatic remission at Week 54.
2. Clinical remission at Week 54 as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).
3. Clinical remission at Week 54 as assessed by the PUCAI score.
4. Clinical remission at Week 6 as assessed by the PUCAI score.
5. Clinical response at Week 6 as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).

6. Endoscopic healing at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).
7. Endoscopic healing at Week 54 (based on Mayo endoscopy subscore assigned by the local endoscopist).
8. Clinical remission at Week 54, as assessed by the Mayo score, for participants who are in clinical remission at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).
9. Participants who were not receiving corticosteroids for at least 12 Weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).

The efficacy endpoint definitions are as follows:

- Symptomatic remission: Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0.
- Clinical response: a decrease from baseline in the Mayo score of ≥30% and ≥3 points, with either a decrease from baseline in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1.
- Clinical remission as measured by the PUCAI score: a PUCAI score <10.
- Endoscopic healing: an endoscopy subscore of the Mayo score of 0 or 1.

HYPOTHESIS

Golimumab is an effective therapy in pediatric UC participants relative to historical placebo outcomes for clinical remission in adults based on the Mayo score.

4. STUDY DESIGN

4.1. Overall Design

This is a multicenter, randomized, open-label golimumab study in pediatric participants aged 2 to 17 years with moderately to severely active UC, defined as a baseline Mayo score of 6 through 12, inclusive, with an endoscopy subscore of ≥2. Additionally, all study participants must have demonstrated an inadequate response to, have failed to tolerate, or have a medical contraindication to conventional therapies (ie, IV or oral corticosteroids or the immunomodulators MTX, AZA, or 6-MP); or, demonstrated corticosteroid dependence; or, require repeated (>3 per year) courses of corticosteroids. Participants with prior exposure to biologic anti-TNFα agents will be ineligible for participation.

In this study, the remission rate on golimumab in pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 UC studies of golimumab and 5 adult Phase 3 studies of other biologic products approved in this indication utilizing similar populations and endpoints. For additional details see Sections 4.2.1, 9.1, and 9.2.

This study also includes an infliximab arm. Upon implementation of Amendment 4, no additional participants will be randomized to the infliximab arm; all newly enrolled participants will receive golimumab. No formal comparisons between golimumab and infliximab will be performed.

Prior to Amendment 4, approximately 125 participants who satisfy inclusion/exclusion criteria were to be included in the study at sites located globally, including in North and South America, Asia, and Europe. At least 24 golimumab participants with body weight <45 kg, and at least 5 golimumab participants with body weight <30 kg will be included.

In order to ensure that at least 5 participants <30 kg receive golimumab, participants who weigh <30 kg were to only be allocated to the golimumab treatment arm. The remaining 120 participants were to be randomized in a 3:1 ratio to golimumab or infliximab, respectively.

Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.

Upon implementation of Amendment 5, no new participants will be enrolled. Approximately 70 participants will participate in this study (at least 60 participants will receive golimumab, at least 10 participants will receive infliximab). Of the 60 golimumab participants, at least 15 will have a body weight <45 kg and at least 5 will have a body weight <30 kg.

Participants must weigh ≥10 kg and be >70 cm tall. This is the lower range of weight and height that the Prefilled Pen-Varioject (PFP-V) has been validated for to deliver SC golimumab. This limit accommodates >97% of all 2-year old girls based on published growth charts.[54] If a study participant's weight falls below 10 kg after Week 10, the study intervention must be withheld until their body weight is ≥10 kg. If they miss 2 consecutive doses of golimumab because of body weight below this 10 kg limit, the study intervention should be discontinued.

The following concomitant medications for UC are allowed in this study: 5-ASAs, corticosteroids, and immunomodulators (ie, 6-MP, AZA, MTX). Dosages of these concomitant medications must be stable for 2 weeks prior to first administration of study intervention at Week 0. For participants receiving 5-ASAs at Week 0, the dose must remain stable through Week 54 (except for weight-based adjustments, as treatment for a documented UC flare after Week 6, or if investigator judgment requires dose reduction or cessation because of toxicity or medical necessity (Section 6.5.3)). For participants receiving immunomodulators at Week 0, the dose should not be increased (except for weight-based adjustments) through Week 6. Although immunomodulators may be discontinued or the dose reduced at any time during the study, it is preferred, at the discretion of the investigator, that they be continued at least through Week 14. For participants receiving corticosteroids, the steroids may be tapered beginning at Week 0, although it would be preferable to delay the stopping of steroids until after the Week 6 evaluation if clinically reasonable. UC-specific medical therapies (ie, oral/rectal corticosteroids, oral/rectal 5-aminosalicylate (5-ASA) compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX]) may not be initiated or their dose increased at any time after Week 6 to Week 54 except for weight-based dose adjustments or unless there is a documented UC flare and loss of response

that makes the subject eligible for rescue medication (Section 6.5.3). For additional details regarding UC-specific allowed concomitant therapies, see Section 6.5.1.

This 54-week study will consist of a 6-week short-term phase and a 48-week long-term phase followed by a study extension (for eligible golimumab-treated participants) as presented in Figure 1.

Short-term Phase (Weeks 0 to 6)

Prior to Protocol Amendment 4, the randomization scheme below was followed.

At Week 0, participants ≥30 kg were randomized 3:1 to either Group 1 or Group 2. All participants <30 kg were placed in Group 1.

Group 1 - golimumab SC at Weeks 0 and 2

- Participants with body weight ≥45 kg will receive fixed induction doses of 200 mg at Week 0 and 100 mg at Week 2.
- Participants with body weight <45 kg will receive body-surface area (BSA)-adjusted induction doses of 120 mg/m^2 (up to a maximum of 200 mg) at Week 0 and 60 mg/m^2 (up to a maximum of 100 mg) at Week 2.

Group 2 - Infliximab 5 mg/kg IV at Weeks 0 and 2 (participants ≥30 kg only)

Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.

At Week 6, golimumab and infliximab participants will undergo sigmoidoscopy (or colonoscopy at the investigator's discretion) and will be evaluated for efficacy, PK, and safety. Exposure-response analysis for golimumab participants will be based on the PK and efficacy assessments conducted at Week 6.

Long-term Phase (Week 6 through Week 54)

Group 1 (Golimumab): At Week 6, participants in clinical response to golimumab (as evaluated by the Mayo score using the local read for the sigmoidoscopy subscore) will continue to receive SC golimumab 100 mg or 60 mg/m^2 q4w through Week 50. Participants not in clinical response at Week 6, may (at the discretion of the investigator) receive 2 additional doses of golimumab (ie, at Week 6 and Week 10). Of these participants, those who are partial Mayo responders at Week 14 (defined as a decrease from the Week 0 partial Mayo score of ≥3 points) will continue to receive SC golimumab 100 mg or 60 mg/m^2 q4w through Week 50. Participants who are not in partial Mayo response at Week 14 will be withdrawn from further study intervention administrations and complete a final safety follow-up period of 16 weeks (more than 5.5 half-lives for SC golimumab) following the last administration of study intervention.

Group 2 (Infliximab): At Week 6, participants in clinical response to infliximab (as evaluated by the Mayo score using the local read for the sigmoidoscopy subscore) will continue to receive IV infliximab 5 mg/kg administered q8w through Week 46. The infliximab arm permits flexible dose

escalation based on clinical response. Participants not in clinical response at Week 6 (as evaluated by the Mayo score) may be considered for an increased dose of infliximab (to 10 mg/kg [capped at 1 gm] at Week 6 and q8w thereafter or 5 mg/kg at Weeks 6 and 8, and 10 mg/kg (capped at 1 gm) at Week 14 and q8w thereafter, respectively). Participants who have achieved a partial Mayo response at Week 14 (defined as a decrease from the Week 0 partial Mayo score of ≥3 points) should continue receiving infliximab at 10 mg/kg q8w through Week 46. For participants not in partial Mayo response, they may also be considered for a change of the dosage interval to q4w. At Week 22, those participants who received an escalation in their infliximab dosing to 10 mg/kg q4w will need to demonstrate a partial Mayo response (defined as a decrease from the Week 0 partial Mayo score of ≥3 points) to continue in the study. Participants in partial Mayo response will continue receiving open-label infliximab 10 mg/kg (capped at 1 gm) q4w through Week 46. Participants who are not in partial Mayo response at Week 22 will have study intervention discontinued and should complete a final safety follow-up at least 8 weeks following the last administration of infliximab.

A clinical flare in UC is defined as an increase from the start of the long-term phase ([Week 6] in the partial Mayo score of at least 2 points **and** an absolute partial Mayo score ≥4; **or** an absolute partial Mayo score ≥7 points. Participants who experience a flare in their UC disease (defined in Section 6.5.3) from Week 6 onward may initiate this step-wise dose escalation at any time to the maximum of 10 mg/kg (capped at 1gm) q4w. Participants who dose-escalate in response to a UC flare will be reassessed after 2 administrations at the final escalated dose. Participants in partial Mayo response (ie, a decrease from flare baseline of ≥2 in the partial Mayo score) will continue receiving open-label infliximab through Week 46 at the escalated dose. Participants who have not achieved a partial Mayo response will be discontinued from study intervention administration and should return for a final safety visit at least 8 weeks after their last infliximab administration.

After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have the Week 54 or Early Termination visit.

Lastly, while escalation should be based on clinical criteria as described above, investigators at their discretion, may utilize infliximab serum levels to assist their decision making in this flexible dosing approach.

Assessments during the long-term phase for both groups include efficacy, PK, and safety.

At Week 54, all participants remaining in the study will undergo a sigmoidoscopy (or colonoscopy at the investigator's discretion) to permit a full Mayo score efficacy determination.

Study extension (Week 54 to end of study)

Group 1 (Golimumab): Following the Week 54 evaluations (end of the main pivotal study), participants who are receiving benefit from golimumab, at the discretion of the investigator, may continue to receive SC golimumab q4w in an extension period until one of the following conditions below is met, whichever occurs first:

1. marketing authorization is obtained for golimumab for the treatment of pediatric participants with UC and golimumab is either commercially available or 2 years have lapsed since marketing authorization, or
2. the participant turns 18 years of age and has access to commercially available golimumab, or
3. until a decision is made by the sponsor not to pursue an indication in this pediatric UC population.

Beginning with the Week 54 evaluations, participants in those regions where the adult maintenance posology is weight-based (eg, 50 mg for those weighing ≤80 kg and 100 mg for those weighing >80 kg) may make a one-time reduction in their golimumab dose to 50 mg q4w. Participants may return to the golimumab 100 mg q4w dosing at the discretion of the investigator, but then no additional changes in dosing can be made for the duration of the study extension.

Beginning with Week 58, eligible participants or their caregivers will have the option to administer golimumab at home after being properly trained (see below; At Home Administration).

Group 2 (Infliximab): After the Week 54 evaluations, participants receiving infliximab will be withdrawn from study participation and transition to local standard of care which may include continued commercially available infliximab at the discretion of their physician.

At Home Administration

At any time after Week 54 (Week 58 at the earliest), participants who are eligible to continue receiving golimumab in the study extension will be offered the option for self-administration (at least 12 years old) or caregiver administration (any age; Appendix 18 [Section 10.18]). This is optional; if a pediatric participant or caregiver elects against self- or caregiver administration, the health care professional (HCP) will continue to administer injections in this study.

All participants who elect AHA of the study intervention will receive a face-to-face training from study site staff on the use of the Prefilled Syringe with UltraSafe (PFS-U) or the Prefilled Pen-Varioject (PFP-V). Training for AHA will occur over 3 q4w administration visits beginning as early as Week 58. Participants will complete a training administration at the first visit, using the PFS-U or PFP-V device at the clinic under the observation/supervision of site staff. Site staff will complete an observer checklist (Appendix 10 [Section 10.10]). An HCP will determine whether a participant (≥12 years of age) or their caregiver (participant may be any age) can perform the injections. The 2 remaining self- or caregiver-dose administrations will be performed in the clinic by the participants or their caregivers, with site staff available for any questions, and should be performed by the person who received the appropriate training. Participants may elect at any time during the study extension to have golimumab administered by an HCP or return entirely to HCP administration of study intervention.

Participants will be observed for at least 30 minutes after the administration of study intervention for symptoms of an injection-site reaction at the investigative site.

In addition to recording the details of the study intervention, dosing day, time, anatomic site and if there were any complications of the injection, participants and/or caregivers should be instructed

to monitor the injection-site for any reactions, including, but not limited to swelling, redness/erythema, pain, tenderness, warmth, bruising, or bleeding. All dosing and adverse event (AE) (including injection-site reaction) information, as well as concomitant medications and TB exposure will be documented in an AHA diary, that is to be returned to the site at the upcoming visit and entered by site staff into the electronic case report form (eCRF). For any severe injection-site reactions, or changes at the injection-site, or any mild to moderate to severe golimumab reaction which occur hours to days following injection, the participant/caregiver should contact the study site for consultation. Acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and/or diphenhydramine or locally available alternative may be administered at the investigators' direction. In case of a severe allergic reaction (eg, anaphylaxis, difficulty breathing, light-headedness, hives, or widely spread body rash), participants or their caregivers should call for emergency medical assistance (paramedic or ambulance) first before contacting the study site.

All product quality device complaints (PQC) and device-related AEs will be collected and investigated. For additional details on PQC procedures, see Appendix 16 (Section 10.16).

Usability Assessment Substudy

Participants at certain study sites entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in an Usability Assessment Substudy (Appendix 18 [Section 10.18]). An attempt will be made to enroll approximately 10-20 participants in the Usability Assessment Substudy at Week 58. Participants administering study intervention at home will receive detailed instructions on how to monitor and report potential injection-site reactions.

For all AHAs of golimumab beginning at Week 58, the details of the study intervention, dosing day, time, anatomic site and if there were any complications of the injection, as well as AE (including injection-site reaction), concomitant medications and TB exposure information will be documented in an AHA diary, that is to be returned to the site at the upcoming visit, and entered by site staff into the eCRF.

Details of the Substudy are provided in Appendix 9 (Section 10.9) and Appendix 18 (Section 10.18).

Database Locks (DBL)

There are 2 planned DBLs in this study:

- The first DBL will occur when all participants have either completed the Week 54 visit or terminated the study prior to Week 54. This DBL may also include data from the Usability Assessment Substudy questionnaire.
- A final DBL will occur when all participants who entered the study extension have either completed the final visit or have terminated study participation.

Additional DBLs other than the 2 specified above may be performed.

Data Monitoring Committee (DMC)

An internal DMC (consisting of Sponsor members [a gastroenterologist, a clinician, and a statistician at a minimum] outside of the study team), will be established to monitor safety data (for both golimumab and infliximab treatments arms) on an ongoing basis until all participants reach the Week 54 visit or terminate the study prior to the Week 54 visit (Section 9.5).

4.2. Scientific Rationale for Study Design

4.2.1. Historical Placebo

The primary analysis will involve a formal statistical comparison to a historical adult placebo remission rate derived from a meta-analysis of 2 Phase 2/3 UC studies of golimumab and 5 Phase 3 studies of other products approved in this indication (for additional details see Sections 9.1 and 9.2) utilizing similar endpoints (clinical remission as assessed by the Mayo Score), populations, and methodologies for endpoint determination (clinical remission as determined by the local endoscopy). This approach of comparing to a historical adult placebo control has been discussed with health authorities (both US and EU) and is similar to the approach employed for infliximab approval in pediatric UC.

To ensure a robust estimate of the placebo remission rate, the Sponsor has derived a historical adult placebo remission rate from a meta-analysis of placebo-controlled studies that met the following criteria:

- Supported successful biologic product registration in UC
- Had similar study design and endpoints (ie, Mayo score remission)
- Utilized local (versus central) endoscopic reading
- Enrolled similar participant populations (eg, participants with moderately to severely active UC)
- Enrolled TNFα-naïve populations or had publicly available information on the subgroup of enrolled participants who were TNFα-naïve

Based on the above criteria, a total of 7 adult UC studies including infliximab Phase 3 (C0168T37 and C0168T46), golimumab Phase 2/3 (C0524T16 and C0524T17), adalimumab Phase 3 (ULTRA 1 and ULTRA 2), and vedolizumab Phase 3 (GEMINI 1) are included in the meta-analysis of the historical adult UC placebo remission rate. Combined, these studies have a total of 988 placebo participants.

The meta-analysis was conducted by taking the weighted average of the point estimate for clinical remission from the various studies, where the study weight is the inverse of the standard error. The studies with smaller standard error and larger sample sizes provide more weight. The estimate of the historical adult UC placebo remission rate based on the meta-analysis is 8.3% (95% confidence interval (CI): 6.6%, 10.0%).

4.2.2. Infliximab

Infliximab, a mouse-human chimeric anti-TNFα mAb, was the first anti-TNFα therapy approved for the treatment of adult and pediatric participants with moderately to severely active UC who had an inadequate response to conventional therapies.

In response to a request from health authorities, an infliximab reference arm was included in this proposed study to assess assay sensitivity (primarily relying on PUCAI and partial Mayo scores) in comparison to historical data from the infliximab C0168T72 pediatric UC study. Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab, and assay sensitivity will not be assessed. This amendment to the infliximab arm was discussed with health authorities and it was accepted that enrollment into the infliximab arm could be stopped.

Participants who weigh <30 kg will not be eligible for infliximab, as this rare subpopulation will only be allocated to the golimumab treatment arm.

Participants in the infliximab arm will receive initial treatment of 5 mg/kg Weeks 0, 2, and 6 then q8w through Week 46 if in clinical response. For participants not in clinical response or who have lost clinical response and experience a flare in their UC, a step-wise flexible dosing approach will be permitted in the infliximab arm only. This approach was chosen as it most closely mimics clinical practice in treatment of pediatric UC, allowing investigators some flexibility in dosing to treat their participants.

Specifically, participants in the infliximab arm will receive IV infliximab 5 mg/kg at Weeks 0 and 2. At Week 6, participants in clinical response to infliximab (as evaluated by the Mayo score) will continue to receive IV infliximab 5 mg/kg administered q8w through Week 46. After the Week 54 evaluations, participants receiving infliximab will be transitioned off the study to standard medical care.

Participants not in clinical response at Week 6, will be considered for an increased dose of infliximab (10 mg/kg [capped at 1 gm] at Week 6 and q8w thereafter or 5 mg/kg at Weeks 6 and 8 and 10 mg/kg [capped at 1 gm] starting at Week 14 and q8w thereafter, respectively) at the discretion of the investigator. Participants who demonstrate a partial Mayo response (defined as a decrease from the Week 0 partial Mayo score of ≥3 points) at Week 14 will continue to receive infliximab 10 mg/kg [capped at 1 gm] q8w through Week 46. Participants not in partial Mayo response may also be considered for a change of the dosage interval to q4w. At Week 22, participants who demonstrate a partial Mayo response (defined as a decrease from the Week 0 partial Mayo score of ≥3 points) will be able to continue in the study and receive infliximab 10 mg/kg (capped at 1 gm) q4w through Week 46. Participants who are not partial Mayo responders at Week 22 will have study intervention discontinued and should complete a final safety follow-up at least 8 weeks following the last of infliximab administration.

Participants who experience a flare in their UC disease (defined in Section 6.5.3) after Week 6 may initiate this step-wise dose escalation at any time to the maximum of 10 mg/kg (capped at 1 gm) q4w. Participants who dose-escalate in response to a UC flare will be reassessed after 2

administrations at the final new higher dose. Participants in partial Mayo response (ie, a decrease from flare baseline of ≥2 in the partial Mayo score) will continue receiving open-label infliximab through Week 46 at the escalated dosage. Participants who have not achieved a partial Mayo response will be discontinued from study intervention administration and should return for a final safety visit at least 8 weeks after their last infliximab administration. After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have Week 54 or Early Termination visit. Importantly, while escalation should be based on clinical criteria as described above, investigators, may utilize infliximab serum levels to assist their decision making in this flexible dosing approach.

Lastly, after the Week 54 evaluations, participants receiving infliximab will be withdrawn from study participation and transition to local standard of care which may include continued commercially available infliximab at the discretion of their physician.

4.2.3. Biomarker Collection

Biomarker samples will be collected to explain interindividual variability in clinical outcomes or may help to identify population subgroups that respond differently to an intervention. The goal of the biomarker analyses is to evaluate the PD of golimumab and aid in evaluating the intervention-clinical response relationship.

Biomarker samples may be used to help address emerging issues and to enable the development of safer, more effective, and ultimately individualized therapies. The RNA blood sample should not be collected at any time point for any participant who at Screening has a body weight of 10 kg to <12.3 kg, even if the weight increases to above 12.3 kg during the study. For participants who weighed more at Screening but whose body weight falls to between 10 kg to <12.3 kg, the RNA blood sample should not be collected.

4.2.4. Study-Specific Ethical Design Considerations

Potential participants will be fully informed of the risks and requirements of the study and, during the study, participants will be given any new information that may affect their decision to continue participation. They will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only participants who are fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

When referring to the signing of the Informed Consent Form (ICF), the terms legal guardian and legally acceptable representative refer to the legally appointed guardian of the child with authority to authorize participation in research. For each participant, his or her parent(s) (preferably both parents, if available) or legally acceptable representative(s), as required by local regulations, must give written consent (permission) according to local requirements after the nature of the study has been fully explained and before the performance of any study-related assessments. Assent must be obtained from children (minors) capable of understanding the nature of the study, typically

participants 7 years of age and older, depending on the institutional policies and national/local guidelines. For the purposes of this study, all references to participants who have provided consent (and assent as applicable) refers to the participants and his or her parent(s) or the participant's legal guardian(s) or legally acceptable representative(s) who have provided consent according to this process. Minors who assent to a study and later withdraw that assent should not be maintained in the study against their will, even if their parent(s) still want them to participate.

The total blood volume to be collected is considered to be an acceptable amount of blood to be collected over this time period from the population in this study. Total blood volume to be collected in this study is in line with the allowable blood sample volumes described in the EU guideline on clinical trials conducted with minors (EU Guideline: Ethical considerations for clinical trials on medicinal products conducted with minors [Rev 1; 18 Sep 2017]).[12]

4.3. Justification for Dose

Golimumab: As the pediatric UC development program for golimumab is a global program, the choice of the 100 mg or its BSA equivalent (60 mg/m^2) where applicable, will facilitate evaluation of the efficacy and safety with a dose that is equivalent to the adult UC maintenance dose of golimumab which is relevant across all regions and is consistent with the approach to dosing that was used in study CNTO148UCO1001. After the evaluation of the key maintenance endpoints at Week 54, investigators will have the option to decrease the maintenance dose to mimic local labeling posology as applicable.

The following golimumab doses will be evaluated in this Phase 3 pediatric study:

- Participants ≥45kg: Short-term phase 200 mg at Week 0 and 100 mg at Week 2; Long-term phase 100 mg q4w from Week 6
- Participants <45kg: Short-term phase - 120 mg/m^2 at Week 0 and 60 mg/m^2 at Week 2; Long-term phase 60 mg/m^2 q4w from Week 6

The golimumab dosages planned for this Phase 3 study were determined based on data from the adult golimumab UC studies and the Phase 1 pediatric UC study (CNTO148UCO1001). Based on the assumption of similarity in disease and response to treatment between pediatric and adult participants with UC, the golimumab dosage in this pediatric study aims to attain systemic exposures in children similar to those established to be safe and effective in adult participants with UC.

A BSA-based dose adjustment was conservatively adopted for pediatric participants with lower body weight in order to minimize the variability of golimumab exposure across the pediatric age continuum. The expectation of consistent exposure following BSA-adjusted posology has been confirmed in a clinical trial of golimumab in pediatric participants with pJIA), where similar golimumab exposure was achieved across the pediatric age (2 to 17 years) and body weight (11 to 110 kg) ranges compared with exposures in adults, using a BSA-based adjusted dosing regimen. Unlike the pJIA study which employed BSA-dose adjustment across the entire pediatric weight range, BSA-dose adjustment is limited to those with body weight <45 kg in this pediatric UC

study. This dosing approach in pediatric UC is supported by PK simulations which demonstrated that using a 45-kg body weight cut-off to transition from a BSA-adjusted dose to the corresponding fixed adult dose would achieve golimumab systemic exposures in pediatric participants that are comparable with exposures achieved in adults with UC.

With respect to the short-term phase (induction) in this study, the golimumab dosage is expected to provide exposure similar to that observed for the approved adult dosage of 200 mg → 100 mg at Week 0 and Week 2, respectively. In the Phase 1 pediatric UC study (CNTO148UCO1001), pediatric participants with UC with body weight <45 kg who received golimumab 90 mg/m^2 → 45 mg/m^2 BSA-adjusted dose regimen (at Week 0 and Week 2, respectively) achieved lower relative mean golimumab concentrations when compared with the reference adult UC population who received golimumab 200 mg → 100 mg. Accordingly, in the present Phase 3 study, higher BSA-adjusted doses of 120 mg/m^2 → 60 mg/m^2 will be employed to more closely match the exposure in the reference adult UC population. These higher golimumab BSA-adjusted doses are supported by PK modeling and simulation analyses.

With respect to the long-term phase (maintenance), the reference adult dose of 100 mg (or its BSA equivalent of 60 mg/m^2) q4w will be employed. While the approved induction dose regimen for golimumab in adult participants with UC is the same worldwide, the maintenance posology is not identical across all markets as the 100 mg dose is approved across all body weights in some countries; whereas a body weight tiered dose regimen (50 mg for those with body weight <80 kg and 100 mg in those ≥80 kg) is approved in other markets. In the pivotal adult UC study (C0524T18), both the 100 mg and 50 mg dose regimens met the primary endpoint of maintaining clinical response through Week 54; however, only the 100 mg dosage met the major secondary endpoints of achieving remission and mucosal healing at both Week 30 and Week 54. In addition, the safety of the golimumab 100 mg maintenance dosage in UC was similar to that seen in other indications in which golimumab has been studied.

Infliximab: The conventional weight-based regimen for infliximab in the treatment of pediatric UC is 5 mg/kg. This posology is based on studies in both adult and pediatric subjects with moderately to severely active ulcerative colitis. In 3 completed clinical trials in adult subjects with moderately to severely active UC (C0168T12, C0168T37 [ACT 1], and C0168T46 [ACT 2]), infliximab safety and efficacy has been evaluated. Both ACT 1 and ACT 2 achieved the primary endpoint of clinical response at Week 8 (ACT 1: infliximab 5 mg/kg and 10 mg/kg [69.4% and 61.5%, respectively, versus placebo 37.2%; both $p < 0.001$]; ACT 2: infliximab 5 mg/kg and 10 mg/kg [64.5% and 69.2%, respectively, versus placebo; 29.3%; both $p < 0.001$]). Further, at Week 54 of ACT 1, a significantly greater proportion of subjects in the combined infliximab treatment group were in clinical response (44.9%), in clinical remission (34.6%), and achieved mucosal healing (46.1%) compared with subjects in the placebo treatment group (19.8%, 16.5%, and 18.2% for clinical response, clinical remission, and mucosal healing, respectively). Similar results were observed at Week 30 of ACT 2.

In addition to efficacy, these clinical trials established the safety of infliximab. Of the approximately 500 adult subjects with UC treated with infliximab during these clinical studies, less than 1% died or experienced malignancies. Serious infections did occur in ACT 1 and ACT 2,

with the overall occurrence rate of 3.9% in the combined infliximab group versus 2.5% in the placebo group.

This conventional weight-based posology (5 mg/kg) was evaluated in pediatric UC patients in the C0168T72 clinical study. This was a Phase 3, randomized, open-label, parallel-group, multicenter study to assess the safety and efficacy of induction and maintenance infliximab treatment in pediatric subjects aged 6 through 17 years with moderately to severely active UC (defined as a Mayo score of 6 to 12, inclusive, at baseline, including an endoscopic subscore ≥2), despite current adequate treatment or who had previously failed to respond to or tolerate treatment with 6-MP, AZA, corticosteroids, and/or 5-ASA compounds. A total of 60 pediatric subjects were enrolled at 27 investigational sites in North America and Europe and followed for safety and efficacy through Week 54.

The C0168T72 study showed that infliximab at 5 mg/kg administered at Weeks 0, 2, and 6 was efficacious in these pediatric subjects with UC, with efficacy consistent with that seen in adults with UC in the infliximab 5 mg/kg group (73.3% and 66.9%, respectively, for the proportion of subjects in clinical response). Further, in this 54-week study of pediatric subjects with UC, a notably greater proportion of subjects was in remission at Week 54 in the q8w maintenance group (38.1%) compared with the q12w maintenance group (18.2% p 0.146).

Infliximab was generally well tolerated in the pediatric UC population, with a safety profile consistent with that reported in other studies. There were no reports of deaths, malignancies, opportunistic infections, serious neurologic events, or TB and the safety profiles observed in the q8w and q12w maintenance treatment groups were similar. No new safety signals have been observed in pediatric populations using infliximab.

With respect to the step-wise dose escalation of infliximab (to a maximum of 10 mg/kg [capped at 1gm] q4w) which is available if the participant fails to achieve a clinical response at Week 6 or, after responding, has a flare in their UC disease after Week 6, this dose escalation posology is consistent with current clinical practice. This approach has been discussed and deemed appropriate by US FDA and Pediatric Committee of the European Medicines Association, as well as experts in pediatric IBD in the US and EU. Real world experience has demonstrated that there is a need for more intensive dosing in some patients, particularly in the setting of acute severe colitis or in patients with a UC flare and a secondary loss of response.

The conventional posology is thought to be inadequate for those patients with acute severe colitis. Either because the inflammatory burden is so high, or due to altered pharmacokinetics, trough levels of infliximab tend to be lower in patients with acute severe colitis.[37,51] Higher rates of remission and lower rates of colectomy have been reported in UC patients with the escalated dosing of infliximab in adults[10] and pediatric patients.[1,17] New guidelines developed in a collaboration between the European Society of Paediatric Hepatology, Gastroenterology, and Nutrition (ESPHGAN) and the European Crohn's Colitis Organization (ECCO) support intensive infliximab dosing in this setting.[48]

For the purposes of this study, a flare in UC symptoms (defined Section 6.5.3) is an increase in the partial Mayo score and is consistent with a secondary loss of response (LOR) to infliximab. Secondary LOR to infliximab after an initial response occurs in 20-40% of all IBD patients after 1 year of therapy.[4,5] Several studies in IBD broadly[14] and UC more specifically[38,41] have found significant clinical benefit in escalating infliximab dosing in the setting of secondary LOR, with response rates generally between 25-45% and avoidance of the need for colectomy.[44] Small retrospective studies in psoriasis[45] and IBD[8,15] have found that dose escalation is generally well tolerated and not associated with new safety signals. In one retrospective study in 86 adult patients with Crohn's disease receiving up to 22.5 mg/kg of infliximab q4w, the rate of serious infections was reported to be 7.4 per 100 patient years. These benefits in clinical response and avoidance of colectomy have offset concerns about the risks of infection and other side effects from the enhanced infliximab dosing.

4.3.1. Randomization

Prior to Amendment 4, central randomization was to be implemented in this study. Participants ≥30 kg were randomized in a 3:1 ratio across intervention groups, golimumab and infliximab, respectively. Randomization was to be used to minimize bias in the assignment of participants to intervention groups and to increase the likelihood that known and unknown participant attributes (eg, demographic and baseline characteristics) are evenly balanced across intervention groups.

Participants <30 kg were not to be randomized and offered only golimumab. This was implemented to ensure that the Sponsor enrolled at least 5 participants who weigh <30 kg and received golimumab as this is a rare subpopulation.

Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.

4.4. End of Study Definition

4.4.1. Study Completion

Short-term and long-term phase through Week 54

A participant will be considered to have completed the short-term and long-term phase of the study if he or she has completed study assessments through Week 54 of the study. Participants who prematurely discontinue study interventions for any reason before completion of the Week 54 assessments of the study will not be considered to have completed the study through Week 54.

Study extension

Following the Week 54 evaluations (end of the main pivotal study), participants who are receiving benefit from golimumab, at the discretion of the investigator, may continue to receive SC golimumab q4w in an extension period until one of the following conditions below is met, whichever occurs first:

1. marketing authorization is obtained for golimumab for the treatment of pediatrics participants with UC and golimumab is either commercially available or 2 years have lapsed since marketing authorization, or
2. the participant turns 18 years of age and has access to commercially available golimumab, or
3. until a decision is made by the sponsor not to pursue an indication in this pediatric UC population

4.4.2. End of study

The end of study is considered as the last scheduled study assessment for the last participant in the study extension as shown in the Schedule of Activities. The final data from the study site will be sent to the sponsor (or designee) after completion of the final participant assessment at that study site, in the time frame specified in the Clinical Trial Agreement.

5. STUDY POPULATION

The study population will include pediatric participants aged 2 to 17 years (at the time of the first administration of study intervention at Week 0) with moderately to severely active UC, defined as a baseline Mayo score of 6 through 12, inclusive, with an endoscopy subscore of ≥2. Additionally, participants must have demonstrated an inadequate response to, have failed to tolerate, or have a medical contraindication to conventional therapies (ie, IV or oral corticosteroids or the immunomodulators MTX, AZA, or 6-MP); or, demonstrated corticosteroid dependence; or, require repeated (>3 per year) courses of corticosteroids. Participants with prior exposure to biologic anti-TNFα agents will be ineligible for participation in this study.

Screening for eligible participants should be performed within 6 weeks before administration of the study intervention. Refer to Section 5.4 Screen Failures for conditions under which the repeat of any screening procedures is allowed. On a case-by-case basis, and after consultation with the medical monitor, procedures may exceed the 6-week window and will not be considered protocol deviations.

The inclusion and exclusion criteria for enrolling participants in this study are described below. If there is a question about these criteria, the investigator must consult with the appropriate sponsor representative and resolve any issues before enrolling a participant in the study. Waivers are not allowed.

5.1. Inclusion Criteria

Each potential participant must satisfy all of the following criteria to be enrolled in the study:

1. Must be 2 to 17 years of age (at the time of the first administration of study intervention at Week 0) of either gender with a body weight ≥10 kg and >70 cm height.
2. Must have had UC diagnosed for at least 1 month prior to screening.

3. Must have the diagnosis of UC confirmed by a prior endoscopic biopsy that is consistent with a diagnosis of UC (eg, crypt distortion, crypt abscess, goblet cell depletion, and continuous distribution).

4. Must have moderately to severely active UC (as defined by baseline Mayo score of 6 through 12 [endoscopy {sigmoidoscopy or colonoscopy} subscore assigned by local endoscopist], inclusive).

5. Must have a Mayo endoscopy (sigmoidoscopy or colonoscopy) subscore ≥2 (subscore assigned by local endoscopist) at baseline endoscopy (indicative of moderately to severely active UC). Baseline endoscopy (sigmoidoscopy or colonoscopy) must be performed with study software and occur no more than 2 weeks before first study intervention administration.

6. Criterion modified per Amendment 3.

   6.1. Prior or current medication for UC must include at least 1 of the following (Appendix 2 [Section 10.2]):

      a. Current treatment with at least 1 of the following therapies: oral corticosteroids, or the immunomodulators 6-MP, MTX, or AZA;

         OR

      b. Have a history of failure to respond to or tolerate, or have a medical contraindication to, at least 1 of the following therapies: oral or intravenous corticosteroids or the immunomodulators 6-MP, MTX, or AZA as defined in Appendix 2 (Section 10.2);

         OR

      c. Currently have or have had a history of corticosteroid dependency (ie, an inability to successfully taper corticosteroids without a return of the symptoms of UC) as defined in Appendix 2 (Section 10.2);

         OR

      d. Have required more than 3 courses of oral or intravenous corticosteroids in the past year.

7. Criterion modified per Amendment 3.

   7.1. Must meet concomitant medication dose stability prior to the first administration of study intervention:

      a. Corticosteroids:

         1) If receiving oral, the dose (in prednisone equivalents) must have been stable for at least 2 weeks prior to Week 0.

         2) If receiving rectal corticosteroids, the dose must have been stable for at least 2 weeks prior to Week 0.

3) If oral, IV, or rectal corticosteroids have recently been discontinued, they must have been stopped for at least 2 weeks prior to Week 0.

b. 5-ASA, MTX, 6-MP, and AZA compounds:

1) If receiving oral or rectal 5-ASA compounds, the dose must have been stable for at least 2 weeks prior to Week 0.

2) If oral or rectal 5-ASA compounds have been recently discontinued, they must have been stopped for at least 2 weeks prior to Week 0.

3) If receiving MTX, 6-MP, or AZA compounds, the participant must have been taking them for ≥12 weeks and on a stable dose for 2 weeks prior to Week 0. If the MTX, 6-MP, or AZA have been recently discontinued, they must have been stopped for at least 2 weeks prior to Week 0.

8. Criterion modified per Amendment 3.

8.1. If receiving enteral nutrition, must have been on a stable regimen for at least 2 weeks prior to the first administration of study intervention at Week 0. Participants who receive parenteral nutrition are not permitted to enroll in the trial.

9. Must have discontinued the use of antibiotics for the treatment of UC (eg, ciprofloxacin, metronidazole, or rifaximin) for at least 1 week prior to screening.

10. Must have discontinued the use of 6-thioguanine (6-TG) for at least 4 weeks prior to screening.

11. If at increased risk for colon cancer, must either have had a colonoscopy to assess the presence of dysplasia within 1 year prior to the first administration of study intervention at Week 0 or a colonoscopy to assess the presence of malignancy as the baseline endoscopy. Baseline endoscopy (sigmoidoscopy or colonoscopy) must be performed with study software and occur no more than 2 weeks before first study intervention administration.

Note: All participants who have had extensive colitis for ≥8 years, or disease limited to the left side of the colon for ≥10 years, are considered at increased risk. For participants with a pathology finding of "indefinite dysplasia with reactive atypia" on colonoscopy, the investigator should discuss the case with the medical monitor to determine eligibility.

12. Criterion modified per Amendment 4.

12.1. Before enrollment, a girl must be either:

a. Not of childbearing potential defined as:

1) Premenarchal

a) A premenarchal state is one in which menarche has not yet occurred.

2) Permanently sterile

a) Permanent sterilization methods include hysterectomy, bilateral salpingectomy, bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy.

b. Of childbearing potential and

1) Practicing a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly) during the study and for 6 months after receiving the last dose of study intervention. Both user-independent and user-dependent methods of contraception are allowed.

Examples of highly effective contraceptives include:

a) User-independent methods:

Implantable progestogen-only hormone contraception associated with inhibition of ovulation; intrauterine device; intrauterine hormone-releasing system; vasectomized partner.

b) User-dependent methods:

Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation: oral, intravaginal, and transdermal; progestogen-only hormone contraception associated with inhibition of ovulation: oral and injectable. Sexual abstinence (sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant).

Typical use failure rates may differ from those when used consistently and correctly. Moreover, user-dependent methods of contraception (eg, oral contraceptives) may have higher failure rates than non-user-dependent methods. Participants who employ user-dependent methods are therefore urged to include an additional contraception method, such as a barrier method (eg, condom or diaphragm). Use should be consistent with local regulations regarding the use of contraceptive methods for participants participating in clinical studies.

Note: If the childbearing potential changes after start of the study (eg, girl who is not heterosexually active becomes active, premenarchal girl experiences menarche) a girl must agree to begin using a highly effective method of birth control, as described above.

13. Criterion modified per Amendment 3.

13.1. Boys must agree not to donate sperm for the purpose of reproduction during the study and for a minimum 6 months after receiving the last dose of study intervention. During the study and for a minimum of 6 months after receiving the

last dose of study intervention, in addition to the highly effective method of contraception, a boy:

a. Who is sexually active with a girl of childbearing potential must agree to use a barrier method of contraception (eg, condom with spermicidal foam / gel / film / cream / suppository).

b. Who is sexually active with a girl who is pregnant must use a condom.

14. All girls of childbearing potential must have a negative serum pregnancy test at screening.

15. A girl of childbearing potential must have a negative urine pregnancy test prior to study intervention administration at Week 0.

16. Girls of childbearing age must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction during the study and for a minimum 6 months after receiving the last dose of study intervention.

17. Criterion modified per Amendment 4.

17.1. Are considered eligible according to the following TB screening criteria:

- Have no history of latent or active TB prior to screening.
- Have no signs or symptoms suggestive of active TB upon medical history and/or physical examination.
- Have had no recent close contact with a person with active TB.
- During the screening period have a negative QuantiFERON®-TB test or T-Spot® test result. Within 1 month, prior to the first study intervention administration, a negative tuberculin skin test is additionally required if the QuantiFERON-TB test or T-Spot test is not approved/registered in that country or the tuberculin skin test (Appendix 3 [Section 10.3]) is mandated by local health authorities. The results of the T-Spot test will be acceptable in place of the QuantiFERON-TB test. If the QuantiFERON-TB or T-Spot test cannot be obtained, the tuberculin skin test can be performed instead after discussion with the medical monitor.
- Indeterminate results should be handled as outlined in Section 8.3.6.

18. Have screening laboratory test result as follows:

a.	Hemoglobin	≥7.5 g/dL	
b.	White blood cells	≥2.5 x 10^3 cells/µL	(SI: ≥2.5 x10^9 cells/L)
c.	Neutrophils	≥1.5 x 10^3 cells/µL	(SI: ≥1.5 x10^9 cells/L)
d.	Platelets	≥100 x 10^3 cells/µL	(SI: ≥100 x10^9 cells/L)

e. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels not exceeding 2.0 times the upper limit of normal (ULN) for the central laboratory

f. Serum creatinine not to exceed:

1) 0.5 mg/dL (SI: 44 µmol/L) for ages 2 to 5 years

2) 0.7 mg/dL (SI: 62 µmol/L) for ages 6 to 10 years

3) 1.0 mg/dL (SI: 88 µmol/L) for ages 11 to 12 years

4) 1.2 mg/dL (SI: 106 µmol/L) for ages ≥13 years

19. Criterion modified per Amendment 4.

19.1. Participants must be up to date with all immunizations (ie, measles, mumps, rubella, and varicella) in agreement with current local immunization guidelines for immunosuppressed participants before Week 0.

20. Criterion modified per Amendment 4.

20.1. For participants who have not completed the recommended vaccination schedule for varicella, measles, mumps, and rubella, and the subsequent vaccination falls within the next 4 years, an accelerated vaccination schedule must be completed prior to study enrollment, per local or professional guidelines. If live, attenuated viral vaccine is utilized, it is necessary for at least 4 weeks (or longer as indicated on the package insert of the relevant vaccine) to elapse between the vaccination and receipt of study intervention. Once study intervention has been initiated, at least a 16-week period must elapse after last dose before a live vaccine is utilized. For additional restrictions regarding Bacille Calmette-Guerin (BCG) vaccination, see Exclusion Criterion 41 in Section 5.2.

21. For each participant, his or her parent(s) (preferably both parents, if available) or legally acceptable representative(s), as required by local regulations, must sign an ICF indicating that he or she understands the purpose of, and procedures required for, the study and is willing to allow the child to participate in the study.

22. Assent is also required of children capable of understanding the study (typically participants 7 years of age and older, depending on the institutional policies), as described in Informed Consent Process in Appendix 12 [Section 10.12], Regulatory, Ethical, and Study Oversight Considerations].

23. Must be willing and able to adhere to the lifestyle considerations specified in this protocol.

5.2. Exclusion Criteria

Any potential participant who meets any of the following criteria will be excluded from participating in the study:

1. Have severe, extensive colitis as evidenced by:

    a. Investigator judgment that the participant is likely to require a colectomy within 12 weeks of Week 0;

    OR

    b. Symptom complex at screening or Week 0 visit that includes at least 4 of the following:

        1) Diarrhea with ≥6 bowel movements/day with macroscopic blood in stool
        2) Focal severe or rebound abdominal tenderness
        3) Persistent fever (≥37.5°C) for more than 5 days
        4) Persistent tachycardia for more than 5 days
        5) Anemia (hemoglobin <8.5 g/dL)

2. Participants with very severe active UC disease who are currently hospitalized for UC disease exacerbation when initiating study screening and who have a Mayo score of 12 should be excluded from the study.

3. History of liver or renal insufficiency; significant cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric (including suicidality), or metabolic disturbances.

4. History of malignancy or macrophage activation syndrome or hemophagocytic lymphohistiocytosis.

5. A serious allergic reaction to latex.

6. Contraindications to the use of golimumab or infliximab or anti-TNFα therapy per local prescribing information.

7. Taken any disallowed therapies as noted in Section 6.5, Concomitant Therapy before the planned first dose of study intervention.

8. Criterion modified per Amendment 4.

    8.1. Received an investigational vaccine or used an invasive investigational medical device within 3 months before the planned first dose of study intervention or is currently enrolled in an investigational study. Receipt of an investigational vaccine for Coronavirus Disease 2019 (COVID-19) is not an automatic exclusion criterion, discuss with the medical monitor.

9. Pregnant, or breast feeding, or planning to become pregnant while enrolled in this study or within 6 months after the last dose of study intervention.

10. Plans to father a child while enrolled in this study or within 6 months after the last dose of study intervention.

11. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

12. Had major surgery, (eg, requiring general anesthesia) within 3 months before screening, or will not have fully recovered from surgery, or has surgery planned during the time the participant is expected to participate in the study or within 3 months after the last dose of study intervention administration.

    Note: Participants with planned surgical procedures to be conducted under local anesthesia may participate if the surgery is to be performed after the Week 14 visit.

13. Have UC limited to the rectum only or to <20% of the colon.

14. Presence of a stoma.

15. Presence or history of a fistula.

16. Have severe, fixed symptomatic stenosis of the large or small intestine.

17. Require, or required within the 2 months prior to screening, surgery for active gastrointestinal bleeding, peritonitis, intestinal obstruction, or intra-abdominal or pancreatic abscess requiring surgical drainage, or other conditions possibly confounding the evaluation of benefit from study intervention treatment.

18. Presence or history of colonic or small bowel obstruction within 6 months prior to screening, confirmed by objective radiographic or endoscopic evidence of a stricture with resulting obstruction (dilation of the colon or small bowel proximal to the stricture on barium radiograph or an inability to traverse the stricture at endoscopy).

19. History of extensive colonic resection (eg, less than 30 cm of colon remaining) that would prevent adequate evaluation of the effect of study intervention on clinical disease activity.

20. Presence on screening endoscopy of adenomatous colonic polyps, if not removed prior to study entry, or history of adenomatous colonic polyps that were not removed.

21. Have evidence of Crohn's disease:

    a. Small intestinal or ileal disease by upper gastrointestinal small bowel follow-through, ileocolonoscopy with histology, videocapsule endoscopy, or Magnetic Resonance Enterography

b. Noncaseating and non-mucin granulomas that are suggestive of a diagnosis of Crohn's disease on colonoscopy

c. Skip lesions on colonoscopy including absolute rectal sparing, with a normal rectum both endoscopically and histologically

d. Perianal disease

Concomitant or previous medical therapies received

22. Have received any anti-TNFα biologic agents (eg, monoclonal antibody therapies).

23. Has received other agents intended to suppress or eliminate TNFα <8 weeks prior to first administration of study intervention.

24. Have received natalizumab within 12 months of first study intervention administration.

25. Have received vedolizumab within 12 weeks of the first study intervention.

26. Have received agents that deplete B or T cells (eg, rituximab, alemtuzumab, or visilizumab) within 12 months of first study intervention administration or continue to manifest depletion of B or T cells more than 12 months after completion of therapy with lymphocyte depleting agents.

27. Are receiving oral corticosteroids at a dose >50 mg of prednisone or its equivalent per day.

28. Require routine use (≥2 times per week) of antimotility agents for control of diarrhea (ie, diphenoxylate hydrochloride with atropine sulfate, loperamide, or other opioids).

29. Have used laxatives, except preparations for endoscopy or other procedures, within 1 week prior to Mayo screening procedures.

30. Other oral immunomodulatory agents (eg, 6-TG, cyclosporine, tacrolimus, sirolimus, or mycophenolate mofetil) within 8 weeks prior to first administration of study intervention.

31. Have used any investigational drug within 4 weeks prior to first administration of study intervention or within 5 half-lives of the investigational agent, whichever is longer, or is currently enrolled in an investigational study.

32. Received thalidomide or related agent within 8 weeks of screening.

33. Have used apheresis (ie, Adacolumn apheresis, Cellsorba apheresis) within 4 weeks prior to first administration of study intervention.

Infections or predisposition to infections

34. Criterion modified per Amendment 4.

    34.1. Has a stool culture or other examination positive for an enteric pathogen, including *Clostridium difficile* toxin in the previous 4 months, unless a repeat examination is negative and there are no signs of ongoing infection with that pathogen.

    Note: For participants who have a positive *C. difficile* test during the screening period, participant may be treated and retested during the screening period (extensions of the screening period can be discussed with the medical monitor). If repeat test is negative and there are no signs of ongoing infection, participant can be considered for enrollment. If repeat *C. difficile* test remains positive during the screening period, the participant must be a screen failure and may be treated and rescreened.

35. Have a history of, or ongoing, chronic or recurrent infectious disease, including but not limited to, chronic renal infection, chronic chest infection (eg, bronchiectasis), sinusitis, recurrent urinary tract infection (eg, recurrent pyelonephritis, chronic cystitis), an open, draining, or infected skin wound, or an ulcer.

36. Have immune deficiency syndrome (eg, severe combined immunodeficiency syndrome, T-cell deficiency syndromes, B-cell deficiency syndromes, or chronic granulomatous disease).

37. Have a known history of infection with HIV.

38. Have a known history of hepatitis C infection.

39. Participants must undergo screening for hepatitis B virus (HBV). At a minimum, this includes testing for HBV surface antigen (HBsAg), HBV surface antibody (anti-HBs), and HBV core antibody (anti-HBc total) (Appendix 15 [Section 10.15]):

    a. Participants who test **positive** for surface antigen (HBsAg+) **are not eligible** for this study, regardless of the results of other hepatitis B tests.

    b. Participants who test **negative** for surface antigen (HBsAg-) and test **positive** for core antibody (anti-HBc+) **and** surface antibody (anti-HBs+) **are eligible** for this study.

    c. Participants who test **positive only** for **surface antibody** (anti-HBs+) **are eligible** for this study.

    d. Participants who test **positive only** for **core antibody** (anti-HBc+) must undergo further testing for hepatitis B deoxyribonucleic acid (HBV DNA test). If the HBV DNA test is **positive**, the participant **is not eligible** for this study. If the

HBV DNA test is **negative,** the participant **is eligible** for this study. In the event the HBV DNA test cannot be performed, the participant **is not eligible** for this study.

Note: For participants who **are not eligible for this study due to HBV test results**, consultation with a physician with expertise in the treatment of HBV infection is recommended.

40. Have a history of latent or active granulomatous infection, including histoplasmosis or coccidioidomycosis, prior to screening.

41. Have had a BCG vaccination within 12 months of screening.

42. Criterion modified per Amendment 3.

    42.1. Have a chest radiograph during screening or 6 months prior to screening that shows an abnormality suggestive of an undiagnosed pulmonary pathology that may include manifestations of IBD, malignancy, prior or current active infection, including TB.

43. Have had a nontuberculous mycobacterial infection or opportunistic infection (eg, cytomegalovirus, pneumocystosis, aspergillosis).

44. Criterion modified per Amendment 4.

    44.1. Have persistently indeterminate (indeterminate on repeat sampling) QuantiFERON-TB or T-Spot test results. Indeterminate results should be handled as outlined in Section 8.3.6.

45. Have had a serious infection (eg, hepatitis, pneumonia, or pyelonephritis), have been hospitalized for an infection, or have been treated with parenteral antibiotics for an infection within 2 months prior to first administration of study intervention.

46. Criterion modified per Amendment 4.

    46.1. Have had 2 or more serious infections requiring hospitalization or treatment with parenteral antibiotics within the past year. Less serious infections (eg, acute upper respiratory tract infection, simple urinary tract infection) need not be considered exclusionary at the discretion of the investigator. Prior parenteral antibiotics administered for the indication of UC are acceptable and not a reason for exclusion.

47. Criterion modified per Amendment 4.

    47.1. Must not have received, or are expected to receive, any live vaccination within 8 weeks (or longer as indicated in the package insert of the relevant vaccine) prior to the first administration of study intervention, during the study, or within 16 weeks (more than 5.5 half-lives of SC golimumab) after the last administration

of study intervention. Receipt of a live SARS-CoV-2 vaccine (against the virus that causes COVID-19) is *not* automatically an exclusion criterion and must be discussed with the medical monitor.

Malignancy or increased potential for malignancy

48. Presence or history of any malignancy.

49. Presence or history of lymphoproliferative disease including lymphoma, or signs and symptoms suggestive of possible lymphoproliferative disease, such as lymphadenopathy of unusual size or location (eg, nodes in the posterior triangle of the neck, infraclavicular, epitrochlear, or periaortic areas) and monoclonal gammopathy of undetermined significance, or clinically significant hepatomegaly or splenomegaly.

Coexisting medical conditions or past medical history

50. Have known allergies, a known hypersensitivity to human immunoglobulin proteins or other components of golimumab, or intolerance to golimumab or its excipients (refer to golimumab IB).

51. Have known allergies, a known hypersensitivity to human immunoglobulin proteins or other components of infliximab, or intolerance to infliximab or its excipients (refer to infliximab IB).

52. Is currently undergoing or has previously undergone allergy immunotherapy for a history of anaphylactic reactions.

53. Fever of greater than 3 weeks duration of unknown origin within 3 months prior to screening.

54. Concomitant diagnosis or history of congestive heart failure.

55. Concomitant diagnosis or history of systemic lupus erythematosus.

56. Have a transplanted organ (with the exception of a corneal transplant performed >3 months prior to first administration of study intervention).

57. Concomitant diagnosis or history of demyelinating disease, such as multiple sclerosis or optic neuritis.

58. Have or have had a history of substance abuse (drug or alcohol).

Other

59. Have poor tolerability of venipuncture or lack of adequate venous access for required blood sampling.

60. Employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.

Infections or predisposition to infections

61. During the 6 weeks prior to baseline, have had ANY of:

    a. Confirmed SARS-CoV-2 (COVID-19) infection (test positive);

    OR

    b. Suspected SARS-CoV-2 infection (clinical features without documented test results);

    OR

    c. Close contact with a person with known or suspected SARS-CoV-2 infection.

    - Exception: may be included with a documented negative result for a validated SARS-CoV-2 test:

      1) obtained at least 2 weeks after conditions (a), (b), (c) above (timed from resolution of key clinical features if present, eg, fever, cough, dyspnea);

      AND

      2) with absence of ALL conditions (a), (b) (c) above during the period between the negative test result and the baseline study visit.

    NOTES on COVID-19-related exclusion:

    - The field of COVID-19-related testing (for presence of, and immunity to, the SARS-CoV-2 virus) is rapidly evolving. Additional testing may be performed as part of screening and/or during the study if deemed necessary by the investigator and in accordance with current regulations/guidance from authorities/standards of care.
    - Precaution: for those who may carry a higher risk for severe COVID-19 illness, follow guidance from local health authorities when weighing the potential benefits and risks of enrolling in the study, and during participation in the study.

NOTE: Investigators should ensure that all available study enrollment criteria have been met at screening. If a participant's clinical status changes (including any available laboratory results or receipt of additional medical records) after screening but before the first dose of study intervention is given such that he or she no longer meets all eligibility criteria, then the participant must be excluded from participation in the study. The required source documentation to support meeting the enrollment criteria are noted in Appendix 12 (Section 10.12), Regulatory, Ethical, and Study Oversight Considerations.

5.3. Lifestyle Considerations

Potential participants must be willing and able to adhere to the following lifestyle restrictions during the course of the study to be eligible for participation:

1. Refer to Section 6.5, Concomitant Therapy for details regarding prohibited and restricted therapy during the study.

2. Agree to follow all requirements that must be met during the study as noted in the Inclusion and Exclusion Criteria (eg, contraceptive requirements).

3. If sexually active, all participants must agree to follow the contraceptive requirements as noted in Inclusion Criterion #12.

5.4. Screen Failures

Participant Identification, Enrollment, and Screening Logs

The investigator agrees to complete a participant identification and enrollment log, which reports on all participants who were seen to determine eligibility for inclusion in the study, to permit easy identification of each participant during and after the study. This document will be reviewed by the sponsor study site contact for completeness.

The participant identification and enrollment log will be treated as confidential and will be filed by the investigator in the study file. To ensure participant confidentiality, no copy will be made. All reports and communications relating to the study will identify participants by participant identification number and age at initial informed consent. In cases where the participant is not randomized into the study the date seen and age at initial informed consent will be used.

If, during the screening phase, a participant has not met all inclusion criteria or has met any exclusion criteria or is unable or unwilling to adhere to the lifestyle considerations of the study, the participant is considered to be a screen failure and is not eligible to be enrolled in the study.

In general, if a participant is a screen failure, but at some-point in the future meets all of the participant eligibility criteria, the participant may be rescreened after a new informed consent/assent has been obtained. Participants who are rescreened should be assigned a new participant number and will restart a new screening phase.

Screening and enrollment procedures should typically be completed within the specified screening window of within 6 weeks; extensions can be discussed with the medical monitor.

If any delay leads to the expiration of time-specific assessments (eg, TB, chest radiograph, stool analysis, sigmoidoscopy) further discussion with the Sponsor should occur before the participant is considered for rescreen, the participant will be considered a screen failure because he/she will not meet eligibility criteria, and the expired assessments (along with the non-time-specific laboratory tests) will have to be repeated on rescreening.

Additional criteria for retesting and rescreening are outlined below and in the Retesting and Rescreening Plan.

Retesting

Retesting of abnormal laboratory values that may lead to exclusion will be allowed once. Retesting can occur at an unscheduled visit during the screening phase, as long as this is done within the specified screening window of within 6 weeks (6 weeks may be exceeded on a case-by-case basis).

Rescreening

Participants who do not meet the criteria for participation in this study (screen failure) may be rescreened 1 time. In rare cases, a participant may be screened a third time after discussion with the medical monitor. Participants who are rescreened will be assigned a new participant number, undergo the informed consent/assent process, and then start a new screening phase. On a case-by-case basis, after consultation with the medical monitor, rescreening procedures may exceed the 6-week window and will not be considered protocol deviations.

6. STUDY INTERVENTION

Study intervention administrations must be captured in the source documents and the electronic case report form (eCRF). Study site personnel will instruct eligible participants on how to store study intervention for AHA in the study extension as indicated for this protocol.

Golimumab and infliximab will be manufactured and provided under the responsibility of the sponsor. Refer to the IB for a list of excipients.

6.1. Study Interventions Administered

Golimumab

During the short-term phase, pediatric participants will receive dose regimens of SC golimumab at Week 0 and Week 2 based on body weight as shown in Table 5. Participants must weigh ≥10 kg and be >70 cm tall. This is the lower range of weight and height that the PFP-V has been validated for to deliver SC golimumab. This limit accommodates >97% of all 2-year-old girls based on published growth charts (www.cdc.gov/growthcharts). Participants' golimumab doses for all administrations through Week 10 (inclusive) will be based on the participants' weight and height at Week 0 or, if not available, the most recent height and weight from screening. The same weight and height should be used through Week 10. **Golimumab doses from Week 14 through Week 54 will be based on the participants' weight and height obtained with that week's visit or the last recorded height and weight.** In the study extension, golimumab doses will be based on the participants' most current weight and height or the last recorded height and weight.

Table 5: SC Golimumab Dosage by Body Weight		
Pediatric participants with ulcerative colitis (2 to 17 years of age)	**Short-term phase**	**Long-term phase†**
With body weight <45 kg	120 mg/m^2 at Week 0* 60 mg/m^2 at Week 2*	60 mg/m^2 every 4 weeks from Week 6*†
With body weight ≥45 kg	200 mg at Week 0 100 mg at Week 2	100 mg every 4 weeks from Week 6†
† Participants in clinical response to golimumab at Week 6 or partial Mayo response at Week 14 *BSA doses are capped at 200 mg and 100 mg for the 120 mg/m^2 and 60 mg/m^2 doses, respectively.		

At Week 6, all participants will be evaluated for clinical response; participants in clinical response will continue receiving open-label golimumab during the long-term phase (Table 5).

Participants not in clinical response (defined as decrease from baseline in the Mayo score of ≥30% and ≥3 points, with either a decrease from baseline in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1; Section 3.1 and Section 8.1.1) at Week 6 may have study intervention discontinued (and complete a safety follow-up at least 16 weeks after the last administration of golimumab) or may continue receiving golimumab for up to 2 additional doses at Weeks 6 and 10 at the discretion of the investigator, as specified in Table 5. At Week 14, these participants will be evaluated for partial Mayo response (defined as a decrease from the Week 0 partial Mayo score of ≥3 points); participants in partial Mayo response will continue receiving open-label golimumab (q4w) during the long-term phase (Table 5). Participants who are not partial Mayo responders at Week 14 will have study intervention discontinued and should complete a final safety follow-up at least 16 weeks following the last administration of study intervention.

After the Week 54 evaluations, at the discretion of the investigator, if participants receiving golimumab are able to benefit from continued SC golimumab, the participants will enter the study extension. Participants will continue to receive SC golimumab q4w under the study extension at the doses specified in Table 5 until marketing authorization is obtained for golimumab for the treatment of pediatric participants with UC, the participant turns 18 and has access to commercially available golimumab, or until a decision is made not to pursue an indication in this pediatric UC population, whichever occurs first.

At entry into the study extension (Week 54) or any time thereafter during the study extension, participants will have the option to decrease their dose one-time, at the discretion of the investigator, to mimic the approved local product label for adult UC. After this decrease in dose, participants can, at the discretion of the investigator, resume their original study intervention dosage, but no further dose adjustments are permitted while the participant is enrolled in the study.

In the study extension beginning at Week 58 participants will have the option of AHA of golimumab by participants and/or their caregivers after being properly trained.

Infliximab

All participants in the infliximab treatment arm will be administered infliximab 5 mg/kg at Weeks 0 and 2. Starting at Week 6, infliximab administrations of 5 mg/kg will continue q8w

through Week 46 for those participants in clinical response at the Week 6 assessments. Infliximab doses for all administrations through Week 8 (inclusive) will be based on the participants' weight at Week 0 or, if not available, the most recent weight from screening. The same weight should be used through Week 8. Infliximab doses from Week 14 through Week 46 will be based on the participants' weight obtained with that week's visit or the last recorded weight.

Additionally, a step-wise flexible dose escalation approach (to a maximum dose of 10 mg/kg [capped at 1 gm] at an interval of q4w) will be permitted in the infliximab arm, at the investigator's discretion, for those participants not in clinical response at Week 6 (defined by the Mayo score), or participants who were in response at Week 6 but have a worsening of their UC signs and symptoms during the study period. This approach was chosen as it most closely mimics clinical practice in treatment of pediatric UC, allowing investigators some flexibility in dosing to treat their patients. Also, if an investigator wants to dose-escalate using a different regimen than listed above, discuss the plan with the medical monitor.

After the Week 54 efficacy and safety evaluations, participants receiving infliximab will be transitioned to standard medical care. At the investigator's discretion a separate blood sample may be obtained and submitted to the central laboratory to evaluate infliximab dose levels and anti-infliximab antibodies (at a maximum of 2 timepoints at Week 6 or later) to inform dose escalations.

Infliximab will be supplied in a 20 mL disposable glass vial. Infliximab will be administered as an IV infusion by qualified study site personnel and the details of each administration will be recorded in the source notes and in the eCRF (including date, start and stop times of the IV infusion, and volume infused).

After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have Week 54 or Early Termination visit.

At Home Administration

Beginning at Week 58, for eligible participants in the golimumab treatment arm, participants/caregivers will have the option to receive training to administer golimumab at home; the training must be documented. Training of the participants/caregivers will occur at the investigative site under the supervision of a health care professional.

Participants/caregivers who are unable or unwilling to administer golimumab at home will return to the investigative site for each administration of golimumab.

Participants will be trained in the recognition and documentation of adverse events (AE) including injection-site reactions (eg, swelling, redness/erythema, pain, tenderness, warmth, bruising, or bleeding). Participants (and caregivers) will be given instructions and encouraged to contact the investigator promptly if an AE occurs. Investigative site personnel will instruct participants (and caregivers) on how to store medication for at home use and how to dispose of used syringes.

For all AHAs of golimumab beginning at Week 58, the details of the study intervention, dosing day, time, anatomic site and if there were any complications of the injection, as well as Adverse Event (including injection-site reaction), Concomitant Medications and TB exposure information will be documented in an AHA diary, that is to be returned to the site at the upcoming visit, and entered by site staff into the eCRF.

Usability Assessment Substudy

At Sponsor identified sites, the participant and/or caregiver will have the option to be enrolled in a Usability Assessment Substudy at Week 58. At Weeks 62 and 66, after self-dosing, the sponsor will collect data on their experience using PFS-U for administrations of golimumab. For additional details see Appendix 18 (Section 10.18).

6.1.1. Dosing Devices

Golimumab will be supplied as a sterile liquid for SC injection in single use prefilled syringes or prefilled pen. Each prefilled syringe contains either 100 mg (1 mL of liquid) or 50 mg (0.5 mL of liquid) of golimumab, with each 0.1 mL of liquid containing 10 mg of golimumab. The prefilled pen for pediatric use can deliver a dose between 10 and 45 mg in 5 mg increments.

Prefilled Syringe with UltraSafe (PFS-U): The UltraSafe Passive Delivery System (UltraSafe) is a manually-operated, single use, disposable needle guard system that is an accessory to the PFS. Each 50 mg or 100 mg-single dose prefilled glass syringe (27-gauge ½ inch needle) contains 50 mg or 100 mg of golimumab per 0.5 or 1.0 mL of solution, respectively.

Prefilled Pen for Pediatric Use (PFP-V): The PFP-V is a variable single dose injection for pediatric use to deliver doses less than 50 mg. It includes an integrated needle guard. Each product can deliver a variable dose between 10 and 45 mg in 5 mg increments. Each PFP-V is assembled with a SIMPONI glass prefilled syringe (27-gauge ½ inch needle) contains 50 mg of golimumab per 0.5 mL of solution.

Dosing device incidents, including those resulting from malfunctions of the device, must be detected, documented, and reported by the investigator throughout the study.

The needle-cover on the PFS assembled with the UltraSafe and PFP-V are manufactured from dry natural rubber containing latex and may cause allergic reactions in individuals who are sensitive to latex.

6.2. Preparation/Handling/Storage/Accountability

All study intervention must be stored at controlled temperatures ranging from 36°F to 46°F (2°C to 8°C).

Refer to the Instructions for Use and Site Investigational Product Procedures Manual for additional guidance on study intervention preparation, handling, and storage.

The investigator is responsible for ensuring that all study intervention received at the site is inventoried and accounted for throughout the study.

For the short- and long-term phases of the study the study intervention will be administered at the study site. The study intervention administered to the participant must be documented on the accountability form. All study intervention will be stored and disposed of according to the sponsor's instructions. Study site personnel must not combine contents of the study intervention containers.

During the study extension, study intervention may be provided to participants for AHA. The dispensing of study intervention to the participant, and the return of study intervention from the participant (if applicable), must be documented on the accountability form. Participants or their legally acceptable representatives where applicable, must be instructed to return all original containers, whether empty or containing study intervention.

Study intervention must be handled in strict accordance with the protocol and the container label and must be stored at the study site in a limited access area or in a locked cabinet under appropriate environmental conditions. Unused study intervention, and study intervention returned by the participant, must be available for verification by the sponsor's study site monitor during on-site monitoring visits. The return to the sponsor of unused study intervention, or used returned study intervention for destruction, will be documented on the intervention return form. When the study site is an authorized destruction unit and study intervention supplies are destroyed on-site, this must also be documented on the intervention return form.

For at site study intervention administrations, potentially hazardous materials such as used ampules, needles, syringes and vials containing hazardous liquids, should be disposed of immediately in a safe manner and therefore will not be retained for accountability purposes. For AHA of study intervention, appropriate hazardous waste disposal containers will be provided to participants. These containers will be collected by the study site for safe disposal of their contents.

Study intervention should be dispensed under the supervision of the investigator or a qualified member of the study site personnel, or by a hospital/clinic pharmacist when administered at the site. Study intervention will be supplied only to participants participating in the study. Returned study intervention must not be dispensed again, even to the same participant. Study intervention may not be relabeled or reassigned for use by other participants. The investigator agrees neither to dispense the study intervention from, nor store it at, any site other than the study sites agreed upon with the sponsor.

6.3. Measures to Minimize Bias: Randomization and Blinding

Intervention Allocation

Procedures for Randomization and Stratification

Prior to implementation of Amendment 4, participants weighing ≥30 kg were to be randomly assigned to 1 of 2 intervention groups based on a computer-generated randomization schedule prepared before the study by or under the supervision of the sponsor. Participants were to be randomized in a 3:1 ratio to golimumab or infliximab. Based on this randomization code, study intervention was assigned and administered to each participant.

Permuted block randomization was used. The interactive web response system (IWRS) assigned a unique treatment code, which dictated the treatment assignment and matching study intervention kit for the participant. The requestor used his or her own user identification and personal identification number when contacting the IWRS and gave the relevant participant details to uniquely identify the participant.

Participants <30 kg were not to be randomized and offered only golimumab. This ensured that at least 5 participants who weighed <30 kg received golimumab treatment.

Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.

Blinding

This is an open-label study, and therefore blinding procedures are not applicable.

6.4. Study Intervention Compliance

Because golimumab and infliximab will be administered at the investigational site by trained study site staff or golimumab will be self-administered by the participant or their caregiver, treatment compliance for these study interventions will be controlled by site personnel.

Visit window: From Week 0 through Week 54, it is expected that all visits will occur within a range of ±7 days of the scheduled visit. Any visits outside of these ranges should be discussed with the sponsor. After Week 54 the follow-up study visits should occur within ±14 days of the scheduled study visit. Any out-of-range visits after Week 54 should be documented in the participant's source notes.

Dosing window: From Week 0 through the end of the trial, any doses that are planned to occur outside of ±7 day dosing window should be discussed with the sponsor. Golimumab should be administered as close as possible to the q4w dosing schedule.

Study site personnel will maintain a log of all study intervention administered. Study intervention supplies for each participant will be inventoried and accounted for. Information regarding study intervention administrations that are administered outside of the scheduled windows or missed will be recorded. Participant charts and worksheets may be reviewed and compared with the data

entries on the eCRFs to ensure accuracy. Although it is understood that treatment may be interrupted for many reasons, compliance with the treatment schedule is strongly encouraged.

When golimumab is administered by the participant or caregiver away from the site, the amount of study intervention dispensed will be recorded and compared with number of injection devices returned and the and the participant or caregiver will be asked to record administration information on the AHA diary. Participants (and parent/caregiver) will receive instructions on compliance with study treatment when they begin self-administration of golimumab at home. During the course of the study, the investigator or designated study research personnel will be responsible for providing additional instruction to reeducate any participant who is not compliant with taking the study intervention.

6.5. Concomitant Therapy

Prestudy therapies, including prescription or over-the-counter medications, vaccines, vitamins, herbal supplements; non-pharmacologic therapies such as electrical stimulation, acupuncture, special diets, exercise regimens administered up to 30 days before first dose of study intervention must be recorded at screening.

The following are permitted medications; their use at any time during study must be recorded in the eCRF. The recorded information will include a description of the type of therapy, duration of use, dosing regimen, route of administration, and indication.

- Over-the-counter medications, vitamins, herbal supplements
- Prescription therapies, including antibiotics, special diets or dietary supplements

Concomitant therapies must be recorded throughout the study beginning with the screening process and through the final safety visit after the last dose of study intervention. This includes medications given for endoscopies and sedation that occur during the study.

All concomitant medications will be recorded in the eCRF through Week 54. After Week 54, only concomitant medications associated with AEs and SAEs (ie, used to treat event or suspected in causing event) and/or with the treatment of UC will be recorded in the eCRF.

Modification of an effective preexisting therapy should not be made for the explicit purpose of entering a participant into the study.

6.5.1. Ulcerative Colitis-Specific Allowed Concomitant Therapies

The following concomitant medications for UC are allowed in this study: 5-ASAs, corticosteroids, and immunomodulators (ie, 6-MP, AZA, MTX). For participants receiving concomitant therapy with 5-ASAs, immunomodulators and/or corticosteroids for UC, the dosage of these medications must be stable for 2 weeks before the first administration of study intervention at Week 0 (Section 5.1). For participants receiving 5-ASAs at Week 0, the dose must remain stable through Week 54 (except for weight-based adjustments, as treatment of a documented UC flare after Week 6, or if investigator judgment requires dose reduction or cessation because of toxicity or medical necessity).

Immunomodulators (ie, 6-MP, AZA, or MTX) should not be initiated between Week 0 and Week 6. For participants receiving immunomodulators at Week 0, the dose should not be increased (except for weight-based adjustments) through Week 6. Although immunomodulators may be discontinued at any time during the study, it is preferred, at the discretion of the investigator, that they be continued at least through Week 14.

For participants receiving corticosteroids (including budesonide), the steroids may be tapered beginning at Week 0, although it would be preferable to delay the stopping of steroids until after the Week 6 evaluation if clinically reasonable. Corticosteroids cannot be started to treat UC disease flare until after Week 6 study assessments (Section 6.5.3).

UC-specific medical therapies (ie, oral/rectal corticosteroids, oral/rectal 5-aminosalicylate (5-ASA) compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX]) may not be initiated or their dose increased at any time from Week 6 to Week 54 except for weight-based dose adjustments or unless there is a documented UC flare and loss of response that makes the subject eligible for rescue medication (Section 6.5.3).

Rare postmarketing cases of hepatosplenic T-cell lymphoma have been reported in participants treated with other TNFα-blocking agents. This rare type of T-cell lymphoma has a very aggressive disease course and is usually fatal. Nearly all of these cases have occurred in participants with UC or Crohn's disease. The majority were in adolescent and young adult males. Almost all these participants had received treatment with AZA or 6-MP concomitantly with a TNFα blocker at or prior to diagnosis. The potential risk with the combination of AZA or 6-MP and golimumab should be carefully considered. A risk for the development for hepatosplenic T-cell lymphoma in participants treated with TNFα blockers cannot be excluded.

6.5.2. Ulcerative Colitis-Specific Prohibited Concomitant Medications

The following are prohibited medications; participants who initiate any of these treatments at any time during study participation will have their study intervention discontinued:

- Immunomodulatory agents other than 6-MP, AZA, or MTX (including, but not limited to, 6-TG, cyclosporine, mycophenolate mofetil, tacrolimus, and sirolimus)
- Immunomodulatory biologic agents (including, but not limited to, TNFα antagonists (eg, etanercept, adalimumab), ustekinumab, abatacept, anakinra, rituximab, alemtuzumab, vedolizumab, natalizumab, and visilizumab)
- Thalidomide or related agents
- Investigational drugs

The sponsor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered.

6.5.3. Rescue Medication

The sponsor will not supply rescue medication.

During the long-term phase of the study, participants who meet the following criteria will be considered to be in clinical flare:

- For study subjects who responded at Week 6 - an increase of the partial Mayo score from Week 6 of at least 2 points and an absolute partial Mayo score ≥4; or an absolute partial Mayo score ≥7 points, or

- For study subjects who did not have a Week 6 response but achieved a response at Weeks 14 or 22 (after additional discretionary doses of golimumab or infliximab [Section 4.1]) - an increase in the partial Mayo score from Weeks 14 or 22 of at least 2 points and an absolute partial Mayo score ≥4; or an absolute partial Mayo score ≥7 points.

In the study extension, the determination that a subject is in clinical flare will be at the discretion of the investigator. However, the basis for this determination should be consistent with the criteria used in the long-term phase, namely an increase in the partial Mayo score by 2 points **and** an absolute partial Mayo score ≥4; **or** an absolute partial Mayo score of ≥7 and based on the study participant (or caregiver)-reported stool frequency and degree of rectal bleeding, as well as a global assessment of UC disease activity made by a study primary- or sub-investigator. These findings supporting a determination of UC disease flare in the study extension should be recorded in the study source documents.

UC-specific medical therapies (ie, oral/rectal corticosteroids, oral/rectal 5-aminosalicylate (5ASA) compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX]) may not be initiated or their dose increased at any time from Week 6 to Week 54 except for weight-based dose adjustments or unless there is a documented UC flare and loss of response that makes the subject eligible for rescue medication (Section 6.5.1).

Participants who flare while enrolled in the study will be eligible to receive rescue medication (ie, corticosteroids, 6-MP, AZA, MTX, and/or 5-ASAs) while continuing to receive study intervention administration as scheduled. Participants who flare between Weeks 6 and 54 (at the discretion of the investigator) can receive rescue treatment with 2 limited courses (prednisolone/prednisone at 1 mg/kg/d [max 40 mg] once daily for up to 3 weeks followed by a tapering period of up to 8 to 10 weeks) of corticosteroids for UC as clinically indicated. Second-generation oral steroids with lower systemic effect such as beclomethasone and budesonide may be used to treat a UC disease flare in place of systemic steroids. Their use counts towards the 2 steroid courses. After Week 54, participants may receive 2 additional steroid courses at the discretion of the investigator to treat a UC disease flare. The date and time of rescue corticosteroid administration as well as the name and dosage regimen of the rescue medication must be recorded.

Participants who are receiving infliximab and experience a flare in their UC disease after Week 6 may initiate the step-wise dose escalation to the maximum of 10 mg/kg (capped at 1 gm) q4w as defined in Section 4, Study Design.

Other UC-specific rescue therapies (ie, rectal corticosteroids, oral/rectal 5-aminosalicylate [5-ASA] compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX]) may be initiated or their dose increased at the discretion of the investigator to manage symptoms in the setting of a documented UC flare. The use of rectal steroids does not count toward the permitted steroid courses.

However, any participant who uses UC-prohibited medications (Section 6.5.2) or requires more than 2 courses of corticosteroids (including budesonide) or requires parenteral (IV) steroids for UC during the 54-week study will be discontinued from further administration of study intervention.

6.6. Dose Modification

During the early and late-phases of the study, 2 types of dose adjustments are permissible. Weight-based dosing adjustments are required for all participants receiving infliximab, and for those participants receiving golimumab who weigh <45 kg. In addition, for participants receiving infliximab, dose escalation (to 10 mg/kg to a maximum of 1 gm, q4w) is permitted using the protocol as defined in Section 4, Study Design. In the study extension, participants in certain jurisdictions who weigh between 45 kg and 80 kg can, at the discretion of the investigator, reduce their 100 mg q4w golimumab dose to 50 mg SC q4w. This reflects permitted posologies and clinical practice in these specific jurisdictions and is not applicable to all study participants. After this dose de-escalation, participants are permitted to return to the 100 mg q4w dosing, but no additional dose adjustments for golimumab are permitted. Any dose/dosage adjustment should be overseen by medically-qualified study site personnel.

The decision to proceed to the next dose level of golimumab or infliximab (either an increase or a decrease) will be made by the investigator based on safety, tolerability, and clinical judgment. Infliximab dosing will not exceed 10 mg/kg (capped at 1 gm) at an interval more frequent than q4w.

6.7. Intervention After the End of the Study

The study extension is described in Section 4.1, Overall Design.

After the Week 54 evaluations, at the discretion of the investigator, if participants receiving golimumab are able to benefit from continued SC golimumab, the participants will continue to receive SC golimumab q4w starting at Week 54 under this protocol's study extension until marketing authorization is obtained for golimumab for the treatment of pediatric participants with UC, the participant turns 18 and has access to commercially available golimumab, or until a decision is made not to pursue an indication in this pediatric UC population, whichever occurs first. Participants who continue golimumab treatment as part of the study extension will be intermittently evaluated per the protocol for efficacy, PK, and safety.

After the Week 54 evaluations, participants receiving infliximab will be withdrawn from study participation and transition to local standard of care which may include continued infliximab at the discretion of their physician.

Participants who discontinue the study and are not transitioning to commercially available golimumab must complete a final safety visit at the study site about 8 weeks (infliximab) or 16 weeks (golimumab) after the last dose of study intervention, unless the participant has died, is lost to follow-up, is continuing golimumab after exiting the study, or has withdrawn consent. Participants who are planning to continue golimumab treatment after exiting the study should have all final safety visit assessments done during the last study visit while on study golimumab. If the participant has died, the date and cause of death will be collected and documented on the eCRF.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

A participant's study intervention must be discontinued if:

1. The investigator believes that for safety reasons or tolerability reasons (eg, AE) it is in the best interest of the participant to discontinue study intervention.
2. The participant initiates treatment with prohibited therapies for UC (Section 6.5.2).
3. The participant requires the addition of parenteral (IV) steroids or more than 2 courses of corticosteroids (including budesonide) for UC flares during the 54-week study.
4. The participant fails to meet Week 6, Week 14, or Week 22 criteria to continue study intervention.
5. The participant has a disease-related surgery that represents a lack of efficacy of study intervention (ie, colectomy) or that will preclude the future ability to assess efficacy using the Mayo score or other instruments required for demonstration of efficacy endpoints.
6. The participant becomes pregnant or plans a pregnancy within the study period. Refer to Appendix 14 (Section 10.14, Contraceptive and Barrier Guidance and Collection of Pregnancy Information).
7. The participant develops a clinically significant cardiovascular event, including but not limited to congestive heart failure, at any time during the study.
8. The participant (or the participant's representative) withdraws consent for administration of study intervention.
9. The participant develops a systemic opportunistic infection.
10. The participant misses 2 consecutive doses of golimumab after Week 10 because of body weight below the 10 kg limit.
11. The participant is deemed ineligible according to the following TB screening criteria:
    - A diagnosis of active TB is made.

- A participant has symptoms suggestive of active TB based on follow-up assessment questions and/or physical examination or has had recent close contact with a person with active TB and cannot or will not continue to undergo additional evaluation.
- A participant undergoing evaluation has a chest radiograph with evidence of current active TB and/or a positive QuantiFERON-TB or T-Spot test result (and/or a positive tuberculin skin test result in countries in which the QuantiFERON-TB or T-Spot test is not approved/registered or the tuberculin skin test is mandated by local health authorities), unless active TB can be ruled out and appropriate treatment for latent TB can be initiated prior to the next study intervention administration and continued to completion (see also Section 8.3.6, and Appendix 3 [Section 10.3]). Indeterminate QuantiFERON-TB test or T-Spot test results should be handled as in Section 8.3.6.
- A participant whose first QuantiFERON-TB test result or T-Spot test result is indeterminate should have the test repeated. In the event that the second QuantiFERON-TB or T-Spot test result is also indeterminate, the participant should be excluded from the study.

12. The participant has a serious adverse reaction that is related to an injection or an infusion, including an injection-site or infusion reaction, resulting in bronchospasm with wheezing and/or dyspnea that requires ventilatory support **OR** that results in symptomatic hypotension with a decrease in systolic blood pressure >40 mm Hg or blood pressure <90/60 mm Hg.
13. The participant has a reaction resulting in myalgia and/or arthralgia with fever and/or rash (suggestive of serum sickness and not representative of signs and symptoms of other recognized clinical syndromes) occurring 1 to 14 days after an injection of study intervention. These may be accompanied by other events including pruritus, facial, hand, or lip edema, dysphagia, urticaria, sore throat, and/or headache.
14. The participant has severe hepatic function abnormalities, as described in Section 8.2.3 and Appendix 13 (Section 10.13).
15. The participant has a malignancy including squamous cell skin cancer. Consideration may be given to allowing participants who develop ≤2 basal cell skin cancers that are adequately treated with no evidence of residual disease to continue to receive study intervention.

Participants will not be automatically withdrawn from the study if they discontinue study intervention before the end of the treatment regimen.

Discontinuation of a participant's study intervention must be <u>strongly considered</u> under the following conditions:

1. Persistent inadequate response or worsening of UC:
   a. Participants in the long-term or study extension phases of the study who meet the criteria as defined Section 6.5.3 will be considered to be in clinical flare. A sigmoidoscopy (or colonoscopy) can be considered to aid clinical judgment and should be performed using study software and submitted for central review.
   b. Participants in clinical flare will be eligible to receive rescue medication (ie, corticosteroids, 5-ASA, 6-MP, AZA, MTX, Section 6.5.3 or infliximab dose escalation Section 6.6) while continuing to receive study intervention administration as scheduled.

c. Participants will be reassessed after 2 administrations of study intervention after the visit at which the loss of clinical response criteria was met or, for infliximab receiving participants, after 2 administrations at the escalated dose using the protocol as defined in Section 4, Study Design. During this interval, clinical flare criteria will not be applied. Participants in the long-term phase who have not achieved a partial Mayo response (ie, a decrease from the flare baseline of ≥2 in the partial Mayo score) at this visit despite rescue medications will be discontinued from study intervention administration and should return for a final safety visit approximately 8 (infliximab) or 16 (golimumab) weeks after their last study intervention administration.

   For participants in the study extension, a clinical response to rescue therapy will be at the discretion of the study investigator but should be consistent with a partial Mayo score of ≤4 based on participant (or caregiver)-reported stool frequency and degree of rectal bleeding, as well as a global assessment of UC disease activity determined by a study primary- or sub-investigator. These findings demonstrating a clinical response should be recorded in the study source documents. Participants in the study extension who do not achieve a clinical response despite rescue medications will be discontinued from the study interventions and should return for a final safety visit 16 weeks after the last administration of study intervention.

   Participants who are assessed as having responded to rescue therapy will continue in the study.

d. After the clinical flare, participants who remain in the study will continue to be assessed for clinical flare. Participants who subsequently meet the criteria for clinical flare again may receive rescue medication a second time and be assessed for an adequate response and managed as described above.

e. If a third clinical flare occurs or the participant experiences AEs consistent with clinically significant worsening of UC at any time during the study, discontinuation of study intervention should be strongly considered.

These events should be evaluated by the investigator and the Sponsor to decide on discontinuation of study intervention. Discontinuation of study intervention should be considered in participants with clinically significant worsening of UC disease where continuation of the study intervention is not in the best interest of the participant.

2. The participant develops a serious infection, including but not limited to sepsis or pneumonia.

If a participant discontinues study intervention for any reason before Week 14, they should return for all scheduled visits through Week 14 (including endoscopy at Week 6) and a final safety visit, 16 weeks after the last dose of golimumab or 8 weeks after the last dose of infliximab. During the long-term phase of the study, if a participant discontinues study intervention for any reason before the Week 54 assessments, the early discontinuation assessments should be obtained if possible as specified in the Schedule of Activities (Table 1), and a final safety visit completed 16 weeks after the last dose of golimumab or 8 weeks after the last dose of infliximab. If a participant discontinues study intervention during the study extension, a final safety visit, 16 weeks after the last dose of golimumab should be completed as specified in the Schedule of Activities (Table 2). If the reason for discontinuation of study intervention is withdrawal of consent, every effort should be made to conduct the efficacy and safety visit assessments, as indicated in the Schedule of Activities, prior

to terminating study participation. After termination of consent, no additional protocol assessments are allowed.

7.2. Participant Discontinuation/Withdrawal from the Study

Participant discontinuation/withdrawal from the study is defined as no longer following up for study visits. It is different from discontinuation from study intervention, as described in Section 7.1.

A participant will be withdrawn from the study for any of the following reasons:

- Lost to follow-up
- Withdrawal of consent
- Sponsor decision (eg, participating in any other clinical study with an investigational intervention)
- Death
- Noncompliance with scheduled study activities as deemed appropriate by the sponsor

When a participant withdraws before completing the study, the reason for withdrawal is to be documented in the eCRF and in the source document. Study intervention assigned to the withdrawn participant may not be assigned to another participant. Additional participants will not be entered. If a participant discontinues study intervention and withdraws from the study, end-of-intervention efficacy and safety assessments should be obtained. If the reason for withdrawal from the study is withdrawal of consent, then no additional assessments are allowed.

7.2.1. Withdrawal from the Main Study and the Use of Biomarker Samples

A participant who withdraws from the study will have the following options regarding the biomarker sample:

- The collected samples will be retained and used in accordance with the participant's original informed consent/assent.
- The participant may withdraw consent for biomarker sample, in which case the sample will be destroyed, and no further testing will take place. To initiate the sample destruction process, the investigator must notify the sponsor study site contact of withdrawal of consent for the biomarker samples and to request sample destruction. The sponsor study site contact will, in turn, contact the biomarker representative to execute sample destruction. If requested, the investigator will receive written confirmation from the sponsor that the samples have been destroyed.

Withdrawal from the Biomarker Samples While Remaining in the Main Study

The participant may withdraw consent for biomarker samples while remaining in the study. The participant may refuse the collection of biomarker samples or may withdraw consent after samples have been obtained. In such a case, the biomarker samples will be destroyed. The sample destruction process will proceed as described above.

Withdrawal from the Use of Samples in Future Research

The participant may withdraw consent for use of samples for research (refer to Appendix 12 [Section 10.12, Regulatory, Ethical, and Study Oversight Considerations]). In such a case, samples will be destroyed after they are no longer needed for the clinical study. Details of the sample retention for research are presented in the main ICF.

7.3. Lost to Follow-up

If a participant is lost to follow-up, every reasonable effort must be made by the study site personnel to contact the participant and determine the reason for discontinuation/withdrawal. Such efforts should include repeated telephone calls, certified letters, and email requests. The measures taken to follow-up must be documented. Refer to Section 7.2, Participant Discontinuation/Withdrawal from the Study.

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

The Schedule of Activities (Table 1 and Table 2) summarizes the frequency and timing of efficacy, PK, immunogenicity, PD, biomarker, and safety measurements applicable to this study.

All visit-specific patient-reported outcomes (PRO) assessments should be conducted/completed after the PUCAI is administered but before any other tests, procedures, or other consultations for that visit to prevent influencing participant perceptions. All other efficacy evaluations should be completed before study intervention administrations.

Actual dates of visit-specific assessments will be recorded in the source documentation and eCRF as required.

The following efficacy outcomes (PUCAI and IMPACT III) will be captured electronically in a tablet device at the appropriate visits, as outlined in the Schedule of Activities (Section 1.3 [Table 1 and Table 2]).

Information about how and when data are filed, stored, and transmitted to or from the study site is provided in the electronic patient-reported outcome (ePRO) electronic tablet device and User Manual.

Additional serum or urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulation, to establish the absence of pregnancy at any time during the participation in the study.

The total blood volume to be collected from each participant will be approximately 105 mL blood over 54 weeks and an additional approximately 5 to 10 mL (depending upon the visit) during study extension. Participants with body weight of 10 kg to <12.3 kg will not have the RNA blood sample collected and will have lesser total volume.

Repeat or unscheduled samples may be taken for safety reasons or for technical issues with the samples.

Sample Collection and Handling

The actual dates and times of sample collection must be recorded in the eCRF or laboratory requisition form.

Refer to the Schedule of Activities (Section 1.3 [Table 1 and Table 2]) for the timing and frequency of all sample collections.

Instructions for the collection, handling, storage, and shipment of samples are found in the laboratory manual. Collection, handling, storage, and shipment of samples must be under the specified, and where applicable, controlled temperature conditions as indicated in the laboratory manual.

Study-Specific Materials

The investigator will be provided with the following:

- Golimumab IB
- Infliximab IB
- Instructions for Use
- Site Investigational Product Procedures Manual
- Laboratory manual
- Retesting and rescreening plan
- NCI-CTCAE
- PRO questionnaires and PRO completion guidelines
- IWRS Manual
- eCRF guidelines
- Sample ICF/assent forms
- Participant diaries
- Imaging kit (laptop) and manual
- ePRO electronic tablet device and User Manual
- iPad® and site user guide, if the study site is participating in electronic informed consent/assent.

8.1. Efficacy Assessments

Efficacy evaluations will include the following:

- Mayo score
- Partial Mayo score
- PUCAI score
- C-reactive protein (CRP)
- Fecal calprotectin
- IMPACT III
- TUMMY-UC and Observer TUMMY-UC

The Schedule of Activities summarizes the frequency and timing of efficacy measurements applicable to this study (Section 1.3 [Table 1 and Table 2]).

8.1.1. Mayo Score

The Mayo score[40] was developed from the criteria of Truelove and Witts[46] for mild, moderate, and severe UC; and from the criteria of Baron et al[3] for grading the mucosal appearance. The Mayo score consists of 4 subscores (stool frequency, rectal bleeding, endoscopy findings, and physician's global assessment), each of which is rated on a scale from 0 to 3, indicating normal to severe activity. The Mayo score is calculated as the sum of the 4 subscores and values range from 0 to 12. The Mayo scoring system is provided in Appendix 4 (Section 10.4).

A score of 3 to 5 points indicates mildly active disease; a score of 6 to 10 indicates moderately active disease; and a score of 11 to 12 indicates severe disease.

Mayo scores are calculated using the following:

1. The stool frequency and rectal bleeding data collected in a study diary over 7 consecutive days within the 14 days prior to the visit. Stool frequency and rectal bleeding subscores will be calculated using the average of the 3-consecutive day period in the diary closest to the study visit. Refer to the study reference study binder on how to proceed when a consecutive 3-day period is not available. Days on which the following conditions are met should be excluded from the calculation:
    a. The day medications for constipation, diarrhea, or irregularity were taken (For participants maintained on a stable dose of bulking or stool softening agents throughout the study, the days on which these agents are taken should not be excluded from consideration in calculating the Mayo score).
    b. The day(s) of a procedure or preparation for a procedure (eg, enemas, other laxatives, a clear liquid diet) that would affect bowel frequency and/or blood content of the stool.
    c. The 48 hours after the use of antimotility agents (ie, diphenoxylate hydrochloride with atropine sulfate, loperamide, or other opioids).

d. The 48 hours immediately following a colonoscopy.

2. The Physician's Global Assessment.

3. The results of a sigmoidoscopy or colonoscopy. Endoscopies are to be performed using study software and submitted for central review. Scoring for disease activity based on endoscopic appearance is to be performed both by the local endoscopist and the central reviewer. All decisions to initiate (Week 0) or continue therapy (Weeks 6 and 54) based on mucosal disease activity will be based on local reads.

Approaches to calculating Mayo and partial Mayo scores in participants who have missing subscores will be detailed in the Statistical Analysis Plan (SAP).

8.1.2. Partial Mayo Score

The partial Mayo score is the Mayo score without the endoscopy subscore and values range from 0 to 9. Partial Mayo scores are calculated using data from items 1 and 2 of the Mayo score calculation (Section 8.1.1).

8.1.3. Pediatric Ulcerative Colitis Activity Index Score

The PUCAI, a noninvasive measure of UC disease activity, is calculated using variables listed in Appendix 5 (Section 10.5). It comprises 6 scales and ranges between 0 and 85 points. The scales are: abdominal pain, rectal bleeding, stool consistency, number of stools, nocturnal bowel movement, and activity level.[47]

The PUCAI score is calculated as the sum of the 6 subscores. The PUCAI score will be calculated if at least 3 of the 6 subscores are available from the visit at which the PUCAI score is measured. For missing PUCAI subscores, the last available subscore value will be carried forward to calculate the score. If the PUCAI score cannot be calculated, it will be considered missing (insufficient data) for that visit.

A PUCAI score of <10 indicates remission, and a decrease of 20 points is considered a minimally clinically important change.[46,47]

8.1.4. C-reactive Protein

C-reactive protein has been demonstrated to be useful as a marker of inflammation in participants with IBD. In UC, elevated CRP has been associated with severe clinical activity, an elevated sedimentation rate, and active disease as detected by colonoscopy.[42,53] C-reactive protein will be assayed using a validated, high sensitivity CRP assay.

8.1.5. Fecal Calprotectin

Fecal calprotectin has been demonstrated to be sensitive and specific marker of intestinal inflammation and response to treatment in participants with IBD.[7,9,23] Assays for fecal calprotectin concentration will be performed using a validated method.

8.1.6. IMPACT III

Quality of life measures will be assessed in participants who are 10 to 17 years of age at Week 0 using the IMPACT-III questionnaire (Appendix 7 [Section 10.7]). The questionnaire comprises 35 questions on a variety of topics, from mood, self-image, and school absences to self-perceptions of weight and height. It has been validated in many studies and is applicable for children 10 to 17 years of age with UC or Crohn's disease. The score ranges from 35 to 175.[36]

8.1.7. Exploratory Evaluations

8.1.7.1. TUMMY-UC and Observer TUMMY-UC

The TUMMY-UC is an exploratory noninvasive PRO for the measurement of signs and symptoms for pediatric UC which is undergoing validation.[32] It is calculated using variables listed in Appendix 8 (Section 10.8). It includes 6 components similar to the PUCAI index and ranges from 0 to 114. The Observer TUMMY-UC is for participants under age 8 and is completed by caregivers. The version used at the Week 0 assessment will be used at all subsequent assessments regardless of if participant age changes.

8.2. Safety Assessments

Adverse events will be reported and followed by the investigator as specified in Section 8.3, Adverse Events and Serious Adverse Events and Appendix 16 (Section 10.16), Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting.

Any clinically significant abnormalities persisting at the end of the study/early withdrawal will be followed by the investigator until resolution or until a clinically stable endpoint is reached.

The study will include the following evaluations of safety and tolerability according to the time points provided in the Schedule of Activities (Section 1.3 [Table 1] and [Table 2]).

8.2.1. Physical Examination

Physical examinations (including skin examinations) will be performed as specified in the Schedule of Activities. Height and weight will be recorded at screening; height, weight and other vital signs will also be recorded at timepoints specified in the Schedule of Activities (Section 1.3 [Table 1] and [Table 2]).

8.2.2. Vital Signs

Vital signs (including temperature, pulse/heart rate, respiratory rate, and blood pressure) should be obtained before and approximately 30 minutes after every SC golimumab administration when administered by a healthcare provider. Vital signs will be obtained before, approximately every 30 minutes during, and twice (at approximately 30-minute intervals) after completion of the IV infusion(s) of infliximab.

8.2.3. Clinical Safety Laboratory Assessments

Blood samples will be collected for routine hematology and blood chemistry laboratory analyses at timepoints specified in the Schedule of Activities (Section 1.3. [Table 1] and [Table 2]).

The investigator must review the laboratory report in a timely manner, document this review, and record any clinically relevant changes occurring during the studies in the adverse event section of the eCRF. The laboratory reports must be filed with the source documents.

The following tests will be performed by the central laboratory:

- **Hematology panel**
  - Hemoglobin
  - Hematocrit
  - White blood cell count with differential
  - Platelet count
- **Serum chemistry panel**
  - sodium
  - potassium
  - chloride
  - blood urea nitrogen
  - creatinine
  - aspartate aminotransferase (AST)
  - alanine aminotransferase (ALT)
  - gamma glutamyl transferase (GGT)
  - total and direct bilirubin
  - alkaline phosphatase
  - calcium
  - phosphate
  - albumin
  - total protein
- **Abnormal liver function tests:** If laboratory testing for a participant who is enrolled in the study and receiving study intervention reveals an increase of serum aminotransferases (ALT or AST) to >3 x upper limit of normal (ULN) and an increase of bilirubin to >2 x ULN, study intervention should be suspended immediately. In addition, laboratory tests for ALT, AST, alkaline phosphatase, and total bilirubin should be confirmed by a retest within 24 hours if possible, but no later than 72 hours following notification of test results. See Appendix 13 (Section 10.13; Liver Safety: Suggested Actions and Follow-up Assessments) for additional information on monitoring and assessment of abnormal liver function tests.

- **Pregnancy testing:** Girls of childbearing potential will undergo a serum β-human chorionic gonadotropin pregnancy test at screening, and a urine pregnancy test before all study intervention administration visits.
- Serology for HBV: HBsAg, anti-HBs, and anti-HBc total at screening.
- HBV DNA detection will only be performed for participants who test positive for core antibody and negative for surface antibody.
- Serology for hepatitis C virus (HCV) at screening.
- Serology for HIV at screening: HIV testing in study participants who are less than 6 years of age is not universally required. It is required in those study participants who are less than 6 years of age and the birth history is unknown (ie, adopted) or has exposure risks (parents with HIV or with risk factors) or at the discretion of the study investigator. In subjects who are less than 6 years of age where testing would be required, if there is a record of a negative HIV test at birth this is acceptable at the discretion of the study physician as long as it is entered into the study record.
- Serology for antinuclear antibodies (ANA) and anti-dsDNA.

8.2.4. Concomitant Medication Review

Concomitant medications will be reviewed at each visit.

All concomitant medications will be recorded in the eCRF through Week 54. After Week 54, only concomitant medications associated with AEs and SAEs (ie, used to treat event or suspected in causing event) and/or with the treatment of UC will be recorded in the eCRF.

8.2.5. Injection-site Reactions

A study intervention injection-site reaction is any adverse reaction at a SC study intervention injection-site. Through Week 54, the injection sites will be evaluated by site staff for reactions and any injection-site reactions will be recorded as an AE in the eCRF and source data. In addition, the duration of injection-site reactions, including injection-site pain, will be captured with the standard AE information which includes information on the start and end date, as well as the start and end time of the AE. Discontinuations due to injection-site reactions, including injection-site pain, will also be recorded. Participants will be observed for at least 30 minutes after the administration of study intervention for symptoms of an injection-site reaction at the investigative site.

Beginning at Week 58, participants administering study intervention at home will receive detailed instructions on how to monitor and report potential injection-site reactions. Any adverse reaction (eg, swelling, redness/erythema, pain, tenderness, warmth, bruising, or bleeding) should be noted in the AHA diary and in the AE page of the eCRF.

Reactions temporarily associated with an infusion

An infusion reaction is defined as an AE that occurs during or within 1 hour after the infusion of study intervention, with the exception of laboratory abnormalities. Minor infusion reactions may be managed by slowing the rate of the IV infusion and/or treating with antihistamines and/or acetaminophen (paracetamol) as clinically indicated. If an IV infusion of study intervention is stopped because of an infusion reaction and the reaction, in the opinion of the investigator, is not severe or does not result in a serious adverse event (SAE; Section 8.3) the infusion may be restarted with caution.

Allergic Reactions

Before any on-site SC injection or IV infusion, appropriately trained personnel and medications must be available to treat allergic reactions, including anaphylaxis. Appropriate medical personnel must be in attendance at the time of the injection and for at least 30 minutes after the SC injection.

Appropriate medical personnel must remain in close proximity to the infusion center for the remaining duration of the infusion, and for 1 hour after the end of the infusion in the event that emergency resuscitation is required. All participants must be observed carefully for symptoms of an allergic reaction (eg, urticaria, itching, hives).

If a mild or moderate allergic reaction is observed, paracetamol, NSAIDs, and/or diphenhydramine or locally available alternative may be administered. In the case of a severe allergic reaction (eg, anaphylaxis), SC aqueous epinephrine, corticosteroids, respiratory assistance, and other proper resuscitative measures are essential and must be available at the study site where the injections or infusions are being given.

Participants who experience severe adverse reactions related to an injection or infusion must be discontinued from further study intervention administrations.

For moderate or lesser adverse reactions related to an injection or infusion, the participant may be permanently discontinued from further study interventions at the discretion of the investigator.

Participants who experience serious adverse reactions after an injection or infusion that result in bronchospasm with wheezing and/or dyspnea that requires ventilatory support OR that result in symptomatic hypotension with a decrease in systolic blood pressure >40 mm Hg or blood pressure <90/60 mm Hg will not be permitted to receive additional study intervention.

8.2.6. Infections

Study intervention should not be administered to a participant with a clinically important, active infection. Investigators are required to evaluate participants for any signs or symptoms of infection at scheduled visits as specified in the Schedule of Activities. If a participant develops a serious infection, including but not limited to sepsis or pneumonia, discontinuation of study intervention administration must be considered. For an active varicella-zoster infection or a significant exposure to varicella-zoster infection in a participant without a history of chickenpox, study

intervention administration should be interrupted until the symptoms have resolved and no active infection is present.

8.3. Adverse Events and Serious Adverse Events

Timely, accurate, and complete reporting and analysis of safety information from clinical studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide. The sponsor has established Standard Operating Procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of safety information; all clinical studies conducted by the sponsor or its affiliates will be conducted in accordance with those procedures.

Adverse events will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally acceptable representative) for the duration of the study. At each visit, participants (or, when appropriate, a caregiver, surrogate, or the participant's legally acceptable representative) will be questioned about any AEs (eg, "side effects") occurring since the previous visit and the outcomes for any AEs reported at previous visits.

Anticipated events will be recorded and reported as described in Appendix 6 (Section 10.6).

For further details on AEs and SAEs (Definitions and Classifications; Attribution Definitions; Severity Criteria; Special Reporting Situations; Procedures) as well as product quality complaints, refer to Appendix 16 (Section 10.16 Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting).

8.3.1. Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information

All Adverse Events

All AEs and special reporting situations, whether serious or non-serious, will be reported from the time a signed and dated ICF is obtained until completion of the participant's last study-related procedure, which may include contact for follow-up of safety. Serious adverse events, including those spontaneously reported to the investigator within 8 (infliximab) or 16 (golimumab) weeks after the last dose of study intervention, must be reported using the Serious Adverse Event Form. The sponsor will evaluate any safety information that is spontaneously reported by an investigator beyond the time frame specified in the protocol.

Serious Adverse Events

All SAEs occurring during the study must be reported to the appropriate sponsor contact person by study site personnel within 24 hours of their knowledge of the event.

Information regarding SAEs will be transmitted to the sponsor using the Serious Adverse Event Form and Safety Report Form of the eCRF, which must be completed and reviewed by a physician from the study site and transmitted to the sponsor within 24 hours. The initial and follow-up reports of a SAE should be transmitted electronically or by facsimile (fax).

8.3.2. Method of Detecting Adverse Events and Serious Adverse Events

Care will be taken not to introduce bias when detecting AEs or SAEs. Open-ended and nonleading verbal questioning of the participant and the participant's caregiver is the preferred method to inquire about adverse event occurrence.

Solicited Adverse Events

Solicited AEs are predefined local events occurring at the injection-site and systemic events for which the participant is specifically questioned and which are noted by participants in their diary (see Section 8; Study Assessments and Procedures).

Unsolicited Adverse Events

Unsolicited AEs are all adverse events for which the participant is not specifically questioned.

8.3.3. Follow-up of Adverse Events and Serious Adverse Events

Adverse events, including pregnancy, will be followed by the investigator as specified in Appendix 16 (Section 10.16, Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting).

8.3.4. Regulatory Reporting Requirements for Serious Adverse Events

The sponsor assumes responsibility for appropriate reporting of AEs to the regulatory authorities. The sponsor will also report to the investigator (and the head of the investigational institute where required) all suspected unexpected serious adverse reactions (SUSARs). For anticipated events reported as individual SAEs the sponsor will make a determination of relatedness in addition to and independent of the investigator's assessment Appendix 17 (Section 10.17). The sponsor will periodically evaluate the accumulating data and, when there is sufficient evidence and the sponsor has determined there is a reasonable possibility that the intervention caused a serious anticipated event, they will submit a safety report in narrative format to the investigators (and the head of the institute where required). The sponsor assumes responsibility for appropriate reporting of anticipated events to the regulatory authorities according to requirements of the countries in which the studies are conducted. The investigator (or sponsor where required) must report SUSARs to the appropriate Independent Ethics Committee/Institutional Review Board (IEC/IRB) that approved the protocol unless otherwise required and documented by the IEC/IRB.

8.3.5. Pregnancy

All initial reports of pregnancy in girls or partners of boys must be reported to the sponsor by the study site personnel within 24 hours of their knowledge of the event using the appropriate pregnancy notification form. Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs and must be reported using the Serious Adverse Event Form. Any participant who becomes pregnant during the study must discontinue further study treatment.

Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required.

8.3.6. Tuberculosis Evaluation

8.3.6.1. Initial Tuberculosis Evaluation

During the screening period, participants must undergo testing for TB and their medical history assessment must include specific questions about a history of TB or known occupational or other personal exposure to individuals with active TB. The participant should be asked about past testing for TB, including chest radiograph results and responses to tuberculin skin or other TB testing.

Participants with a negative QuantiFERON-TB or T-Spot test result (and/or a negative tuberculin skin test result in countries in which the QuantiFERON-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities) are eligible to continue with prerandomization procedures. Participants with a newly identified positive QuantiFERON-TB or T-Spot or tuberculin skin test result must be excluded from the study (see Appendix 3 [Section 10.3]).

If the QuantiFERON-TB or T-Spot cannot be obtained, the tuberculin skin test can be performed instead after discussion with the medical monitor. The tuberculin skin test will be required in addition to the QuantiFERON-TB or T-Spot in countries where QuantiFERON-TB or T-Spot is not registered/approved or if the tuberculin skin test is mandated by local health authorities.

Investigators have the option to use 2 TB screening tests (selecting from the QuantiFERON-TB test, the T-Spot test, and the tuberculin skin test) to screen for latent TB if they believe, based on their judgment, that the use of 2 tests is clinically indicated in order to evaluate a participant who has high risk of having latent TB. If a single test is positive, the participant is considered to have latent TB infection for the purposes of eligibility for this study and must be excluded from the study.

A participant whose first QuantiFERON-TB or T-Spot or tuberculin skin test result is indeterminate should have the test repeated. In the event that the second QuantiFERON-TB or T-Spot or tuberculin skin test result is also indeterminate, the participant should be excluded from the study.

In select circumstances as approved by the Sponsor, a local laboratory may be used to perform the QuantiFERON-TB or T-Spot test.

8.3.6.2. Ongoing Tuberculosis Evaluation

Early Detection of Active Tuberculosis

To aid in the early detection of TB reactivation or new TB infection during study participation, participants must be evaluated for signs and symptoms of active TB at scheduled visits (refer to the Schedule of Activities). The following series of questions is suggested for use during the evaluation:

- "Has your child had a new cough of >14 days duration or a change in a chronic cough?"
- Has your child had any of the following symptoms:
  - Persistent fever?
  - Unintentional weight loss?
  - Night sweats?"
- Has your child had close contact with an individual with active TB?" (If there is uncertainty as to whether a contact should be considered "close," a physician specializing in TB should be consulted).

If the evaluation raises suspicion that a participant may have TB reactivation or new TB infection, an immediate and thorough investigation should be undertaken, including, where possible, consultation with a physician specializing in TB.

Investigators should be aware that TB reactivation in immunocompromised participants may present as disseminated disease or with extrapulmonary features. Participants with evidence of active TB should be referred for appropriate treatment.

Participants who experience close contact with an individual with active TB during the conduct of the study must have a chest radiograph, a repeat QuantiFERON-TB or T-Spot test, a repeat tuberculin skin test in countries in which the QuantiFERON-TB or T-Spot test is not approved/registered or the tuberculin skin test is mandated by local health authorities, and if possible, referral to a physician specializing in TB to determine the participant's risk of developing active TB and whether treatment for latent TB is warranted. If the QuantiFERON-TB or T-Spot test result is indeterminate, the test should be repeated. In the event that the second QuantiFERON-TB or T-Spot test result is also indeterminate, the participant must immediately discontinue further administration of study intervention and be encouraged to return for all subsequent scheduled study visits according to the protocol.

Adverse Event Reporting

Any newly identified case of active TB occurring after the first study intervention administration(s) in participants participating in this clinical study must be reported by the investigator according to the procedures in (Section 7). Investigators are also advised that active TB is considered a reportable disease in most countries. These events are to be considered serious only if they meet the definition of a serious adverse event.

8.4. Treatment of Overdose

For this study, any dose of golimumab or infliximab greater than 15% higher than planned or indicated based on the participants weight will be considered an overdose. If this happens during the AHA portion of the study, parents/caregivers should immediately contact study site personnel.

In the event of an overdose, the investigator or treating physician should:

- Contact the medical monitor immediately.
- Closely monitor the participant for AE/SAE and laboratory abnormalities.
- Document the quantity of the excess dose as well as the duration of the overdosing in the CRF.

Decisions regarding dose interruptions or modifications will be made by the investigator in consultation with the medical monitor based on the clinical evaluation of the participant.

8.5. Pharmacokinetics

Serum samples will be used to evaluate the PK of golimumab and infliximab. Samples collected for the analyses of serum concentrations of golimumab or infliximab may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period, or for the evaluation of relevant biomarkers. Genetic analyses will not be performed on these serum samples. Participant confidentiality will be maintained.

Evaluations

Venous blood samples of approximately 55 mL will be collected for measurement of serum concentrations of golimumab or infliximab and anti-golimumab or anti-infliximab antibodies over 54 weeks and final safety visits. An additional approximately 50 mL will be collected for other study measurements including CRP, complete blood count, chemistries, and biomarker studies through study Week 54. An additional approximately 5 mL per visit will be collected during study extension when laboratory assessments are indicated in the Schedule of Assessments.

Pharmacokinetic Analytical Procedures

Serum samples will be analyzed to determine concentrations of golimumab or infliximab using respective validated, specific, and sensitive assay methods by or under the supervision of the sponsor.

Pharmacokinetic Parameters

Serum samples will be used to evaluate various golimumab PK parameters based on blood drawn from participants receiving golimumab according to the Schedule of Activities (Section 1.3 [Table 1] and [Table 2]).

8.5.1. Immunogenicity (Antibodies to Golimumab and Infliximab)

Antibodies to golimumab or infliximab will be evaluated on blood drawn from all participants according to the Schedule of Activities. Additionally, samples should also be collected at the final visit for participants who are discontinued from intervention or withdrawn from the study.

Serum samples will be screened for antibodies binding to golimumab or infliximab and the titer of confirmed positive samples will be reported as applicable. Other analyses may be performed to further characterize the immunogenicity of golimumab or infliximab.

Immunogenicity Analytical Procedures

The detection and characterization of antibodies to golimumab or infliximab will be performed using validated assay methods by or under the supervision of the sponsor.

All samples collected for detection of anti-drug antibodies will also be evaluated for the respective serum drug concentration to enable interpretation of the antibody data.

8.6. Biomarkers

Exploratory biomarker assessments will be performed to identify RNA (mRNA or microRNA) expression patterns and microbial activities that are relevant to golimumab and/or infliximab treatment and/or pediatric UC, to correlate histologic and immunohistochemical assessments of disease and healing, and to evaluate whether biomarkers can be developed to predict a golimumab response and/or UC disease activity. Biomarker assessments (described below) will include the evaluation of relevant markers in tissue biopsies, blood, and feces for all participants as specified in the Schedule of Activities.

Instructions for the collection and shipment of biomarker samples will be provided in the laboratory manual.

Mucosal Biopsy Histology and RNA

Mucosal biopsy samples will be collected from all participants during endoscopy according to the Schedule of Activities. Total RNA will be isolated and used for differential gene expression analyses to identify mRNA expression patterns that are relevant to golimumab or infliximab treatment and/or pediatric UC, and to evaluate markers that can predict clinical response and/or monitor UC disease activity. The biopsy samples collected will also be used for the histologic and immunohistochemical assessment of disease and healing. Genetic (DNA) analyses will not be performed on these biopsy samples.

Whole Blood RNA

Whole blood samples will be collected from all participants according to the Schedule of Activities. Total RNA will be isolated and used for differential gene expression analyses to identify mRNA or microRNA expression patterns that are relevant to golimumab or infliximab treatment and/or pediatric UC, and to identify markers that can predict clinical response and/or monitor disease activity. Genetic (DNA) analyses will not be performed on these blood samples.

Fecal Biomarkers

Fecal samples will be collected from all participants as specified in the Schedule of Activities. Microbiome and associated products analysis will be conducted to evaluate the association between microbial activities and golimumab and/or pediatric UC. The relationships between microbiome, metabolites, and biomarkers in other tissue samples will also be assessed.

Stopping Analysis

Biomarker analyses are dependent upon clinical response rates. Biomarker analysis may be deferred or not performed, if there are not enough samples or responders to allow for adequate biomarker evaluation. In the event the study is terminated early or shows poor clinical efficacy, completion of biomarker assessments is based on justification and intended utility of the data.

9. STATISTICAL CONSIDERATIONS

Statistical analysis will be done by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be used to analyze the efficacy and safety data is outlined below. Specific details will be provided in the SAP.

9.1. Statistical Hypotheses

The primary hypothesis is that golimumab is an effective therapy in pediatric UC relative to a historical placebo control as assessed by clinical remission at Week 6 based on the Mayo score. The historical placebo clinical remission rate is based on a meta-analysis of 7 adult UC studies including infliximab Phase 3 (C0168T37 and C0168T46), golimumab Phase 2/3 (C0524T16 and C0524T17), adalimumab Phase 3 (ULTRA 1 and ULTRA 2), and vedolizumab Phase 3 (GEMINI 1).

9.2. Criteria for Success

The success of the study will ultimately be based on the totality of evidence. The primary analysis will be based on the proportion of golimumab pediatric participants in clinical remission at Week 6 based on the Mayo score and its associated 90% CI. The criteria for the primary analysis will have been met if the lower limit of the two-sided 90% CI for the proportion of golimumab participants in clinical remission at Week 6 is >10.0% (ie, the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 derived from a meta-analysis of 7 adult UC studies including 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints).

9.3. Sample Size Determination

Sample size calculations were based on the need to have a sufficient number of participants assigned to the golimumab treatment arm to achieve the criteria defined in Section 9.2. In addition, collecting sufficient PK data to adequately characterize the PK of golimumab in participants with UC is also considered.

A sample size of 60 participants in the golimumab arm will ensure that the lower bound of the 90% CI for the pediatric golimumab remission rate is above 10.0% (ie, the upper bound of the 95% CI for the historical placebo control) as long as the observed remission rate is at least 18.3%. The probability of observing a remission rate of ≥18.3%, given different assumptions for the true rate of clinical remission is shown in Table 6.

With 60 golimumab-treated participants, the probability of observing a remission rate of ≥18.3% ranges from 50% (if the golimumab adult UC remission rate of 17.8% is assumed) to greater than

99% (if the remission rate of 42.9% from the first golimumab study in pediatric UC is assumed). It is reasonable to assume that the true remission rate in pediatric UC participants is greater than the remission rate observed in the adult UC study, as the remission rate in the first golimumab pediatric UC study was at least twice that observed in the adult UC study. Therefore, if we assume the remission rate to be 22.5%, then the probability of observing a remission rate of ≥18.3% is at least 80% (Table 6).

Table 6: Probability of Observing a Clinical Remission Rate of ≥18.3% With Differing Assumptions for the True Remission Rate

Clinical Remission as Assessed by the Mayo Score	Probability of Observing ≥18.3% N=60
17.8% (observed adult remission rate; C0524T17)	50%
20.0%	68%
22.5%	82%
25.0%	91%
42.9% (observed pediatric remission rate; CNTO148UCO1001)	>99.9%

The precision (ie, half width of the CI) based on this sample size of 60 golimumab participants is 8.1% (assuming a clinical remission rate of 17.8% at Week 6) and 10.5% (assuming a clinical remission rate at Week 6 of 42.9%).

Furthermore, the Fisher Information Matrix-based optimal design analysis indicates that PK data from a total of 60 participants (including 45 participants in the ≥45 kg subgroup and 15 participants in the <45 kg subgroup) would be sufficient to adequately characterize the PK of golimumab in pediatric participants with UC.

Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.

9.4. Statistical Analyses

Descriptive statistics (eg, mean, median, standard deviation, interquartile range, minimum, and maximum) will be used to summarize continuous variables. Counts and percentages will be used to summarize categorical variables. Graphical data displays may also be used to summarize the data. Listings may also be utilized to present data at participant level. Specific details will be provided in the SAP.

In general, efficacy and participant information analyses will be based on all participants (including the youngest weight cohort [<30 kg]) who received at least 1 dose (complete or partial) of study treatment.

Safety analyses will include all participants who received at least 1 dose (complete or partial) of study treatment and participants will be analyzed based on the treatment they actually received, regardless of the treatment group they were assigned to.

Pharmacokinetics analysis for golimumab and infliximab will include participants who received at least one complete dose of golimumab (or infliximab) and have at least one postdose sample collection. Antibodies to golimumab or infliximab will be analyzed for participants who received at least one dose of study intervention and have at least one postdose sample collection.

9.4.1. Efficacy Analyses

A formal comparison is planned for the primary endpoint. Summary statistics will be provided for all efficacy endpoints for golimumab and infliximab. Unless otherwise specified, all endpoints that involve the Mayo endoscopy subscore will be based on the subscore assigned by the local endoscopists.

No comparisons of infliximab to golimumab will be performed.

Upon implementation of Amendment 4, participants will not be randomized to the infliximab arm. However, summary statistics will still be provided for the infliximab group.

9.4.1.1. Primary Endpoint

The primary endpoint is clinical remission at Week 6.

Treatment failure rules will override the clinical remission status based on the Mayo score. Participants who meet any of the following criteria for treatment failure through Week 6 will be considered to not have achieved clinical remission at Week 6:

- Had a colectomy (partial or full) or ostomy,

  OR
- Discontinued study intervention due to lack of efficacy or an AE of worsening of UC,

  OR
- Had protocol prohibited medication changes including increase above the baseline corticosteroid dose due to worsening UC (detailed in the SAP).

In addition, participants who do not return for evaluation or have insufficient data to calculate their Mayo score at Week 6 (ie, all 4 Mayo subscores are missing) will be considered to not have achieved clinical remission (based on the Mayo score) at Week 6.

The primary analysis population includes all participants (including the youngest weight cohort [<30 kg]) who were treated with golimumab. The success of the study will ultimately be based on the totality of evidence. The primary analysis will be based on the proportion of pediatric participants who received golimumab and who were in clinical remission at Week 6 based on the Mayo score (endoscopy subscore assigned by local endoscopist) and its associated 90% CI. The criteria for the primary analysis will have been met if the lower limit of the two-sided 90% CI for the proportion of pediatric golimumab participants in clinical remission at Week 6 is greater than the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 (ie, >10.0%) derived from a meta-analysis of 7 adult UC studies (2 adult Phase 2/3 UC

studies of golimumab and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints).

9.4.1.2. Major Secondary Endpoints

For endpoints beyond Week 6, analyses will be performed on participants who are in clinical response at Week 6 as assessed by the Mayo score.

1. Symptomatic remission at Week 54.
2. Clinical remission at Week 54, as assessed by the Mayo score (based on the Mayo endoscopy subscore assigned by the local endoscopist).
3. Clinical remission at Week 54 as assessed by the PUCAI score.
4. Clinical remission at Week 6 as assessed by the PUCAI score.
5. Clinical response at Week 6 as assessed by the Mayo score (based on the Mayo endoscopy subscore assigned by the local endoscopist).
6. Endoscopic healing at Week 6 (based on the Mayo endoscopy subscore assigned by the local endoscopist).
7. Endoscopic healing at Week 54 (based on the Mayo endoscopy subscore assigned by the local endoscopist).
8. Clinical remission at Week 54, as assessed by the Mayo score, for participants who are in clinical remission at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).
9. Participants who were not receiving corticosteroids for at least 12 Weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).

Treatment failure rules will be applied as specified in the primary efficacy analysis. In addition, participants who use rescue medication for a clinical flare after Week 6 will be considered a treatment failure for endpoints after Week 6 (detailed in the SAP). Participants who have any treatment failure events prior to the timepoint of interest will be considered to not have achieved the endpoints at that timepoint. These rules will override the response status based on the Mayo, PUCAI, and endoscopy score.

Participants who do not return for evaluation or have insufficient data to calculate their Mayo score or PUCAI Score at Week 6 or Week 54 will be considered not to be in clinical response or clinical remission, and not to have endoscopic healing at these timepoints. Participants who do not have sufficient data to calculate their stool frequency and rectal bleeding subscores at Week 54 will be considered to not have achieved symptomatic remission at these timepoints. Approaches to participants with missing subscores, including those missing an endoscopy subscore at Week 6 or Week 54, will be detailed in the SAP.

9.4.1.3. Other Endpoints

For endpoints beyond Week 6, analyses will be performed on participants who are in clinical response at Week 6 as assessed by the Mayo score.

Remission

1. Symptomatic remission at Week 6.
2. Clinical remission at Week 30, as assessed by the PUCAI score, for participants who are in clinical remission at Week 6.
3. Clinical remission at Week 54, as assessed by the PUCAI score, for participants who are in clinical remission at Week 6.
4. Symptomatic remission at Week 54 for participants who are in symptomatic remission at Week 6.
5. Corticosteroid-free clinical remission at Week 54, as assessed by the PUCAI score.
6. Corticosteroid-free clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).
7. Corticosteroid-free symptomatic remission at Week 54.
8. Remission at Week 6 based on a Mayo score less than or equal to 2, with no individual subscore greater than 1, a stool frequency subscore of 0, and a rectal bleeding subscore of 0.
9. Partial Mayo remission at Week 6.
10. Partial Mayo remission at Week 54.
11. Participants who were not receiving corticosteroids for at least 12 weeks prior to Week 54 and in symptomatic remission at Week 54.
12. Participants who were not receiving corticosteroids for at least 12 weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the PUCAI score.

Partial Mayo remission is defined as a partial Mayo score $\leq$2.

Other Clinical Efficacy endpoints

1. Clinical response at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).
2. Baseline and postbaseline values and the change from baseline in the Mayo score at Week 6 and at Week 54 (based on Mayo endoscopy subscore assigned by the local endoscopist).
3. Baseline and postbaseline values in the Mayo subscores at Week 6 and at Week 54 (based on Mayo endoscopy subscore assigned by the local endoscopist).
4. Baseline and postbaseline values and the change from baseline in the PUCAI score through Week 6 and during the long-term phase through Week 54.
5. Baseline and postbaseline values and the change from baseline in the Partial Mayo score through Week 6 and during the long-term phase through Week 54.
6. Clinically important change at Week 6 as assessed by the PUCAI score.
7. Clinically important change at Week 30 as assessed by the PUCAI score.
8. Clinically important change at Week 54 as assessed by the PUCAI score.

Clinically important change is defined as a decrease of ≥20 from Week 0 in the PUCAI score.

CRP and Fecal Marker Endpoints

1. Baseline and postbaseline values and the change from baseline in CRP through Week 6 and during the long-term phase through Week 54.
2. Baseline and postbaseline values and the change from baseline in fecal calprotectin concentrations through Week 6 and during the long-term phase through Week 54.
3. Normalization of CRP concentration (≤3 mg/L) through Week 6 and during the long-term phase through Week 54 among participants with abnormal CRP concentration (>3 mg/L) at baseline.
4. Normalization of fecal calprotectin concentration (≤250 mg/kg) through Week 6 and during the long-term phase through Week 54 among participants with abnormal fecal calprotectin concentration (>250 mg/kg) at baseline.

Quality of Life

1. Baseline and postbaseline values and the change from baseline in IMPACT III over time through Week 54 for participants ≥10 years at Week 0.

Analyses of the primary and major secondary endpoints will also be conducted utilizing the centrally read endoscopy measures. Additional sensitivity analyses in which subjects with friability present on endoscopy are considered nonresponders in the analysis are detailed in the SAP.

Alternate definitions of clinical remission will be explored. Details will be provided in the SAP.

Exploratory analyses of the TUMMY-UC and the Observer TUMMY-UC scores and analyses based on different approaches to handling missing endoscopies at Week 54 will also be performed. Details will be provided in the SAP.

Treatment failure rules will be applied as specified in the primary efficacy analysis. Participants who use rescue medication for a clinical flare after Week 6 will be considered a treatment failure for endpoints after Week 6 (detailed in the SAP). For continuous endpoints (ie, PUCAI score, Mayo score, partial Mayo score, fecal markers and CRP), the same treatment failure rules that will be applied for the dichotomous efficacy endpoints will also be applied to these endpoints. The baseline value will be carried forward from the time the treatment failure occurs onward.

Missing data rules for these endpoints will be specified in the SAP.

For endpoints beyond Week 6, analyses will also be conducted on all golimumab participants including partial Mayo responders at Week 14 and separately for all infliximab participants including partial Mayo responders at Week 14 or Week 22. Details will be provided in the SAP.

9.4.1.4. Analyses of Study Extension

The proportion of participants in clinical remission based on the PUCAI score will be summarized over time. The change from study extension baseline in the PUCAI score will be summarized over time. Treatment failure and missing data rules will be detailed in the SAP.

For the Usability Assessment Substudy, data from the questionnaire will be descriptively summarized. Details will be provided in the SAP.

9.4.2. Safety Analyses

Adverse Events

The verbatim terms used in the eCRF by investigators to identify AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Intervention-emergent AEs are adverse events with onset during the intervention phase or that are a consequence of a preexisting condition that has worsened since baseline. All reported intervention-emergent AEs will be included in the analysis. For each AE, the percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group.

The following analyses of AEs will be used to assess the safety of participants:

- Frequency and type of AEs.
- Frequency and type of SAEs.
- Frequency and type of reasonably related AEs as assessed by the investigator.
- Frequency and type of AEs leading to discontinuation of study intervention.
- Frequency and type of infections, serious infections, and infections requiring oral or parenteral antimicrobial treatment.
- Frequency and type of AEs temporally associated with an infusion.
- Frequency and type of injection-site reactions.

In addition, the following targeted events will also be assessed:

- Malignancy, study participant death, pregnancy in a girl or the partner of a boy, TB diagnosis or treatment.

Summaries, listings, datasets, or participant narratives may be provided, as appropriate, for those participants who die, who discontinue intervention due to an AE, or who experience a SAE.

Clinical Laboratory Tests

Laboratory data will be summarized by type of laboratory test. Reference ranges and Common Terminology Criteria for Adverse Events (CTCAE) grade results (specified in the SAP) will be used in the summary of laboratory data. Descriptive statistics will be calculated for selected laboratory analytes at baseline and for observed values and changes from baseline at scheduled time points. Frequency tabulations of abnormalities will be made.

The following summaries of clinical laboratory tests will be used to assess participant safety:

- Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry)
- Summary of maximum CTCAE toxicity grade for postbaseline laboratory values (hematology and chemistry)

Listings of participants with any abnormal postbaseline laboratory values of CTCAE Grade ≥2 will also be provided.

9.4.3. Other Analyses

9.4.3.1. Pharmacokinetic Analyses

Descriptive statistics of the serum golimumab or infliximab concentrations will be calculated at each sampling time point. These concentrations will be summarized over time.

All concentrations below the lowest quantifiable concentration or missing data will be labeled as such in the concentration database or data presentations. Concentrations below the lowest quantifiable concentration will be treated as zero in the summary statistics.

A population PK analysis approach for golimumab using nonlinear mixed effects modeling (NONMEM) will be used to evaluate PK parameters. The influence of important covariates on the population PK parameter estimates may be evaluated. The results of the population PK analysis will be presented in a separate technical report.

Participants will be excluded from the PK analysis if their data do not allow for accurate assessment of the PK (eg, incomplete administration of the study intervention; missing time of study intervention administration). Detailed rules for the analysis will be specified in the SAP.

Exposure-response analyses will be performed to evaluate the relationship between serum golimumab concentrations and clinical efficacy endpoints using summary statistics and a modeling approach.

9.4.3.2. Immunogenicity Analyses

Golimumab

The incidence of anti-golimumab antibodies will be summarized for all participants who receive at least 1 dose of golimumab and have appropriate samples for detection of antibodies to golimumab (ie, participants with at least 1 sample obtained after their first dose of golimumab).

A listing of participants who are positive for antibodies to golimumab will be provided. The maximum titers of antibodies to golimumab will be summarized for participants who are positive for antibodies to golimumab.

Infliximab

The incidence of anti-infliximab antibodies will be summarized for all participants who receive at least 1 dose of infliximab and have appropriate samples for detection of antibodies to infliximab (ie, participants with at least 1 sample obtained after their first dose of infliximab).

A listing of participants who are positive for antibodies to infliximab will be provided. The maximum titers of antibodies to infliximab will be summarized for participants who are positive for antibodies to infliximab.

Other immunogenicity

Other immunogenicity analyses may be performed to further characterize the immune responses that are generated.

9.4.3.3. Biomarkers Analyses

Changes in serum/RNA or other biomarkers over time will be summarized by intervention group. Associations between baseline levels and changes from baseline in select biomarkers and clinical response at screening and Weeks 0, 2, 6, and 54 will be explored.

Biomarker analyses are considered exploratory and results will be presented in a separate report.

9.4.3.4. Pharmacodynamic Analyses

Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information. Any pharmacodynamics (PD) samples received by the contract vendor or sponsor after the cut-off date will not be analyzed, and therefore, excluded from the PD analysis.

9.5. Data Monitoring Committee

An internal DMC (consisting of Sponsor members [a gastroenterologist, a clinician and a statistician at a minimum] outside of the study team), will be established to monitor safety data (for both golimumab and infliximab treatments arms) on an ongoing basis until all participants reach the Week 54 visit or terminate the study prior to the Week 54 visit.

The major function of the DMC is to monitor the safety of the study intervention by reviewing the SAEs each month and by reviewing the interim study safety data every 3-months.

The content of the safety summaries, the DMC role and responsibilities and the general procedures (including communications) and their recommendations on the study conduct are defined and documented in the DMC charter, which will be finalized prior to the first DMC review. The first DMC meeting will occur approximately 4 months after the first participant is dosed with study intervention.

In addition, during the study, the sponsor's study responsible physician (or designee) will regularly review safety data from the sites and notify the DMC and appropriate Sponsor personnel of any issues.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Abbreviations

5-ASA	5-aminosalicylate
6-MP	6-mercaptopurine
6-TG	6-thioguanine
AE	adverse event
AHA	at home administration
ALT	alanine aminotransferase
ANA	antinuclear antibodies
anti-HBc	HBV core antibody total
anti-HBs	HBV surface antibody
ARC	anticipated event review committee
AS	ankylosing spondylitis
AST	aspartate aminotransferase
AZA	azathioprine
BCG	Bacille Calmette-Guerin
BSA	body-surface area
CI	confidence interval
COVID-19	Coronavirus Disease 2019
CRP	C-reactive protein
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DBL	database lock
DCS	data collection system
DMC	Data Monitoring Committee
DNA	deoxyribonucleic acid
eCRF	electronic case report form
ePRO	electronic patient-reported outcome
E-R	exposure-response
EU	European Union
FDA	Food and Drug Administration
FSH	follicle stimulating hormone
HBsAg	HBV surface antigen
HBV	hepatitis B virus
HCP	health care professional
HCV	hepatitis C virus
HRT	hormone replacement therapy
IB	Investigator's Brochure
IBD	inflammatory bowel disease
ICF	informed consent form
ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
IV	intravenous
IWRS	interactive web response system
LOR	loss of response
mAb	monoclonal antibody
MTX	methotrexate
NSAIDs	nonsteroidal anti-inflammatory drugs
PD	pharmacodynamics
PFP-V	prefilled pen-Varioject
PFS	prefilled syringe
PFS-U	prefilled syringe with UltraSafe
pJIA	polyarticular juvenile idiopathic arthritis
PK	pharmacokinetics
PPD	purified protein derivative

PQC	product quality complaint
PRO	participant-reported outcomes
PUCAI	Pediatric Ulcerative Colitis Activity Index Score
q4w	every 4 weeks
q8w	every 8 weeks
q12w	every 12 weeks
QoL	quality of life
RNA	ribonucleic acid
SAE	serious adverse event
SAP	Statistical Analysis Plan
SC	subcutaneous
SUSAR	suspected unexpected serious adverse reactions
TB	tuberculosis
TNFα	tumor necrosis factor alpha
TU	tuberculin units
UC	ulcerative colitis
ULN	upper limit of normal
US	United States

10.2. Appendix 2: Definitions of Inadequate Response to or Intolerance of Corticosteroids, MTX, or AZA/6-MP and Corticosteroid Dependence

CORTICOSTEROIDS

Participants have failed to respond to corticosteroids if they have had evidence of an initial inadequate response, recurrent disease, or a relapse despite receiving at least 1.0 mg/kg/day or a maximum of 40 mg/day of prednisone (or corticosteroid equivalent, given orally or intravenously) for 2 weeks; or ≥9 mg/day of budesonide or ≥5 mg/day of beclomethasone dipropionate given orally for at least 4 weeks.

Participants are intolerant of corticosteroids if:

- They have developed clinically significant adverse events (eg, osteonecrosis or osteoporosis, psychosis, uncontrolled diabetes) unresponsive to dose reduction that, in the judgment of the investigator, precluded the use of corticosteroids to treat UC.

OR

- They have a medical condition that precludes the use of corticosteroids as a treatment for UC.

Participants are corticosteroid dependent if they have failed to successfully taper their corticosteroid (ie, had a flare of disease) within 3 months of starting therapy, or if a relapse occurs within 3 months after stopping corticosteroids or if they are unable to discontinue these agents without flare within 3 months after starting them.

METHOTREXATE, 6-MERCAPTOPURINE (6-MP) OR AZATHIOPRINE (AZA)

Participants have failed to respond to MTX, 6-MP or AZA if they have had evidence of an initial inadequate response, recurrent disease, or a relapse despite receiving:

- At least 3 months of therapy before screening on MTX or at least 3 months of therapy before screening with 1 mg/kg/day of 6-MP or 2 mg/kg/day of AZA.

OR

- At least 3 months before screening at lower dosage of 6-MP or AZA when country or local guidelines specify a different treatment regimen. (In such an event, the country or local guidelines needs to be included in the source document).

OR

- At least 3 months before screening at a dosage of 6-MP or AZA confirmed to be therapeutic for the participant with whole blood thioguanine nucleotide levels >200 pmol/8 x 10^8 red blood cells.

OR

- At least 3 months before screening at the highest tolerated dosage due to leukopenia, elevated liver enzymes, or nausea.

Participants are intolerant of MTX, 6-MP or AZA if:

- They have developed clinically significant adverse events (eg, pancreatitis, arthritis accompanied by high fever and/or rash, leukopenia, or persistently elevated liver enzymes) unresponsive to dose reduction that, in the judgment of the investigator, precluded the use of MTX, 6-MP or AZA to treat UC within the past 5 years.

OR

- They have a medical condition that precludes the use of MTX, 6-MP or AZA.

10.3. Appendix 3: Tuberculin Skin Testing

Administering the Mantoux Tuberculin Skin Test

The Mantoux tuberculin skin test (CDC, 2000) is the standard method of identifying persons infected with *Mycobacterium tuberculosis*. Multiple puncture tests (Tine and Heaf) should not be used to determine whether a person is infected because the amount of tuberculin injected intradermally cannot be precisely controlled. Tuberculin skin testing is both safe and reliable throughout the course of pregnancy. The Mantoux tuberculin test is performed by placing an intradermal injection of 0.1 mL of tuberculin into the inner surface of the forearm. The test must be performed with tuberculin that has at least the same strength as either 5 tuberculin units (TU) of standard purified protein derivative (PPD)-S or 2 TU of PPD-RT 23, Statens Seruminstitut, as recommended by the World Health Organization. PPD strengths of 1 TU or 250 TU are not acceptable (Menzies, 2000). Using a disposable tuberculin syringe with the needle bevel facing upward, the injection should be made just beneath the surface of the skin. This should produce a discrete, pale elevation of the skin (a wheal) 6 mm to 10 mm in diameter. To prevent needle-stick injuries, needles should not be recapped, purposely bent or broken, removed from disposable syringes, or otherwise manipulated by hand. After they are used, disposable needles and syringes should be placed in puncture-resistant containers for disposal. Institutional guidelines regarding universal precautions for infection control (eg, the use of gloves) should be followed. A trained health care worker, preferably the investigator, should read the reaction to the Mantoux test 48 to 72 hours after the injection. Participants should never be allowed to read their own tuberculin skin test results. If a participant fails to show up for the scheduled reading, a positive reaction may still be measurable up to 1 week after testing. However, if a participant who fails to return within 72 hours has a negative test, tuberculin testing should be repeated. The area of induration (palpable raised hardened area) around the site of injection is the reaction to tuberculin. For standardization, the diameter of the induration should be measured transversely (perpendicular) to the long axis of the forearm. Erythema (redness) should not be measured. All reactions should be recorded in millimeters, even those classified as negative.

Interpreting the Tuberculin Skin Test Results

In the US and many other countries, the most conservative definition of positivity for the tuberculin skin test is reserved for immunocompromised participants, and this definition is to be applied in this study to maximize the likelihood of detecting latent TB, even though the participants may not be immunocompromised at baseline.

In the US, an induration of 5 mm or greater in response to the intradermal tuberculin skin test is considered to be a positive result and evidence for either latent or active TB.

In countries outside the US, country-specific guidelines for immunocompromised participants should be consulted for the interpretation of tuberculin skin test results. If no local country guidelines for immunocompromised participants exist, US guidelines must be followed.

Treatment of Latent Tuberculosis

Local country guidelines for immunocompromised participants should be consulted for acceptable anti-tuberculous treatment regimens for latent TB. If no local country guidelines for immunocompromised participants exist, US guidelines must be followed.

References

Centers for Disease Control and Prevention. Core curriculum on tuberculosis: What the clinician should know (Fourth Edition). Atlanta, GA: Department of Health and Human Services; Centers for Disease Control and Prevention; National Center for HIV, STD, and TB Prevention; Division of Tuberculosis Elimination; 2000:25-86.

Menzies RI. Tuberculin skin testing. In: Reichman LB, Hershfield ES (eds). *Tuberculosis, a comprehensive international approach*. 2nd ed. New York, NY: Marcel Dekker, Inc; 2000:279-322.

10.4. Appendix 4: Mayo Score

Mayo scoring system for assessment of ulcerative colitis activity

Stool frequency[a]
- 0 Normal number of stools for this participant
- 1 1-2 stools more than normal
- 2 3-4 stools more than normal
- 3 5 or more stools more than normal

Rectal bleeding[b]
- 0 No blood seen
- 1 Streaks of blood with stool less than half the time
- 2 Obvious blood with stool most of the time
- 3 Blood alone passed

Findings of endoscopy
- 0 Normal or inactive disease
- 1 Mild disease (erythema, decreased vascular pattern, mild friability)
- 2 Moderate disease (marked erythema, absent vascular pattern, friability, erosions)
- 3 Severe disease (spontaneous bleeding, ulceration)

Physician's global assessment[c]
- 0 Normal
- 1 Mild disease
- 2 Moderate disease
- 3 Severe disease

[a] Each participant serves as his or her own control to establish the degree of abnormality of the stool frequency.
[b] The daily bleeding score represents the most severe bleeding of the day.
[c] The physician's global assessment acknowledges the 3 other criteria, the participant's recall of abdominal discomfort and general sense of well-being, and other observations, such as physical findings and the participant's performance status.

10.5. Appendix 5: Pediatric Ulcerative Colitis Activity Index (PUCAI)

ITEM	POINTS
1. Abdominal pain	
No pain	0
Pain can be ignored	5
Pain cannot be ignored	10
2. Rectal bleeding	
None	0
Small amount only, in less than 50% of stools	10
Small amount with most stools	20
Large amount (>50% of the stool content)	30
3. Stool consistency of most stools	
Formed	0
Partially formed	5
Completely unformed	10
4. Number of stools per 24 hours	
0-2	0
3-5	5
6-8	10
>8	15
5. Nocturnal bowel movement (any diarrhea episode causing wakening)	
No	0
Yes	10
6. Activity level	
No limitation of activity	0
Occasional limitation of activity	5
Severe restricted activity	10
SUM OF PUCAI (0-85)	

10.6. Appendix 6: Attribution Definitions and Severity Criteria

Attribution Definitions

Not Related

An AE that is not related to the use of the drug.

Doubtful

An AE for which an alternative explanation is more likely, eg, concomitant drug(s), concomitant disease(s), or the relationship in time suggests that a causal relationship is unlikely.

Possible

An AE that might be due to the use of the drug. An alternative explanation, eg, concomitant drug(s), concomitant disease(s), is inconclusive. The relationship in time is reasonable; therefore, the causal relationship cannot be excluded.

Probable

An AE that might be due to the use of the drug. The relationship in time is suggestive (eg, confirmed by dechallenge). An alternative explanation is less likely, eg, concomitant drug(s), concomitant disease(s).

Very Likely

An AE that is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation, eg, concomitant drug(s), concomitant disease(s). The relationship in time is very suggestive (eg, it is confirmed by dechallenge and rechallenge).

Severity Criteria

An assessment of severity grade will be made using the following general categorical descriptors:

Mild: Awareness of symptoms that are easily tolerated, causing minimal discomfort and not interfering with everyday activities.

Moderate: Sufficient discomfort is present to cause interference with normal activity.

Severe: Extreme distress, causing significant impairment of functioning or incapacitation. Prevents normal everyday activities.

The investigator should use clinical judgment in assessing the severity of events not directly experienced by the participant (eg, laboratory abnormalities).

Note that seriousness and severity should not be confused. A participant could experience a severe headache that would not qualify as an SAE, while another might experience a mild stroke that, while not severe, would be considered serious.

10.7. Appendix 7: IMPACT III Questionnaire

IMPACT-III

English–North America

A QUALITY OF LIFE QUESTIONNAIRE FOR CHILDREN WITH INFLAMMATORY BOWEL DISEASE

INSTRUCTIONS

Below you will find a questionnaire containing 35 questions for children who have inflammatory bowel disease (Crohn's disease or ulcerative colitis). The questions are about your life with inflammatory bowel disease. Some questions deal with, for example, pains you may suffer from, others are about feelings or worries you may have.

After each question you will see boxes above five possible answers. Please put a cross in the box above the answer that best fits your answer.

First an example:
The question is: How afraid are you of tigers?

☐	☐	☒	☐	☐
Not at all afraid	A little afraid	Afraid	Quite afraid	Very much afraid

So, this person is afraid of tigers.

☐	☒	☐	☐	☐
Not at all afraid	A little afraid	Afraid	Quite afraid	Very much afraid

This person is **a little afraid** of tigers.

Please answer **all the questions**! If you do not understand a question, ask someone for help.

Good luck with filling in the questionnaire and....many thanks in advance for your efforts!

Contact: Dr. Anthony Otley impact@iwk.nshealth.ca
Version: June 2013

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Question 1.	How much has your stomach been hurting you in the past two weeks?

☐	☐	☐	☐	☐
Not at all	Hardly hurting at all	Hurting somewhat	Hurting quite a bit	Hurting very much

Question 2.	Taking medicines or tablets bothers you

☐	☐	☐	☐	☐
Not at all	**Hardly bothers at all**	**Bothers somewhat**	**Bothers quite a bit**	**Bothers very much**

Question 3.	**How often has your inflammatory bowel disease prevented you from eating what you want in the past two weeks?**

☐	☐	☐	☐	☐
Never	**Rarely**	**Sometimes**	**Often**	**Very often**

Question 4.	**How often have you been worrying about having a flare-up (increase of symptoms) in the last two weeks?**

☐	☐	☐	☐	☐
Never	**Rarely**	**Sometimes**	**Often**	**Very often**

Question 5.	**How much does it bother you that you have an illness that does** not just go away?

☐	☐	☐	☐	☐
Not at all	Hardly bothers at all	Bothers somewhat	Bothers quite a bit	Bothers very much

Question 6.	How much energy did you have during the past two weeks?

☐ Very much energy	☐ Quite a bit of energy	☐ Some energy	☐ A little energy	☐ No energy at all

Question 7.	How do you feel about your weight?

☐ I feel great about my weight	☐ I feel good about my weight	☐ I don't feel good or bad about my weight	☐ I feel bad about my weight	☐ I feel awful about my weight

Question 8.	How has your inflammatory bowel disease affected your family?

☐ The effect has been great	☐ The effect has been good	☐ It has not affected our family	☐ The effect has been bad	☐ The effect has been awful

Question 9.	How often did you have to miss out on certain things (hobbies, play, parties) because of your inflammatory bowel disease in the past two weeks?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 10.	How often have you been bothered by diarrhea (loose or frequent bowel movements) in the past two weeks?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 11.	**How often do you worry about health problems you might have in the future?**

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 12.	**How often do you think it is unfair that you have inflammatory bowel disease?**

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 13.	**During the past two weeks, were you ever angry that you have inflammatory bowel disease?**

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 14.	**Do you think too many rules or limits are placed on you because of your inflammatory bowel disease?**

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 15.	How do you feel about the way you look?

☐ I think I look great	☐ I think I look good	☐ I don't think I look good or bad	☐ I think I look bad	☐ I think I look awful

Question 16.	Are you embarrassed because of your bowel condition?

☐ Not at all	☐ Hardly embarrassed at all	☐ Embarrassed somewhat	☐ Embarrassed quite a bit	☐ Embarrassed very much

Question 17.	Did you have fun during the past two weeks?

☐ Very often	☐ Often	☐ Sometimes	☐ Rarely	☐ Never

Question 18.	Is it harder to make friends because of your inflammatory bowel disease?

☐ Not at all harder	☐ A little harder	☐ Quite a bit harder	☐ Much harder	☐ Very much harder

Question 19.	How often do you worry about your stool (bowel movement) containing blood?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 20.	Are you worried you cannot go out on a date or have a boyfriend or girlfriend because of your inflammatory bowel disease?

☐ Not at all worried	☐ Hardly worried at all	☐ Worried somewhat	☐ Worried quite a bit	☐ Worried very much

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Question 21.	How often did you feel sick to your stomach in the past two weeks?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 22.	How do you feel about the tests you have to go through?

☐ I do not mind them at all	☐ I mind them a tiny bit	☐ I mind them a little	☐ I mind them a lot	☐ I hate them

Question 23.	Do other children bully you or leave you out of things because of your inflammatory bowel disease or its treatment?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 24.	How often do you worry about having an operation?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 25.	In the past two weeks how often were you afraid you may have an accident or not get to the toilet in time?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 26.	**Do you try to keep your inflammatory bowel disease a secret from other people?**

☐ No, I do not try at all	☐ I don't try much	☐ I try a little	☐ I try hard	☐ Yes, I try very hard

Question 27.	**Does your inflammatory bowel disease make it difficult to travel or go on a holiday?**

☐ No, not difficult	☐ A little difficult	☐ Quite difficult	☐ Very difficult	☐ Yes, extremely difficult

Question 28.	**How did you feel during the past two weeks?**

☐ Great	☐ Good	☐ Not good or bad	☐ Bad	☐ Awful

Question 29.	**Are you happy with your life?**

☐ Yes, very happy	☐ Happy	☐ Not happy or unhappy	☐ Unhappy	☐ Very unhappy

Question 30.	Do you feel there is someone you can talk to about your inflammatory bowel disease?

☐ Always	☐ Often	☐ Sometimes	☐ Rarely	☐ Never

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Question 31.	How often did you have to pass gas in the past two weeks?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Very often

Question 32.	How tired have you felt in the past two weeks?

☐ Not at all tired	☐ A little tired	☐ Tired	☐ Quite tired	☐ Very tired

Question 33.	How do you feel about your height?

☐ I feel great about my height	☐ I feel good about my height	☐ I don't feel good or bad about my height	☐ I feel bad about my height	☐ I feel awful about my height

Question 34.	Does your inflammatory bowel disease get in the way of playing sports the way you would like to?

☐ Never	☐ Rarely	☐ Sometimes	☐ Often	☐ Always

Question 35.	In the past two weeks how often were you able to go to school ? (If you are in the middle of a school break or the summer holidays, answer as if school was on)

☐ Always	☐ Most days	☐ Half the days	☐ A few days	☐ Never

End of questionnaire

This completes the questionnaire. Do you have anything else to add which you feel is important about having inflammatory bowel disease, or do you have any other remarks? Please write them below.

10.8. Appendix 8: Examples of the TUMMY-UC and the Observer TUMMY-UC Questionnaires

TUMMY-UC

User's guide (for the investigator)
Relating to both the TUMMY-UC and the Observer TUMMY-UC

1. The TUMMY-UC should reflect the last 24 hours.
2. It is best completed at bedtime to provide a clear time point. However, if the subject did not complete it at bedtime, it may be completed at any time during the day on condition that the time during the day remains the same.
3. Caregiver version- urgency: for the youngest children with a diaper, impute the score by the average score of the 4 other items with a maximal score of 6 (i.e. abdominal pain, stool consistency, weakness, nocturnal stooling), rounded to the nearest numbers 0, 2, 4, 6 (round up numbers in the middle).
4. Weighting of the items (total score range 0-114 points):
   a. Abdominal pain (item I): score the 5 response options of the items as 0, 3, 6, 9, 12 points
   b. Stool frequency (item II): score the 4 response options as 0, 6, 12, 18 points
   c. Amount of rectal bleeding (item III): score the 5 response options as 0, 0, 6, 12, 18 points
   d. Frequency of rectal bleeding (item IV): score the 4 response options as 0, 0, 9, 18 points
   e. Bristol stool consistency chart (item V): score the 6 response options as 0, 0, 0, 4, 8, 12 points
   f. Weakness (item VI): score the 3 response options as 0, 6, 12 points
   g. Nocturnal stools (item VII): score the 3 response options as 0, 6, 12 points
   h. Urgency (item VIII): score the 5 response options as 0, 0, 4, 8, 12 points

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TUMMY-UC (PRO for children 8-18 years)

1. These questions ask about how you have been feeling because of your colitis since yesterday at this time (last 24 hours).
2. It is best that you complete the TUMMY-UC before you go to bed at night and report the time since you went to bed last night until now. However, this is not mandatory and it may be completed at any time during the day on condition that the time during the day remains the same.
3. Please answer honestly. There are no right or wrong answers.

Please write down the time you completed the TUMMY:

___ / ___ A.M. / P.M.
HH MM

___ / _____ / _____
DD MMM YYYY

I. What is the worst your tummy has hurt *since yesterday at this time (last 24 hours)*?

0 **1** **2** **3** **4**

No pain **Worst Possible pain**

II. How many times did you poop since yesterday at this time (last 24 hours)? (Count the number of all visits to the bathroom when you pooped, including accidents (e.g., in your underwear or pants). If you poop a few times during one visit to the bathroom, count them as one time)

a. 0-2 times
b. 3-5 times
c. 6-8 times
d. More than 8 times

III. When thinking about your poop, please choose the best answer that describes the most blood you have seen since yesterday at this time (last 24 hours)?

a. I had no poops
b. There was no blood at all
c. There was more poop than blood
d. There was more blood than poop
e. There was only blood (without any poop)

IV. How often did you see blood in your poop since yesterday at this time (last 24 hours)?

a. I had no poops
b. There was no blood in any of my poops
c. There was blood in only some of my poops (half, or less than half of my poops)
d. There was blood in most of my poops

V. What did most of your poops look like since yesterday at this time (last 24 hours)? Circle the picture that describes what most of your poops looked like.

0		No poops
1		Separate hard lumps, like nuts (hard to pass)
2		Sausage- shaped but lumpy
3		Like a sausage or snake, smooth and soft
4		Fluffy pieces with ragged edges, a mushy poop
5		Watery, no solid pieces

VI. Did your colitis make you feel weak since yesterday at this time (last 24 hours)? *We are asking about weakness related to colitis and not being tired from not sleeping enough*

a. I am not weak at all. I can do everything I regularly do
b. I am a little bit weak. I can do everything I regularly do but I am not as good as usual.
c. I am weak and I am not able to do most of the things I regularly do; I stay at home all day

VII. Did you wake up to go poop last night?

a. No
b. Yes- the need to poop caused me to wake up once
c. Yes- the need to poop caused me to wake up more than once

VIII. How badly have you needed to poop when you got the feeling to poop since yesterday at this time (last 24 hours)?

a. I did not feel like I needed to poop
b. I could hold it and wait
c. I could hold it for a short while, but I needed to find a toilet/bathroom quickly
d. When I felt like I needed to poop, it was almost too late to get to the toilet/bathroom in time before it was about to come out
e. I could not hold it. It was too late to get to the toilet/bathroom in time and I had an accident (i.e., poop came out) outside the toilet

THE END…THANK YOU!

Observer TUMMY-UC (for children ≥2 but <8 years)

1. These questions should be completed by the caregiver.
2. We ask how your child has been doing because of the colitis since yesterday at this time (last 24 hours).
3. It is important that the time the TUMMY-UC is completed each day is kept consistent; ideally at the end of the day, when your child goes to sleep.
4. Please answer the questions based on behaviors that you have observed in your child and things that he/she may have said to you that indicate how he/she has been feeling.

Please indicate the time you completed the TUMMY:

___ / ___ A.M. / P.M.
HH MM

___ / _____ / _____
DD MMM YYYY

I. Which of the following best describes your child's behaviors relating to stomach pain since yesterday at this time (last 24 hours)?

My child behaves in a way that shows me that he/she has:

a. No stomach pain- Acts and plays normally, no complaints of stomach pain
b. Minimal stomach pain- Complains infrequently about stomach pain but no other related behavior - acts normally, plays, does not hold stomach and does not curls up
c. Mild stomach pain- Still active but less than usual, holds stomach, seems less cheerful, may complain of stomach pain
d. Moderate stomach pain- Stops playing, eats less than usual, complains a lot of pain, lies down from time to time, may hold stomach but does not curl up and no obvious crying
e. Severe stomach pain- Holds stomach, freezes in place or curls up, may cry, lots of complaints of pain or may become quite and withdrawn, lies down often

II. How many times did your child poop since yesterday at this time (last 24 hours)? Count the number of all visits to the bathroom when he/she pooped, including accidents in the underwear or pants. If he/she pooped a few times during one visit to the bathroom count them as one time)

a. 0-2 times
b. 3-5 times
c. 6-8 times
d. More than 8 times

1

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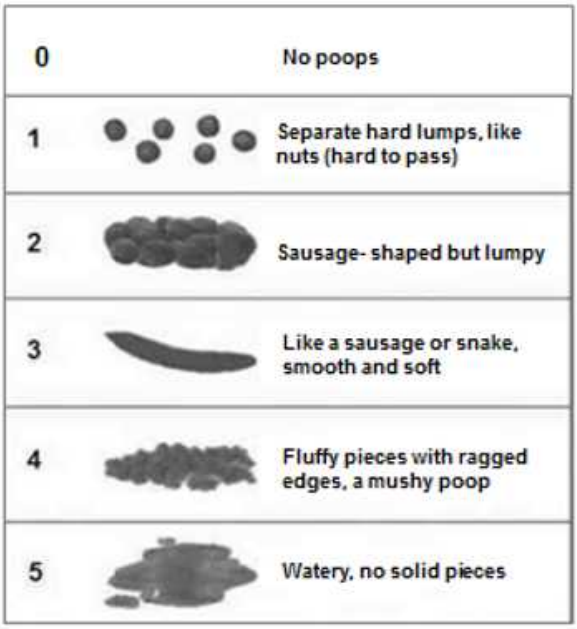
III. When thinking about your child's poop, please choose the best answer that describes the most blood you have seen since yesterday at this time (last 24 hours)?

a. He/she had no poops
b. There was no blood at all
c. There was more poop than blood
d. There was more blood than poop
e. There was only blood (without any poop)

IV. How often did you see blood in your child's poop since yesterday at this time (last 24 hours)?

a. He/she had no poops
b. There was no blood in any of my child's poops
c. There was blood in only some of my child's poops (half, or less than half of the poops)
d. There was blood in most of my child's poops

V. What have most of your child's poops looked like since yesterday at this time (last 24 hours)?



2

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VI. Which of the following best describes your child's behaviours relating to weakness, since yesterday at this time (last 24 hours)? *We are now asking about weakness related to colitis and not being tired from not sleeping enough*

My child behaves in a way that shows me that he/she is:

a. Not weak- Acts, eats and plays normally, sleeping as usual, energetic, can do regular activities and everything he/she likes
b. A little bit weak- Can do regular activities but gets tired quickly, sleeps more than usual, has less energy
c. Weak- Stays at home all day, doesn't want to do even fun activities, sleeps much more than usual, has no energy

VII. Did your child wake up to go poop last night?

a. No
b. Yes- the need to poop caused my child to wake up once
c. Yes- the need to poop caused my child to wake up more than once

VIII. Which of the following best describes your child's behaviors relating to urgency since yesterday at this time (last 24 hours)?

My child behaves in a way that shows me that he/she:

a. No poop at all
b. Doesn't have urgency- Can hold it without difficulty and wait, doesn't run to the toilet
c. Has mild urgency- Can hold it, but has some difficulty holding it; cannot hold it for a long time; would prefer not to hold it
d. Has moderate urgency-Runs to the toilet, scared to have an accident, but no accidents; may hold the bum or shake legs
e. Has severe urgency- Runs to the toilet but still has accidents

□ Tick here if your child has a diaper and thus it is not possible to answer this question

THE END…THANK YOU!

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10.9. Appendix 9: PFS-U and PFP-V Actual Use Data Collection

Introduction

The PFS-U and PFP-V Actual Use Data Collection is designed to capture and document real-life handling and use experience data from injections administered by pediatric participants or caregivers in a home-like setting, including complaints and failures in use. The actual use data to be collected is intended as additional support of the human factors and labeling comprehension data obtained during Summative Human Factors Studies but is not itself considered a human factors study. Following the second independent self- or caregiver- administration by appropriately trained pediatric participants capable of self-administration or their caregivers, all study participants performing the injection will be asked to complete a questionnaire (provided below) regarding their experience using either the PFS-U or the PFP-V. Evaluation of the user experience after the second independent administration is considered adequate to evaluate how well participants can understand and recall the dosage instructions, and to assess for any common difficulties with injections.

The Schedule of Activities (Table 2) summarizes the setup of data collection. Pediatric participants aged 12 and older, or caregivers of participants of any age will be offered the option for self- or caregiver administration after the Week 54 study evaluations. This is optional; if a pediatric participant or caregiver elects against self- or caregiver administration, the HCP will administer injections in this study. If a pediatric participant or caregiver does elect self- or caregiver administration, the pediatric participant or caregiver will perform a training administration no earlier than Week 58. Pediatric participants or caregivers will receive face-to-face training by study site staff on the use of the injection device. The training will include a review of the IFU with site staff, a demonstration with a device Trainer (when available) performed by the site staff, and 'hands-on' practice injections performed by the pediatric participants and/or their caregivers using the device Trainer. An Observer Checklist will be completed by the trainer in order to determine that the user is able to correctly administer the injection. Based on this information, the HCP will determine whether the pediatric participant, or their caregiver, is able to administer the injection in a home-like setting at the site.

If caregiver injection is selected, then injections should be continued at subsequent weeks by the caregiver and not be switched to the pediatric participant. Similarly, if pediatric participant self-injection is selected, then injections should be continued at subsequent weeks by the pediatric participant and not be switched to the caregiver. At any time, pediatric participants or caregivers can opt to continue on with self- or caregiver-injections performed at the study site or can return to HCP administration in the clinic after they start self- or caregiver administration, if desired.

Self- or caregiver training injections will occur in 2 subsequent study intervention administrations, the second and third self- or caregiver administration visits. Injections will be performed independently in a home-like setting in the clinic, with the IFU available for reference. Approximately 10-20 participants from Sponsor identified sites who choose AHA will enter the Usability Assessment Substudy at Week 58 and complete an injection device Usability Questionnaire at Weeks 62 and 66 after completion of the second and third self- or caregiver administration visits (Sections 4.1 and 6.1).

10.10. Appendix 10: Injection Device Observer Injection Checklist

This form is intended to be completed to determine if the first AHA training dose was delivered successfully by the caregiver or participant and should be completed by the study staff observing the injections.

Injection Device Observer Injection Checklist

Participant Number:

Type of Injection Device: PFS-U PFP-V

By my signature below, I hereby certify that:

Participant Passed Training OR Caregiver Passed Training

Circle level of training aptitude:

Below Average (must justify passing)	Average	Above Average

- I have trained and/or observed the participant/caregiver whose participant number is listed above to properly comply with each and every one of the methods and procedures for administering the drug via an injection.
- I observed the participant/caregiver perform a successful and simulated injection.
- I observed the participant/caregiver demonstrate adequate learning of the tasks and information relevant for first-time use of this device;
- I observed the participant/caregiver perform the injection without undue effort or frustration;
- I have concluded that the participant/caregiver can safely use the device on their own;
- The participant/caregiver is competent and capable of such use and does not require my further presence or assistance when using the device.

Participant Failed Training OR Caregiver Failed Training

- During training, the participant/caregiver failed for the following reason(s): (Check all that apply)
  - ☐ Participant/caregiver showed an inability to learn how to use the device and did not successfully demonstrate correct use the device, after being trained.
  - ☐ Participant/caregiver showed high levels of frustration, stress or workload that may prevent them from using the device correctly or safely.
  - ☐ Participant/caregiver was not willing to interact with the device per the trainer's instructions.
  - ☐ Participant's/caregiver's behaviors, attitudes and/or abilities were not representative of their typical user group and falls outside of the norm.

Use This Space To Note Additional Information:

Trainer Signature: Date:

10.11. Appendix 11: Injection Device Assessment Questionnaire

Thank you for completing this questionnaire by yourself or with the assistance of a parent or caregiver if necessary, preferably in a quiet environment. Take as much time as you need to complete it. There are no right or wrong answers. Your answers will remain strictly confidential and anonymous.

TYPE OF INJECTION DEVICE

	Prefilled Syringe (PFS-U)	Prefilled Pen-Varioject (PFP-V)
Which type of injection device did you use for this injection?	☐	☐

CONFIRMATION OF SUCCESSFUL INJECTION

	Yes	No
Were you able to successfully inject using the injection device (PFS-U or PFP-V)?	☐	☐

EASE OF USE OF THE INJECTION DEVICE

The following questions ask about the **ease of use** of the injection device (PFS-U or PFP-V).

Please answer each question below by checking the box that best represents your opinion (Check only one box per question).

How difficult or easy was it to:	Very difficult	Difficult	Somewhat difficult	Somewhat easy	Easy	Very easy
position the injection device at the injection-site?	☐	☐	☐	☐	☐	☐
press the plunger on the injection device to inject the liquid?	☐	☐	☐	☐	☐	☐
hold the injection device during the injection?	☐	☐	☐	☐	☐	☐
withdraw the needle into the safety guard after completion of the injection?	☐	☐	☐	☐	☐	☐

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

10.12. Appendix 12: Regulatory, Ethical, and Study Oversight Considerations

REGULATORY AND ETHICAL CONSIDERATIONS

Investigator Responsibilities

The investigator is responsible for ensuring that the study is performed in accordance with the protocol, current International Council on Harmonisation (ICH) guidelines on Good Clinical Practice (GCP), and applicable regulatory and country-specific requirements.

Good Clinical Practice is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human participants. Compliance with this standard provides public assurance that the rights, safety, and well-being of study participants are protected, consistent with the principles that originated in the Declaration of Helsinki, and that the study data are credible.

Protocol Amendments

Neither the investigator nor the sponsor will modify this protocol without a formal amendment by the sponsor. All protocol amendments must be issued by the sponsor and signed and dated by the investigator. Protocol amendments must not be implemented without prior IEC/IRB approval, or when the relevant competent authority has raised any grounds for non-acceptance, except when necessary to eliminate immediate hazards to the participants, in which case the amendment must be promptly submitted to the IEC/IRB and relevant competent authority. Documentation of amendment approval by the investigator and IEC/IRB must be provided to the sponsor or designee. When the change(s) involve only logistic or administrative aspects of the study, the IEC/IRB (where required) only needs to be notified.

During the course of the study, in situations where a departure from the protocol is unavoidable, the investigator or other physician in attendance will contact the appropriate sponsor designee. Except in emergency situations, this contact should be made before implementing any departure from the protocol. In all cases, contact with the sponsor or designee must be made as soon as possible to discuss the situation and agree on an appropriate course of action. The data recorded in the Data Collection System (DCS) and source documents will reflect any departure from the protocol, and the source documents will describe this departure and the circumstances requiring it.

Regulatory Approval/Notification

This protocol and any amendment(s) must be submitted to the appropriate regulatory authorities in each respective country, if applicable. A study may not be initiated until all local regulatory requirements are met.

Required Prestudy Documentation

The following documents must be provided to the sponsor or designee before shipment of study intervention to the study site:

- Protocol and amendment(s), if any, signed and dated by the principal investigator
- A copy of the dated and signed (or sealed, where appropriate per local regulations), written IEC/IRB approval of the protocol, amendments, ICF, any recruiting materials, and if applicable, participant compensation programs. This approval must clearly identify the specific protocol by title and number and must be signed (or sealed, where appropriate per local regulations) by the chairman or authorized designee.
- Name and address of the IEC/IRB, including a current list of the IEC/IRB members and their function, with a statement that it is organized and operates according to GCP and the applicable laws and regulations. If accompanied by a letter of explanation, or equivalent, from the IEC/IRB, a general statement may be substituted for this list. If an investigator or a member of the study site personnel is a member of the IEC/IRB, documentation must be obtained to state that this person did not participate in the deliberations or in the vote/opinion of the study.
- Regulatory authority approval or notification, if applicable
- Signed and dated statement of investigator (eg, Form FDA 1572), if applicable
- Documentation of investigator qualifications (eg, curriculum vitae)
- Completed investigator financial disclosure form from the principal investigator, where required
- Signed and dated Clinical Trial Agreement, which includes the financial agreement
- Any other documentation required by local regulations

The following documents must be provided to the sponsor or designee before enrollment of the first participant:

- Completed investigator financial disclosure forms from all sub-investigators
- Documentation of sub-investigator qualifications (eg, curriculum vitae)
- Name and address of any local laboratory conducting tests for the study, and a dated copy of current laboratory normal ranges for these tests, if applicable
- Local laboratory documentation demonstrating competence and test reliability (eg, accreditation/license), if applicable

Independent Ethics Committee or Institutional Review Board

Before the start of the study, the investigator (or sponsor where required) will provide the IEC/IRB with current and complete copies of the following documents (as required by local regulations):

- Final protocol and, if applicable, amendments
- Sponsor-approved ICF (and any other written materials to be provided to the participants)
- Investigator's Brochure (or equivalent information) and amendments/addenda
- Sponsor-approved participant recruiting materials
- Information on compensation for study-related injuries or payment to participants for participation in the study, if applicable

- Investigator's curriculum vitae or equivalent information (unless not required, as documented by the IEC/IRB)
- Information regarding funding, name of the sponsor, institutional affiliations, other potential conflicts of interest, and incentives for participants
- Any other documents that the IEC/IRB requests to fulfill its obligation

This study will be undertaken only after the IEC/IRB has given full approval of the final protocol, amendments (if any, excluding the ones that are purely administrative, with no consequences for participants, data or study conduct, unless required locally), the ICF, applicable recruiting materials, and participant compensation programs, and the sponsor or designee has received a copy of this approval. This approval letter must be dated and must clearly identify the IEC/IRB and the documents being approved.

Approval for the collection of optional samples for research and for the corresponding ICF must be obtained from the IEC/IRB. Approval for the protocol can be obtained independent of this optional research component.

During the study the investigator (or sponsor where required) will send the following documents and updates to the IEC/IRB for their review and approval, where appropriate:

- Protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data or study conduct)
- Revision(s) to ICF and any other written materials to be provided to participants
- If applicable, new or revised participant recruiting materials approved by the sponsor
- Revisions to compensation for study-related injuries or payment to participants for participation in the study, if applicable
- New edition(s) of the IB and amendments/addenda
- Summaries of the status of the study at intervals stipulated in guidelines of the IEC/IRB (at least annually)
- Reports of AEs that are serious, unlisted/unexpected, and associated with the study intervention
- New information that may adversely affect the safety of the participants or the conduct of the study
- Deviations from or changes to the protocol to eliminate immediate hazards to the participants
- Report of deaths of participants under the investigator's care
- Notification if a new investigator is responsible for the study at the site
- Development Safety Update Report and Line Listings, where applicable
- Any other requirements of the IEC/IRB

For all protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data or study conduct), the amendment and applicable ICF revisions must be submitted promptly to the IEC/IRB for review and approval before implementation of the change(s).

At least once a year, the IEC/IRB will be asked to review and reapprove this study, where required.

At the end of the study, the investigator (or sponsor where required) will notify the IEC/IRB about the study completion (if applicable, the notification will be submitted through the head of investigational institution).

Country Selection

This study will only be conducted in those countries where the intent is to launch or otherwise help ensure access to the developed product if the need for the product persists, unless explicitly addressed as a specific ethical consideration in Section 4.2.4, Study-Specific Ethical Design Considerations.

Other Ethical Considerations

For study-specific ethical design considerations, refer to Section 4.2.4.

FINANCIAL DISCLOSURE

Investigators and sub-investigators will provide the sponsor or designee with sufficient, accurate financial information in accordance with local regulations to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

Refer to Required Prestudy Documentation (above) for details on financial disclosure.

INFORMED CONSENT PROCESS

For each participant, his or her parent(s) (preferably both parents, if available) or legally acceptable representative(s), as required by local regulations, must give written consent (permission) according to local requirements after the nature of the study has been fully explained and before the performance of any study-related assessments. Assent must be obtained from children (minors) capable of understanding the nature of the study, typically participants 7 years of age and older, depending on the institutional policies and national/local guidelines. The ICF(s) must be signed before performance of any study-related activity. The ICF(s) that is/are used must be approved by both the sponsor or designee and by the reviewing IEC/IRB and be in a language that the participant can read and understand. The informed consent should be in accordance with principles that originated in the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory requirements, and sponsor policy.

Before enrollment in the study, the investigator or an authorized member of the study site personnel must explain to potential participants the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort participation in the study may entail. Participants will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the participant will receive. Finally, they will be told that the investigator will maintain a participant identification register for the purposes of long-term follow-up if needed and that their records may be accessed by health authorities and authorized sponsor or designee personnel without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations. By signing the ICF the participant is authorizing such access. It also denotes that the participant agrees to allow his or her study physician to recontact the participant for the purpose of obtaining consent for additional safety evaluations, and subsequent disease-related treatments, if needed.

There will be a second consent/assent process for the optional Usability Assessment Substudy which will utilize the same procedures as the primary study consent/assent process.

The participant will be given sufficient time to read the ICF and the opportunity to ask questions. After this explanation and before entry into the study, consent should be appropriately recorded by means of the participant's personally dated signature. After having obtained the consent, a copy of the ICF must be given to the participant.

A participant may be rescreened 1 time. Participants who are rescreened are required to sign a new ICF. In rare cases, a participant may be screened a third time after discussion with the medical monitor.

Completion of screening and randomization procedures within the specified approximately 6-week window is required. If a participant is approaching the completion of that period, the medical monitor can be contacted to discuss eligibility.

If any delay leads to the expiration of time-specific assessments (eg, TB, chest radiograph, stool analysis), the participant will be considered a screen failure because he/she will not meet eligibility criteria, and the expired assessments (along with the non-time-specific laboratory tests) will have to be repeated on rescreening.

A limited number of study sites will be asked by the Sponsor to obtain informed consent/assent using a validated electronic system instead of a paper-based process. If both parties (Sponsor and the study site) agree, and if participation is allowed by local regulations and EC/IRB requirements, the Sponsor will provide an eTablet device (eg, iPad®) to the study site to use for the electronic informed consent/assent. Overall the consent/assent process will remain the same, as described in this section; however, at the study sites utilizing electronic informed consent/assent, participants or their legally acceptable representatives will be able to review the entire informed consent/assent form content on the eTablet. The ability for participants or their legally acceptable representatives to review the paper informed consent/assent form is always an option at sites utilizing electronic informed consent/assent. Depending on local regulations and EC/IRB requirements, the

participants or their legally acceptable representatives and person obtaining consent/assent will either apply their handwritten signature electronically directly onto the eTablet or apply their handwritten signature to a printed paper copy of the informed consent/assent in accordance with local regulations.

DATA PROTECTION

Privacy of Personal Data

The collection and processing of personal data from participants enrolled in this study will be limited to those data that are necessary to fulfill the objectives of the study.

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of participants confidential.

The informed consent obtained from the participant includes explicit consent for the processing of personal data and for the investigator/institution to allow direct access to his or her original medical records (source data/documents) for study-related monitoring, audit, IEC/IRB review, and regulatory inspection. This consent also addresses the transfer of the data to other entities and to other countries.

The participant has the right to request through the investigator access to his or her personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps will be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Exploratory biomarker, PK, and immunogenicity tests are only for research. They will not be used for medical care of the participant or to make a diagnosis about the participant's health. In addition, the sponsor cannot make decisions as to the significance of any findings resulting from exploratory research. Therefore, exploratory research data will not be returned to participants or investigators, unless required by law or local regulations. Privacy and confidentiality of data generated in the future on stored samples will be protected by the same standards applicable to all other clinical data.

LONG-TERM RETENTION OF SAMPLES FOR ADDITIONAL FUTURE RESEARCH

Samples collected in this study may be stored for up to 15 years (or according to local regulations) for additional research. The start of the storage period is defined as last participant last visit. Samples will only be used to understand golimumab and infliximab, to understand UC, to understand differential intervention responders, and to develop diagnostic tests to identify UC populations that may be responsive or non-responsive to treatment with golimumab or infliximab. The research may begin at any time during the study or the poststudy storage period.

Stored samples will be coded throughout the sample storage and analysis process and will not be labeled with personal identifiers. Participants may withdraw their consent for their samples to be stored for research (refer to Section 7.2.1, Withdrawal from the Use of Research Samples).

COMMITTEES STRUCTURE

Data Monitoring Committee

Details regarding an internal DMC are presented in Section 9.5.

PUBLICATION POLICY/DISSEMINATION OF CLINICAL STUDY DATA

All information, including but not limited to information regarding golimumab or the sponsor's operations (eg, patent application, formulas, manufacturing processes, basic scientific data, prior clinical data, formulation information) supplied by the sponsor to the investigator and not previously published, and any data, including pharmacogenomic or exploratory biomarker research data, generated as a result of this study, are considered confidential and remain the sole property of the sponsor. The investigator agrees to maintain this information in confidence and use this information only to accomplish this study and will not use it for other purposes without the sponsor's prior written consent.

The investigator understands that the information developed in the study will be used by the sponsor in connection with the continued development of golimumab, and thus may be disclosed as required to other clinical investigators or regulatory agencies. To permit the information derived from the clinical studies to be used, the investigator is obligated to provide the sponsor with all data obtained in the study.

The results of the study will be reported in a Clinical Study Report (CSR) generated by the sponsor and will contain eCRF data transmitted from a central laboratory, ePRO, and IWRS data from all study sites that participated in the study into the sponsor's database, as per protocol. Recruitment performance or specific expertise related to the nature and the key assessment parameters of the study will be used to determine a coordinating investigator for the study. Results of pharmacogenomic and exploratory biomarker analyses performed after the CSR has been issued will be reported in a separate report and will not require a revision of the CSR.

Study participant identifiers will not be used in publication of results. Any work created in connection with performance of the study and contained in the data that can benefit from copyright protection (except any publication by the investigator as provided for below) shall be the property of the sponsor as author and owner of copyright in such work.

Consistent with Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines, the sponsor shall have the right to publish such primary (multicenter) data and information without approval from the investigator. The investigator has the right to publish study site-specific data after the primary data are published. If an investigator wishes to publish information from the study, a copy of the manuscript must be provided to the sponsor for review at least 60 days before submission for publication or presentation. Expedited reviews will be arranged for abstracts, poster presentations, or other materials. If requested by the sponsor in

writing, the investigator will withhold such publication for up to an additional 60 days to allow for filing of a patent application. In the event that issues arise regarding scientific integrity or regulatory compliance, the sponsor will review these issues with the investigator. The sponsor will not mandate modifications to scientific content and does not have the right to suppress information. For multicenter study designs and substudy approaches, secondary results generally should not be published before the primary endpoints of a study have been published. Similarly, investigators will recognize the integrity of a multicenter study by not submitting for publication data derived from the individual study site until the combined results from the completed study have been submitted for publication, within 18 months after the study end date, or the sponsor confirms there will be no multicenter study publication. Authorship of publications resulting from this study will be based on the guidelines on authorship, such as those described in the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals, which state that the named authors must have made a significant contribution to the conception or design of the work; or the acquisition, analysis, or interpretation of the data for the work; and drafted the work or revised it critically for important intellectual content; and given final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Registration of Clinical Studies and Disclosure of Results

The sponsor will register and disclose the existence of and the results of clinical studies as required by law.

DATA QUALITY ASSURANCE

Data Quality Assurance/Quality Control

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study sites, review of protocol procedures with the investigator and study site personnel before the study, periodic monitoring visits by the sponsor, direct transmission of clinical laboratory data from a central laboratory as well as direct transmission of IWRS data to the sponsor's database, and direct transmission of PRO and self-injection data to the electronic patient-reported outcome (ePRO) vendor database and then to the sponsor's database.

Guidelines for eCRF completion will be provided and reviewed with study site personnel before the start of the study.

The sponsor or designee will review eCRF for accuracy and completeness during on-site monitoring visits and after transmission to the sponsor; any discrepancies will be resolved with the investigator or designee, as appropriate. After upload of the data into the study database they will be verified for accuracy and consistency with the data sources.

DATA COLLECTION

Data for each study participant will be collected in the eCRF or ancillary data collection systems such as the IWRS, patient-reported outcome (PRO) tablets, laboratory database, and imaging database. Case report forms are prepared and provided by the sponsor for each participant in eCRF. Collectively, all data collection via eCRFs and ancillary systems will comprise what is referred to in this protocol as the DCS.

All DCS entries, corrections, and alterations must be made by the investigator or authorized study site personnel.

The investigator must verify that all data entries in the eCRF are accurate and correct.

Study data will be transcribed by study site personnel from source documentation to an eCRF or the appropriate ancillary DCS, as applicable. Study-specific data from each source will be transmitted in a secure manner to the sponsor.

Worksheets may be used as source documentation to capture data and facilitate completion of the eCRF or entry of data into the applicable ancillary data system. Data must be entered into the DCS in English. The eCRF must be completed as soon as possible after a participant visit and the forms should be available for review at the next scheduled monitoring visit.

Necessary eCRF or ancillary data modifications can only be made by the investigator or appropriate site personnel using eCRF system functionality and/or ancillary data revision procedures. All data changes will be recorded in an audit trail.

SOURCE DOCUMENTS

At a minimum, source documents consistent in the type and level of detail with that commonly recorded at the study site as a basis for standard medical care must be available for the following: participant identification, eligibility, and study identification; study discussion and date of signed informed consent; dates of visits; results of safety and efficacy parameters as required by the protocol; record of all AEs and follow-up of AEs; concomitant medication; intervention receipt/dispensing/return records; study intervention administration information; and date of study completion and reason for early discontinuation of study intervention or withdrawal from the study, if applicable.

The author of an entry in the source documents should be identifiable.

Specific details required as source data for the study and source data collection methods will be reviewed with the investigator before the study and will be described in the monitoring guidelines (or another equivalent document).

The minimum source documentation requirements for Section 5.1, Inclusion Criteria and Section 5.2, Exclusion Criteria that specify a need for documented medical history are as follows:

- Referral letter from treating physician or
- Complete history of medical notes at the site
- Discharge summaries

Inclusion and exclusion criteria not requiring documented medical history must be verified at a minimum by participant interview or other protocol-required assessment (eg, physical examination, laboratory assessment) and documented in the source documents.

Participant- and investigator-completed scales and assessments designated by the sponsor including PRO assessments (PUCAI and IMPACT III) will be recorded into an electronic tablet device during the visit at the study site. These data will be considered electronic source documentation.

An electronic source (eSource) system may be utilized, which contains data traditionally maintained in a hospital or clinic record to document medical care (eg, electronic source documents) as well as the clinical study-specific data fields as determined by the protocol. This data is electronically extracted for use by the sponsor. If eSource is utilized, references made to the eCRF in the protocol include the eSource system but information collected through eSource may not be limited to that found in the eCRF.

MONITORING

The sponsor designee will perform on-site monitoring visits as frequently as necessary. The monitor will record dates of the visits in a study site visit log that will be kept at the study site, as allowed by local regulation. The first postinitiation visit will be made as soon as possible after enrollment has begun. At these visits, the monitor will compare the data entered into the applicable DCS component (as defined in the monitoring guidelines) with the source documents (eg, hospital/clinic/physician's office medical records). The nature and location of all source documents will be identified to ensure that all sources of original data required to complete the applicable DCS component are known to the sponsor or designee and study site personnel and are accessible for verification by the sponsor study site contact. If electronic records are maintained at the study site, the method of verification must be discussed with the study site personnel.

Direct access to source documents (medical records) must be allowed for the purpose of verifying that the recorded data are consistent with the original source data. Findings from this review will be discussed with the study site personnel. The sponsor or designee expects that, during monitoring visits, the relevant study site personnel will be available, the source documents will be accessible, and a suitable environment will be provided for review of study-related documents. The monitor will meet with the investigator on a regular basis during the study to provide feedback on the study conduct.

In addition to on-site monitoring visits, remote contacts can occur. It is expected that during these remote contacts, study site personnel will be available to provide an update on the progress of the study at the site.

Central monitoring will take place for data identified by the sponsor or designee as requiring central review.

ON-SITE AUDITS

Representatives of the sponsor's (or sponsor designee's) clinical quality assurance department may visit the study site at any time during or after completion of the study to conduct an audit of the study in compliance with regulatory guidelines and company policy. These audits will require access to all study records, including source documents, for inspection. Participant privacy must, however, be respected. The investigator and study site personnel are responsible for being present and available for consultation during routinely scheduled study site audit visits conducted by the sponsor or its designees.

Similar auditing procedures may also be conducted by agents of any regulatory body, either as part of a national GCP compliance program or to review the results of this study in support of a regulatory submission. The investigator should immediately notify the sponsor or designee if he or she has been contacted by a regulatory agency concerning an upcoming inspection.

RECORD RETENTION

In compliance with the ICH/GCP guidelines, the investigator/institution will maintain all eCRF and all source documents that support the data collected from each participant, as well as all study documents as specified in ICH/GCP Section 8, Essential Documents for the Conduct of a Clinical Trial, and all study documents as specified by the applicable regulatory requirement(s). The investigator/institution will take measures to prevent accidental or premature destruction of these documents.

Essential documents must be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.

If the responsible investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the investigator relocate or dispose of any study documents before having obtained written approval from the sponsor or designee.

If it becomes necessary for the sponsor or the appropriate regulatory authority to review any documentation relating to this study, the investigator/institution must permit access to such reports.

STUDY AND SITE CLOSURE

Study Termination

The sponsor reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study site closure visit has been performed.

The investigator may initiate study site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the sponsor or investigator may include but are not limited to:

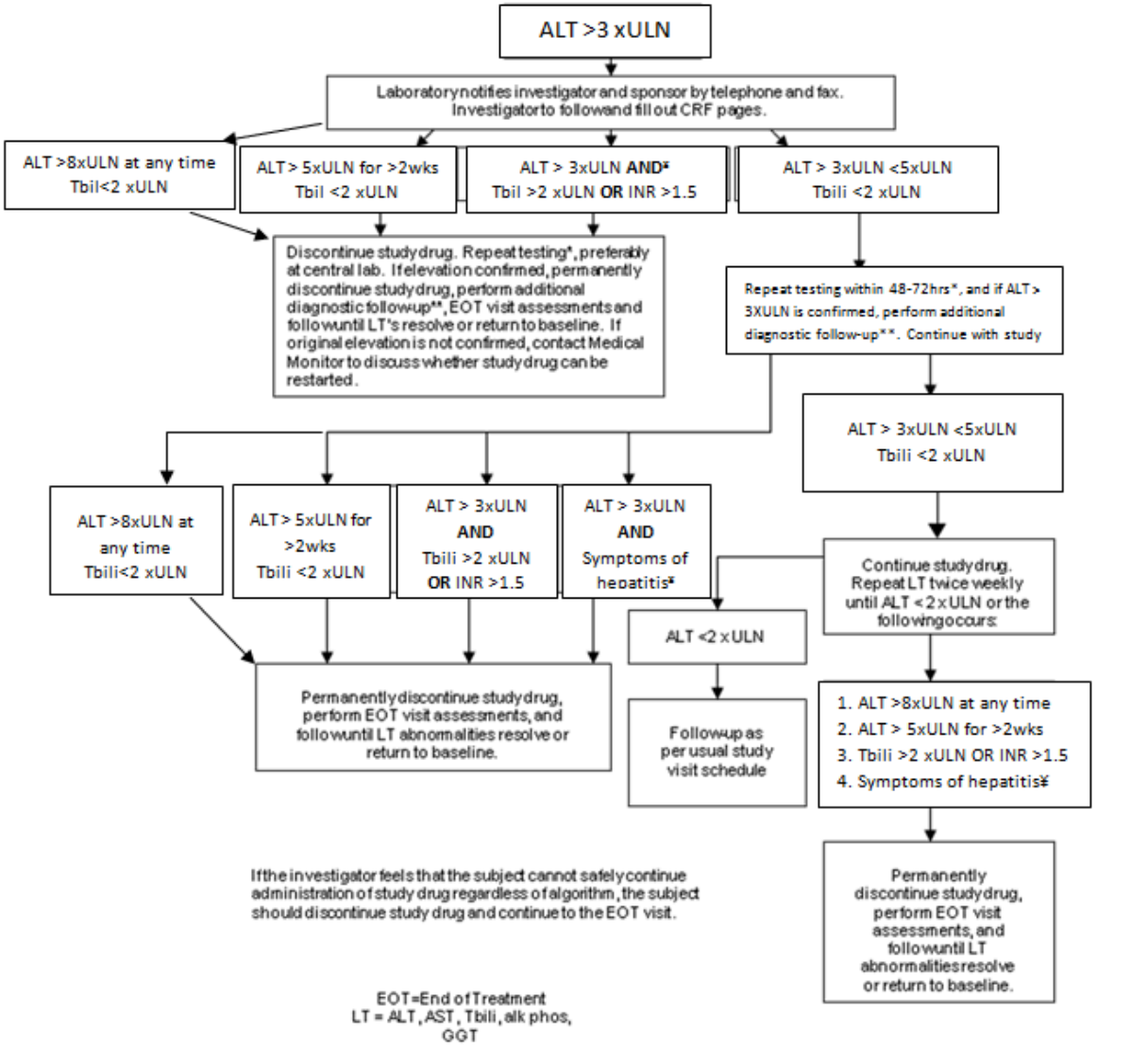
- Failure of the investigator to comply with the protocol, the requirements of the IEC/IRB or local health authorities, the sponsor's procedures, or GCP guidelines
- Inadequate recruitment of participants by the investigator
- Discontinuation of further study intervention development

10.13. Appendix 13: Liver Safety: Suggested Actions and Follow-up Assessments

Guideline Algorithm for Monitoring, Assessment & Evaluation of Abnormal Liver Tests in Participants with no Underlying Liver Disease and normal baseline ALT, AST, Alkaline Phosphatase and Bilirubin

Although this algorithm is still applicable across all populations, it has been developed assuming normal liver function at baseline. For populations with preexisting liver disease and/or AT increases at baseline, product teams are strongly encouraged to consult with Hepatic Safety Group for further guidance particularly for discontinuation criteria.

NOTE: "Liver tests" or "LT's" is the proper name for what are often called "liver function tests" or "LFT's"



*Repeat testing within 48-72 hours in patients with initial ALT elevations, particularly if these are not events reported previously with the drug. If ALT transient elevations have been already established as part of the safety profile, the required frequency of retesting can be decreased

¥ OR ALT >3xULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (>5%)

10.14. Appendix 14: Contraceptive and Barrier Guidance and Collection of Pregnancy Information

Participants must follow contraceptive measures as outlined in Section 5.1, Inclusion Criteria. Pregnancy information will be collected and reported as noted in Section 8.3.5 (Pregnancy), and Appendix 16 (Section 10.16; Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting).

Definitions

Woman of Childbearing Potential (WOCBP)

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

Woman Not of Childbearing Potential

- **premenarchal**
  A premenarchal state is one in which menarche has not yet occurred.
- **postmenopausal**
  A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level (>40 IU/L or mIU/mL) in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT), however in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient. If there is a question about menopausal status in women on HRT, the woman will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if she wishes to continue HRT during the study.
- **permanently sterile**
  Permanent sterilization methods include hysterectomy, bilateral salpingectomy, bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy.

Note: If the childbearing potential changes after start of the study (eg, a premenarchal woman experiences menarche) or the risk of pregnancy changes (eg, a woman who is not heterosexually active becomes active), a woman must begin a highly effective method of contraception, as described throughout the inclusion criteria.

If reproductive status is questionable, additional evaluation should be considered.

As noted in inclusion criterion #12, study participants who are girls of childbearing potential or female partners of boys must be practicing a highly effective method of contraception and remain on a highly effective method while receiving study intervention and until 6 months after last dose. Examples of highly effective methods of contraception are provided below; however, the method selected must meet local/regional regulations/guidelines for highly effective contraception.

Examples of Contraceptives

EXAMPLES OF CONTRACEPTIVES[a] ALLOWED DURING THE STUDY INCLUDE:
USER-INDEPENDENT **Highly Effective Methods That Are User-Independent** *Failure rate of ≤1% per year when used consistently and correctly.*
• Implantable progestogen-only hormone contraception associated with inhibition of ovulation[b]
• Intrauterine device (IUD)
• Intrauterine hormone-releasing system (IUS)
• Bilateral tubal occlusion
• Vasectomized partner *(Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the woman of childbearing potential and the absence of sperm has been confirmed. If not, additional highly effective method of contraception should be used. Spermatogenesis cycle is approximately 74 days.)*
USER-DEPENDENT **Highly Effective Methods That Are User-Dependent** *Failure rate of <1% per year when used consistently and correctly.*
• Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation[b] – oral – intravaginal – transdermal – injectable
• Progestogen-only hormone contraception associated with inhibition of ovulation[b] – oral – injectable
• Sexual abstinence *(Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.)*
NOT ALLOWED AS SOLE METHOD OF CONTRACEPTION DURING THE STUDY (not considered to be highly effective - failure rate of >1% per year)
• Progestogen-only oral hormonal contraception where inhibition of ovulation is not the primary mode of action.
• Male or female condom with or without spermicide[c]
• Cap, diaphragm, or sponge with spermicide
• A combination of male condom with either cap, diaphragm, or sponge with spermicide (double-barrier methods)[c]
• Periodic abstinence (calendar, symptothermal, postovulation methods)
• Withdrawal (coitus-interruptus)
• Spermicides alone
• Lactational amenorrhea method (LAM)
a) Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies. b) Hormonal contraception may be susceptible to interaction with the study intervention, which may reduce the efficacy of the contraceptive method. In addition, consider if the hormonal contraception may interact with the study intervention. c) Male condom and female condom should not be used together (due to risk of failure with friction).

Pregnancy during the study

All initial reports of pregnancy in female participants or partners of male participants must be reported to the sponsor or designee by the study site personnel within 24 hours of their knowledge of the event using the appropriate pregnancy notification form. Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs and must be reported using the Serious Adverse Event Form. Any participant who becomes pregnant during the study must discontinue further study intervention.

Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required.

10.15. Appendix 15: Hepatitis B Virus (HBV) Screening with HBV DNA Testing

Participants must undergo screening for hepatitis B virus (HBV). At a minimum, this includes testing for HBsAg (HBV surface antigen), anti-HBs (HBV surface antibody), and anti-HBc total (HBV core antibody total):

- Participants who test negative for all HBV screening tests (ie, HBsAg-, anti-HBc-, and anti-HBs-) ***are eligible*** for this protocol.
- Participants who test **negative** for surface antigen (HBsAg-) and test **positive** for core antibody (anti-HBc+) ***and*** surface antibody (anti-HBs+) ***are eligible*** for this protocol.
- Participants who test **positive only** for **surface antibody** (anti-HBs+) ***are eligible*** for this protocol.
- Participants who test **positive** for surface antigen (HBsAg+) ***are NOT eligible*** for this protocol, regardless of the results of other hepatitis B tests.
- Participants who test **positive only** for **core antibody** (anti-HBc+) must undergo further testing for the presence of hepatitis B virus deoxyribonucleic acid (HBV DNA) test. If the HBV DNA test is **negative**, the participant ***is eligible*** for this protocol. If the HBV DNA test is **positive**, the participant ***is NOT eligible*** for this protocol. In the event the HBV DNA test cannot be performed, the participant ***is NOT eligible*** for this protocol.

These eligibility criteria based on HBV test results are also represented in Table 1 below.

Table 1: Eligibility based on hepatitis B virus test results

HEPATITIS B TEST RESULT			
Hepatitis B surface antigen (HBsAg)	**Hepatitis B surface antibody (anti-HBs)**	**Hepatitis B core antibody (anti-HBc total)**	**STATUS**
negative	negative	negative	**Eligible**
negative	(+)	negative	
negative	(+)	(+)	
(+)	negative *or* (+)	negative *or* (+)	**Not eligible**
negative	negative	(+)	**(Require testing for presence of HBV DNA*)**

* If HBV DNA is detectable, the participant is not eligible for this protocol. If HBV DNA testing cannot be performed, or there is evidence of chronic liver disease, the participant is not eligible for the protocol.

For participants who **are not eligible for this protocol due to HBV test results**, consultation with a physician with expertise in the treatment of hepatitis B virus infection is recommended.

10.16. Appendix 16: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

ADVERSE EVENT DEFINITIONS AND CLASSIFICATIONS

Adverse Event

An adverse event is any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An adverse event does not necessarily have a causal relationship with the intervention. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product. (Definition per International Council on Harmonisation [ICH] Technical Requirements for Pharmaceuticals for Human Use).

This includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

Note: The sponsor collects adverse events starting with the signing of the ICF (refer to All Adverse Events under Section 8.3.1, Time Period and Frequency for Collecting Adverse Events and Serious Adverse Events Information, for time of last adverse event recording).

Serious Adverse Event

A serious adverse event based on ICH and EU Guidelines on Pharmacovigilance for Medicinal Products for Human Use is any untoward medical occurrence that at any dose:

- Results in death
- Is life threatening
  (The participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe)
- Requires inparticipant hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is a suspected transmission of any infectious agent via a medicinal product
- Is Medically Important*

*Medical and scientific judgment should be exercised in deciding whether expedited reporting is also appropriate in other situations, such as important medical events that may not be immediately life threatening or result in death or hospitalization but may jeopardize the participant or may require intervention to prevent one of the other outcomes listed in the definition above. These should usually be considered serious.

Unlisted (Unexpected) Adverse Event/Reference Safety Information

An adverse event is considered unlisted if the nature or severity is not consistent with the applicable product reference safety information. For golimumab and for infliximab, the expectedness of an adverse event will be determined by whether or not it is listed in the IB for golimumab or for infliximab, respectively.

Adverse Event Associated With the Use of the Intervention

An adverse event is considered associated with the use of the intervention if the attribution is possible, probable, or very likely by the definitions listed below (see Attribution Definitions).

ATTRIBUTION DEFINITIONS

Not Related

An adverse event that is not related to the use of the intervention.

Doubtful

An adverse event for which an alternative explanation is more likely, eg, concomitant treatment(s), concomitant disease(s), or the relationship in time suggests that a causal relationship is unlikely.

Possible

An adverse event that might be due to the use of the intervention. An alternative explanation, eg, concomitant treatment(s), concomitant disease(s), is inconclusive. The relationship in time is reasonable; therefore, the causal relationship cannot be excluded.

Probable

An adverse event that might be due to the use of the intervention. The relationship in time is suggestive (eg, confirmed by dechallenge). An alternative explanation is less likely, eg, concomitant treatment(s), concomitant disease(s).

Very Likely

An adverse event that is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation, eg, concomitant treatment(s), concomitant disease(s). The relationship in time is very suggestive (eg, it is confirmed by dechallenge and rechallenge).

SEVERITY CRITERIA

An assessment of severity grade will be made using the following general categorical descriptors:

Mild: Awareness of symptoms that are easily tolerated, causing minimal discomfort and not interfering with everyday activities.

Moderate: Sufficient discomfort is present to cause interference with normal activity.

Severe: Extreme distress, causing significant impairment of functioning or incapacitation. Prevents normal everyday activities.

The investigator should use clinical judgment in assessing the severity of events not directly experienced by the participant (eg, laboratory abnormalities).

SPECIAL REPORTING SITUATIONS

Safety events of interest on a sponsor study intervention in an interventional study that may require expedited reporting or safety evaluation include, but are not limited to:

- Overdose of a sponsor study intervention
- Suspected abuse/misuse of a sponsor study intervention
- Accidental or occupational exposure to a sponsor study intervention
- Any failure of expected pharmacologic action (ie, lack of effect) of a sponsor study intervention
- Unexpected therapeutic or clinical benefit from use of a sponsor study intervention
- Medication error involving a sponsor product (with or without participant/participant exposure to the sponsor study intervention, eg, name confusion)
- Exposure to a sponsor study intervention from breastfeeding

Special reporting situations should be recorded in the eCRF. Any special reporting situation that meets the criteria of a serious adverse event should be recorded on the serious adverse event page of the eCRF.

PROCEDURES

All Adverse Events

All adverse events, regardless of seriousness, severity, or presumed relationship to study intervention, must be recorded using medical terminology in the source document and the eCRF. Whenever possible, diagnoses should be given when signs and symptoms are due to a common etiology (eg, cough, runny nose, sneezing, sore throat, and head congestion should be reported as "upper respiratory infection"). Investigators must record in the eCRF their opinion concerning the relationship of the adverse event to study therapy. All measures required for adverse event management must be recorded in the source document and reported according to sponsor instructions.

For all studies with an out participant phase, including open-label studies, the participant must be provided with a "wallet (study) card" and instructed to carry this card with them for the duration of the study indicating the following:

- Study number
- Statement, in the local language(s), that the participant is participating in a clinical study
- Investigator's name and 24-hour contact telephone number
- Local sponsor's or designee’s name and 24-hour contact telephone number (for medical staff only)

- Site number
- Participant number
- Any other information that is required to do an emergency breaking of the blind

Serious Adverse Events

All serious adverse events that have not resolved by the end of the study, or that have not resolved upon discontinuation of the participant's participation in the study, must be followed until any of the following occurs:

- The event resolves
- The event stabilizes
- The event returns to baseline, if a baseline value/status is available
- The event can be attributed to agents other than the study intervention or to factors unrelated to study conduct
- It becomes unlikely that any additional information can be obtained (participant or health care practitioner refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts)

Suspected transmission of an infectious agent by a medicinal product will be reported as a serious adverse event. Any event requiring hospitalization (or prolongation of hospitalization) that occurs during the course of a participant's participation in a study must be reported as a serious adverse event, except hospitalizations for the following:

- Hospitalizations not intended to treat an acute illness or adverse event (eg, social reasons such as pending placement in long-term care facility)
- Surgery or procedure planned before entry into the study (must be documented in the eCRF). Note: Hospitalizations that were planned before the signing of the ICF, and where the underlying condition for which the hospitalization was planned has not worsened, will not be considered serious adverse events. Any adverse event that results in a prolongation of the originally planned hospitalization is to be reported as a new serious adverse event.

The cause of death of a participant in a study within 16 weeks of the last dose of study intervention, whether or not the event is expected or associated with the study intervention, is considered a serious adverse event.

CONTACTING SPONSOR REGARDING SAFETY

The names (and corresponding telephone numbers) of the individuals who should be contacted regarding safety issues or questions regarding the study are listed in the Contact Information page(s), which will be provided as a separate document.

PRODUCT QUALITY COMPLAINT HANDLING

A PQC is defined as any suspicion of a product defect related to manufacturing, labeling, or packaging, ie, any dissatisfaction relative to the identity, quality, durability, or reliability of a

product, including its labeling or package integrity. A PQC may have an impact on the safety and efficacy of the product. Timely, accurate, and complete reporting and analysis of PQC information from studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide. The sponsor has established procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of PQC information; all studies conducted by the sponsor or its affiliates will be conducted in accordance with those procedures.

All PFP-V associated with device-related PQCs will be investigated including the return of the device to the sponsor for inspection. PFS-U should be retained for further investigation if requested by the sponsor.

Procedures

All initial PQCs must be reported to the sponsor or designee by the study site personnel within 24 hours after being made aware of the event.

If the defect is combined with a serious adverse event, the study site personnel must report the PQC to the sponsor designee according to the serious adverse event reporting timelines (refer to Section 8.3.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information). A sample of the suspected product should be maintained for further investigation if requested by the sponsor.

Contacting Sponsor Regarding Product Quality

The names (and corresponding telephone numbers) of the individuals who should be contacted regarding product quality issues are listed in the Contact Information page(s), which will be provided as a separate document.

10.17. Appendix 17: Anticipated Events

Anticipated Event

An anticipated event is an adverse event (serious or non-serious) that commonly occurs as a consequence of the underlying disease or condition under investigation (disease-related) or background regimen.

For the purposes of this study, the following events will be considered anticipated events:

- adverse events related to symptoms of UC
- adverse events related to worsening or progression of UC

Reporting of Anticipated Events

All adverse events will be recorded in the eCRF regardless of whether considered to be anticipated events and will be reported to the sponsor or designee as described under All Adverse Events in Section 8.3.1 (Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information). Any anticipated event that meets serious adverse event criteria will be reported to the sponsor or designee as described under Serious Adverse Events in Section 8.3.1 (Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information). These anticipated events are exempt from expedited reporting as individual single cases to health authorities, except where local regulations require expedited reporting of all SUSARs. However, if based on an aggregate review, it is determined that an anticipated event is possibly related to study intervention, the sponsor will report these events in an expedited manner.

Anticipated Event Review Committee (ARC)

An Anticipated Event Review Committee (ARC) will be established to perform reviews of prespecified anticipated events at an aggregate level. The ARC is a safety committee within the sponsor's organization that is independent of the sponsor's study team. The ARC will meet to aid in the recommendation to the sponsor's study team as to whether there is a reasonable possibility that an anticipated event is related to the study intervention.

Statistical Analysis

Details of statistical analysis of anticipated events, including the frequency of review and threshold to trigger an aggregate analysis of anticipated events will be provided in a separate Anticipated Events Safety Monitoring Plan (ASMP).

10.18. Appendix 18: Usability Assessment Substudy

Objectives

The objective of the Substudy is to provide supportive data that the PFS-U or PFP-V as designed, together with the appropriate training and written Instructions for Use, are suitable for at home administration (AHA) by pediatric participants or their caregivers.

Overview of Study Design

The Usability Assessment Substudy will be conducted at Sponsor identified sites. Participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in an Usability Assessment Substudy (Section 4.1). An attempt will be made to enroll approximately 10-20 participants in the Usability Assessment Substudy at Week 58.

Similar for all AHA participants, pediatric participants or their caregivers in CNTO148UCO3003 will be trained in safe AHA the first week, and their self- or caregiver administration observed over 2 subsequent q4w visits. Participants or their caregivers will receive face-to-face training by study site staff on the use of the PFS-U or the PFP-V at the first training visit (at the Week 58 study visit for Usability Assessment Substudy participants). Participants will perform a training administration using the PFS-U or the PFP-V at the clinic under the observation/supervision of site staff. Site staff will complete an Observer Checklist at the Week 58 visit. The health care professional will determine whether a pediatric participant or their caregiver can perform the injections. During the 2 subsequent q4w clinic visits, administrations will be performed in a home-like setting in the clinic by pediatric participants or caregivers and should be performed by the same person (ie, pediatric participant or caregiver) and not switched unless participants opt to return to the HCP administration.

Participants or caregivers performing the injection who are enrolled in the Usability Assessment Substudy will be asked to complete an Injection Device Assessment Questionnaire (Section 10.11) regarding their experience using the PFS-U or the PFP-V at Weeks 62 and 66 after completion of the second and third self- or caregiver administration visits. If the injections have been performed by the caregiver, the questionnaire will be completed by the caregiver. If the self-injections have been performed by the pediatric participant, the participant will complete the questionnaire with parent or caregiver assistance, if needed. Evaluation of the user experience after the second independent self- or caregiver administration is considered adequate to evaluate how well participants can understand and recall the dosage instructions, and to assess for any common difficulties with injections.

Participant Population

This Substudy population will include pediatric participants who are enrolled in the study extension. The inclusion and exclusion criteria of the Substudy are described below.

All participants who satisfy the inclusion and exclusion criteria described in Section 5.1 and Section 5.2 of the main protocol, respectively, as well as satisfying the following criteria:

Inclusion Criteria

1. Participants must be eligible for AHA.
2. Participants and parents or caregivers of the participant must successfully demonstrate the ability to complete a study intervention administration.
3. Must sign a separate informed consent/assent for this Substudy.
4. Agree to complete an AHA diary and return it at the next clinic visit.
5. Contact the site for any safety concerns immediately.

Exclusion Criteria

1. Unable to demonstrate the ability to complete a study intervention administration by self or parent/caregiver. For self-administration, participants must be ≥12 years of age. Participants <12 years of age must have study intervention administrations by the parents or caregiver.

Criteria for Withdrawal from this Substudy

Criteria for withdrawal of participants during the Substudy will be identical to that described in Section 7 of the main protocol.

Safety Evaluations

Participants will be observed for at least 30 minutes after the administration of study intervention for symptoms of an injection-site reaction at the investigative site. Participants administering study intervention at home will receive detailed instructions on how to monitor and report potential injection-site reactions. Any adverse reaction (eg, swelling, redness/erythema, pain, tenderness, warmth, bruising, or bleeding) should be noted on the AHA diary and in the AE page of the eCRF.

Similarly, as for all AHA participants, in addition to recording the details of the study intervention, dosing day, time, anatomic site and if there were any complications of the injection, participants and/or caregivers should be instructed to monitor the injection-site for any reactions, including, but not limited to swelling, redness/erythema, pain, tenderness, warmth, bruising, or bleeding. All dosing and adverse event (including injection-site reaction) information, as well as concomitant medications and TB exposure will be documented in an AHA diary, that is to be returned to the site at the upcoming visit and entered by site staff into the eCRF. For any severe injection-site reactions, or changes at the injection-site, or any mild to moderate to severe golimumab reaction which occur hours to days following injection, the participant/caregiver should contact the study site for consultation. Acetaminophen, NSAIDs, and/or diphenhydramine or locally available alternative may be administered at their direction. In case of a severe allergic reaction (eg, anaphylaxis, difficulty breathing, light-headedness, hives, or widely spread body rash), participants or their caregivers should call for emergency medical assistance (paramedic or ambulance) first before contacting the study site.

All device complaints and device-related AEs will be captured and investigated including the return of the device for inspection.

Schedule

Participants in this study will follow the schedule of events as outlined in Table 3 for collection of actual use data for the PFS-U and PFP-V (Injection Device Assessment Questionnaire).

Statistical Methods

Data from the questionnaire will be descriptively summarized for PFS-U. Further details will be provided in the SAP.

10.19. Appendix 19: Guidance on Study Conduct during the COVID-19 Pandemic

It is recognized that the Coronavirus Disease 2019 (COVID-19) pandemic may have an impact on the conduct of this clinical study due to, for example, self-isolation/quarantine by participants and study site personnel; travel restrictions/limited access to public places, including hospitals; study-site personnel being reassigned to critical tasks.

In alignment with recent health authority guidance, the sponsor is providing options for study -related participant management in the event of disruption to the conduct of the study. This guidance does not supersede any local or government guidelines or requirements or the clinical judgment of the investigator to protect the health and well-being of participants and site staff. If, at any time, a participant's safety is considered to be at unacceptable risk, study intervention will be discontinued, and study follow-up will be conducted.

Scheduled visits that cannot be conducted in-person at the study site will be performed to the extent possible remotely/virtually or delayed until such time that on-site visits can be resumed. At each contact, participants will be interviewed to collect safety data. Key efficacy endpoint assessments should be performed if required and as feasible. Participants will also be questioned regarding general health status to fulfill any physical examination requirement.

Every effort should be made to adhere to protocol-specified assessments for participants on study intervention, including follow-up. Modifications to protocol-required assessments may be permitted via COVID-19 Appendix after consultation between the participant and investigator, and with the agreement of the sponsor (see below).

The sponsor will continue to monitor the conduct and progress of the clinical study, and any changes will be communicated to the sites and to the health authorities according to local guidance. If a participant has tested positive for COVID 19, the investigator should contact the sponsor's responsible medical officer to discuss plans for study intervention and follow-up. Modifications made to the study conduct as a result of the COVID-19 pandemic should be summarized in the clinical study report.

ADDITIONAL ELEMENTS, WHERE APPLICABLE:

- Certain protocol-mandated visits to the study site may not be possible during the COVID-19 outbreak. Therefore, temporary measures may be implemented if considered appropriate by the sponsor and investigator to maintain continuity of participant care and study integrity. Certain measures, such as those listed below, may be necessary and should be instituted in accordance with applicable (including local) laws, regulations, guidelines, and procedures:

    - remote (eg, by phone / telemedicine) or in-person, off-site (eg, in-home) interactions between site staff (or designees) and participants for study procedures eg, those related to safety monitoring / efficacy evaluation / study intervention storage and administration (including training where pertinent)

    - procurement of study intervention by participants (or designee) or shipment of study intervention from the study site directly to participants for AHA (including the potential for self-administration of study intervention)

    - laboratory assessments using a suitably accredited local laboratory; for selected measures (eg, urine pregnancy), home testing may be employed

    - other procedures, eg, imaging, may be conducted at an appropriate facility

- Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented with the prefix "COVID-19-related" in the case report form (CRF).

    - other relevant study data elements impacted by the pandemic should also be documented / labeled as "COVID-19-related" in CRFs and / or other study systems, as directed by detailed sponsor guidance. These may include missed / delayed / modified study visits / assessments / dosing, and instances where temporary measures such as those above are implemented.

- The Sponsor will evaluate the totality of impact of COVID-19 on collection of key study data and additional data analyses will be outlined in study SAP(s).

10.20. Appendix 20: Protocol Amendment History

The Protocol Amendment Summary of Changes Table for the current amendment is located directly before the Table of Contents (TOC).

DOCUMENT HISTORY	
Document	**Date**
Amendment 5	14 October 2022
Amendment 4	16 March 2021
Amendment 3	8 July 2019
Amendment 2	13 May 2019
Amendment 1	27 June 2018
Original Protocol	17 May 2018

Amendment 5 (14 October 2022)

Overall Rationale for the Amendment: Upon implementation of Amendment 5, no new participants will be enrolled. The sample size is being reduced from n=90 to n=60 golimumab-treated participants as 60 participants will provide sufficient safety, efficacy, and PK data.

The changes made to the clinical protocol CNTO148UCO3003 as part of Protocol Amendment 5 are listed below, including the rationale of each change and a list of all applicable sections. Changes made in previous protocol amendments are listed in Section 10.20 Appendix 20: Protocol Amendment History.

Section Number and Name	Description of Change	Brief Rationale
1.1 Synopsis NUMBER OF PARTICIPANTS; 4.1 Overall Design	**Upon implementation of Amendment 5, no new participants will be enrolled.** Approximately ~~100~~**70** participants will participate in this study (at least ~~90~~ **60** participants will receive golimumab, at least 10 participants will receive infliximab). Of the ~~90~~ **60** golimumab participants, at least ~~24~~ **15** will have a body weight <45 kg and at least 5 will have a body weight <30 kg.	The sample size of n=60 for golimumab-treated participants for clinical efficacy and PK data will be sufficient to obtain interpretable results based on the totality of evidence to establish the efficacy, dosing, and safety of golimumab for the treatment of pediatric UC.

Section Number and Name	Description of Change	Brief Rationale
1.1 Synopsis STATISTICAL METHODS, Sample Size Calculation; 9.3 Sample Size Determination	Sample size calculations were based on the need to have a sufficient number of participants assigned to the golimumab treatment arm to achieve the criteria defined in Section 9.2. **In addition, collecting sufficient PK data to adequately characterize the PK of golimumab in participants with UC is also considered.** A sample size of ~~90~~ **60** participants in the golimumab arm will ensure that the lower bound of the 90% CI for the pediatric golimumab remission rate is above 10.0% (ie, the upper bound of the 95% CI for the historical placebo control) as long as the observed remission rate is at least ~~16.5~~**18.3**%. The probability of observing a remission rate of ≥~~16.5~~**18.3**%, given different assumptions for the true rate of clinical remission is shown in Table II below. With ~~90~~ **60** golimumab-treated participants, the probability of observing a remission rate of ≥~~16.5~~**18.3**% ranges from ~~65~~**50**% (if the golimumab adult UC remission rate of 17.8% is assumed) to greater than 99% (if the remission rate of 42.9% from the first golimumab study in pediatric UC is assumed). It is reasonable to assume that the true remission rate in pediatric UC participants is greater than the remission rate observed in the adult UC study, as the remission rate in the first golimumab pediatric UC study was at least twice that observed in the adult UC study. Therefore, if we assume ~~only a slight increase from~~ the ~~adult UC~~ remission rate to ~~a rate of~~ **be** ~~20~~ **22.5**%, then the probability of observing a remission rate of ≥~~16.5~~**18.3**% is at least 80% (Table II). **Table II: Probability of Observing a Clinical Remission Rate of ≥~~16.5~~18.3% With Differing Assumptions for the True Remission Rate**	The reduction in sample size is justified based on the calculations for the probability of observing a clinical remission rate for the success of the primary endpoint.

<table>
<tr><th>Section Number and Name</th><th>Description of Change</th><th>Brief Rationale</th></tr>
<tr><td></td><td>
<table>
<tr><th>Clinical Remission as Assessed by the Mayo Score</th><th>Probability of Observing ≥~~16.5~~ 18.3% N=60</th></tr>
<tr><td>~~15.0%~~</td><td>~~37%~~</td></tr>
<tr><td>17.8% (observed adult remission rate; C0524T17)</td><td>50~~65~~%</td></tr>
<tr><td>20.0%</td><td>68~~82~~%</td></tr>
<tr><td>22.5%</td><td>82~~93~~%</td></tr>
<tr><td>25.0%</td><td>91~~98~~%</td></tr>
<tr><td>42.9% (observed pediatric remission rate; CNTO148UCO1001)</td><td>>99.9%</td></tr>
</table>

The precision (ie, half width of the CI) based on this sample size of ~~90~~ 60 golimumab participants is ~~6.7~~8.1% (assuming a clinical remission rate of 17.8% at Week 6) and ~~8.6~~10.5% (assuming a clinical remission rate at Week 6 of 42.9%).

Furthermore, the Fisher Information Matrix-based optimal design analysis indicates that PK data from a total of 60 participants (including 45 participants in the ≥45 kg subgroup and 15 participants in the <45 kg subgroup) would be sufficient to adequately characterize the PK of golimumab in pediatric participants with UC.</td><td></td></tr>
<tr><td>1.2 Schema</td><td>Figure 1 was updated to indicate that at least n=60 participants will be treated with golimumab</td><td>Figure updated to reflect change in sample size of golimumab-treated participants from n=90 to n=60.</td></tr>
<tr><td>1.1 Synopsis OVERALL DESIGN;
4.1 Overall Design;
10.18 Appendix 18: Usability Assessment Substudy</td><td>An attempt will be made to enroll a~~A~~Approximately ~~15~~10-20 participants ~~will be enrolled~~in the Usability Assessment Substudy at Week 58.</td><td>The reduction in sample size reflects the reduced sample size in the overall study.</td></tr>
<tr><td>1.3 Schedule of Activities, Table 3, footnote a</td><td>Approximately ~~15~~10-20 participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in an Usability Assessment Substudy at Week 58.</td><td>The reduction in sample size reflects the reduced sample size in the overall study.</td></tr>
<tr><td>10.9 Appendix 9: PFS-U and PFP-V Actual Use Data Collection</td><td>Approximately ~~the first 15~~10-20 participants from Sponsor identified sites who choose AHA will enter the Usability Assessment Substudy at</td><td>The reduction in sample size in this substudy reflects the reduced sample size in the overall study.</td></tr>
</table>

Section Number and Name	Description of Change	Brief Rationale
	Week 58 and complete an injection device Usability Questionnaire at Weeks 62 and 66 after completion of the second and third self- or caregiver administration visits.	
1.3 Schedule of Activities, Table 2	Efficacy assessments (IMPACT III, CRP, fecal calprotectin) have been removed from the Study Schedule of Activities in the study extension. Only PUCAI score will be assessed during the study extension.	Efficacy assessments were removed because efficacy data can be extrapolated from adults and to reduce participant burden.
9.4.1.4. Analyses of Study Extension	The proportion of participants in clinical remission based on the PUCAI score will be summarized over time. The change from study extension baseline in the PUCAI score~~, fecal calprotectin, CRP, and IMPACT III~~ will be summarized over time. Treatment failure and missing data rules will be detailed in the SAP.	Efficacy assessments were removed because efficacy data can be extrapolated from adults and to reduce participant burden.
1.3 Schedule of Activities, Table 2, footnote a	a. ~~All p~~Participants **who discontinue the study and are not continuing golimumab treatment after exiting the study** must return for final safety visit (ie, 16 weeks after last administration) for this study. **Participants who are planning to continue golimumab treatment after exiting the study should have all final safety visit assessments done during the last study visit while on study golimumab.**	Clarification provided that only participants who are discontinuing study and not transitioning to commercially available golimumab must return for a final safety visit.
6.7 Intervention After the End of the Study	Participants **who discontinue the study and are not transitioning to commercially available golimumab must** complete a final safety ~~check~~ visit at the study site about 8 weeks (infliximab) or 16 weeks (golimumab) after the last dose of study intervention, unless the participant has died, is lost to follow-up, **is continuing golimumab after exiting the study,** or has withdrawn consent. **Participants who are planning to continue golimumab treatment after exiting the study should have all final safety visit assessments done during the last study visit while on study golimumab**. If the participant has died, the date and cause of death will be collected and documented on the eCRF.	Clarification provided on timing of final safety visit.
1.3 Schedule of Activities, Table 2, footnote o	o. ~~Required only if participant is ≥10 years of age at Week 0~~. **Samples should be collected every 6 months**	Sample collection changed to annual frequency in Year 2 of the

Section Number and Name	Description of Change	Brief Rationale
	during Year 1 of the study extension and, starting at Week 108, annually thereafter.	study extension to reduce participant burden.
1.1 Synopsis Endpoints; 3.1 ENDPOINTS; 9.4.1.2. Major Secondary Endpoints	**8. Clinical remission at Week 54, as assessed by the Mayo score, for participants who are in clinical remission at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).** **9. Participants who were not receiving corticosteroids for at least 12 Weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).**	These endpoints were moved from Other Endpoints to Major Secondary Endpoints based on Health Authority Feedback.
9.4.1.3. Other Endpoints	~~4. Clinical remission at Week 54, as assessed by the Mayo score, for participants who are in clinical remission at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).~~ ~~13. Participants who were not receiving corticosteroids for at least 12 weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).~~	These endpoints were moved from Other Endpoints to Major Secondary Endpoints based on Health Authority Feedback.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted

Amendment 4 (16 March 2021)

Overall Rationale for the Amendment: Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab. Participants already randomized to the infliximab arm prior to Amendment 4 implementation will continue treatment and remain in the study, but no newly enrolled participants will be randomized to infliximab.

The reasons for terminating enrollment into the infliximab arm are the following: interpretable golimumab study data will be available without the infliximab arm, limited ability to interpret the infliximab data, and updated study feasibility assessments.

Corrections reflecting this change, together with other edits to improve structure and readability of the document, have been made.

Section number and Name	Description of Change	Brief Rationale
Synopsis Overall Design, Number of Participants, Statistical Methods;	**OVERALL DESIGN** This is a multicenter, randomized, open-label golimumab study in pediatric participants aged 2 to 17 years with moderately to severely active UC, defined as a baseline Mayo score of 6 through 12, inclusive, with an endoscopy subscore of ≥2.	Enrollment into the infliximab arm will be terminated due to robust totality of the golimumab data, limited utility of infliximab data, and updated study feasibility assessments.

Section number and Name	Description of Change	Brief Rationale
	Prior to Amendment 4, central randomization was implemented in this study. Participants ≥30 kg were randomized in a 3:1 ratio across intervention groups, golimumab and infliximab, respectively. Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab. In this study, the remission rate of golimumab in pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints. This study will also include a**n** ~~reference~~ infliximab arm.~~ for the purpose of determining assay sensitivity only if the success criteria are not met (versus historical placebo).~~ No formal comparisons between golimumab and infliximab will be performed. **NUMBER OF PARTICIPANTS** **Prior to Amendment 4,** ~~A~~**a**pproximately 125 participants who satisfy inclusion/exclusion criteria **were to** ~~will~~ be included in the study at sites located globally, including in North and South America, Asia, and Europe. At least 24 golimumab participants with body weight <45 kg, and at least 5 golimumab participants with body weight <30 kg will be included. In order to ensure at least 5 participants with body weight <30 kg receive golimumab, participants who weigh <30 kg ~~will~~ **were to** only be allocated to the golimumab treatment arm. The remaining 120 participants **were to** ~~will~~ be randomized in a 3:1 ratio to golimumab or infliximab, respectively. **Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.** **Approximately 100 participants will participate in this study (at least 90 participants will receive golimumab, at least 10 participants will receive infliximab). Of the 90 golimumab participants, at least 24 will have a body weight <45 kg and at least 5 will have a body weight <30 kg.** **STATISTICAL METHODS** ~~To ensure that 90 participants are treated with golimumab, at least 90 participants who are at least~~	

Section number and Name	Description of Change	Brief Rationale
1.2. Schema;	~~30 kg will be randomized into the golimumab arm, and at least 5 additional participants who are less than 30 kg will also be enrolled.~~ ~~A sample size of 30 participants for infliximab was determined sufficient to serve as a reference arm to assess assay sensitivity. With 30 infliximab-treated participants, the probability of observing a clinical remission rate at Week 6 (based on the PUCAI score) of ≥25%, given the assumed rate of 32.0% (from Remicade pediatric study [C0168T72]), is approximately 80%. Table III below provides the probability of observing a certain remission rate or higher based on the assumed true remission rate of 32.0%.~~ Table III deleted Study schema for CNTO148UCO3003 updated: Figure 1: Study Schema for CNTO148UCO3003 **(Modified in Amendment 4)** 1) Sample sizes changed Golimumab (n = **at least** 90) Infliximab (n= ~~30~~ **at least 10**) 2) "**X****" added to arrow pointing to infliximab 3) Footnote added: ****Upon implementation of Amendment 4, no new participants will be randomized to the infliximab arm.** 4) ~~Reference arm: Comparison to infliximab pediatric data (assay sensitivity); n~~**N**o formal comparison to golimumab	
2. Introduction;	This Phase 3 study (CNTO148UCO3003) will be a multicenter, randomized, open-label golimumab study in pediatric participants aged 2 to 17 years with moderately to severely active UC. This study will assess the efficacy, safety, and pharmacokinetics (PK) of SC golimumab in pediatric participants. The remission rate of golimumab in these pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved for this indication utilizing similar populations and endpoints. Additionally, the study will include an infliximab ~~reference~~ arm**. Upon implementation of Amendment 4, no additional participants will be randomized to the infliximab arm; all newly enrolled participants will receive golimumab.** ~~for the purpose of demonstrating assay sensitivity~~	

Section number and Name	Description of Change	Brief Rationale
2.1. Study Rationale;	~~(if needed; see Section 9.4.1.4) and will also include a study extension for eligible golimumab-treated participants~~. CNTO148UCO3003 (this study): A multicenter, randomized, open-label study to assess the efficacy, safety, and PK of golimumab treatment in pediatric participants from 2 to 17 years of age with moderately to severely active UC. In this study, the remission rate on golimumab in these pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints. ~~Additionally, open-label infliximab will serve as a reference arm to demonstrate assay sensitivity if the formal comparison for the primary endpoint of this study is not successful; no formal comparisons between golimumab and infliximab will be performed.~~ A study extension is included for eligible golimumab-treated participants. In this study extension, participants ~~≥45 kg~~ will be eligible for at home administration (AHA). Participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in a Usability Assessment Substudy (Appendix 18 [Section 10.18]).	
4.1. Overall Design;	This study ~~will~~ also includ**es** a**n** ~~reference~~ infliximab arm. **Upon implementation of Amendment 4, no additional participants will be randomized to the infliximab arm; all newly enrolled participants will receive golimumab.** ~~for the purpose of determining assay sensitivity if the formal comparison for the primary endpoint of this study is not successful (for additional details, see Section 4.2.2 and Section 9.4.1.4).~~ No formal comparisons between golimumab and infliximab will be performed. **Prior to Amendment 4,** ~~A~~**a**pproximately 125 participants who satisfy inclusion/exclusion criteria ~~will~~ **were to** be included in the study at sites located globally, including in North and South America, Asia, and Europe. At least 24 golimumab participants with body weight <45 kg, and at least 5 golimumab participants with body weight <30 kg will be included. In order to ensure that at least 5 participants <30 kg ~~will~~ receive golimumab, participants who weigh <30 kg ~~will~~ **were to** only be allocated to the golimumab treatment arm. The remaining	

Section number and Name	Description of Change	Brief Rationale
4.2.2. Infliximab;	120 participants ~~will~~ **were to** be randomized in a 3:1 ratio to golimumab or infliximab**, respectively.** **Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.** **Approximately 100 participants will participate in this study (at least 90 participants will receive golimumab, at least 10 participants will receive infliximab). Of the 90 golimumab participants, at least 24 will have a body weight <45 kg and at least 5 will have a body weight <30 kg.** Short-term Phase (Weeks 0 to 6) **Prior to Protocol Amendment 4, the randomization scheme below was followed.** At Week 0, participants ≥30 kg w**ere**~~ill be~~ randomized 3:1 to either Group 1 or Group 2. All participants <30 kg w**ere**~~ill be~~ placed in Group 1. Group 1 - golimumab SC at Weeks 0 and 2 • Participants with body weight ≥45 kg will receive fixed induction doses of 200 mg at Week 0 and 100 mg at Week 2. • Participants with body weight <45 kg will receive body-surface area (BSA)-adjusted induction doses of 120 mg/m^2 (up to a maximum of 200 mg) at Week 0 and 60 mg/m^2 (up to a maximum of 100 mg) at Week 2. Group 2 - Infliximab 5 mg/kg IV at Weeks 0 and 2 (participants ≥30 kg only) **Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.** In response to a request from health authorities, an infliximab reference arm **was**~~is~~ included in this proposed study to assess assay sensitivity (primarily relying on PUCAI and partial Mayo scores) in comparison to historical data from the infliximab C0168T72 pediatric UC study. **Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab, and assay sensitivity will not be assessed. This amendment to the infliximab arm was discussed with health authorities and it was accepted that enrollment into the infliximab arm could be stopped.** ~~The determination of assay~~	

Section number and Name	Description of Change	Brief Rationale
4.3.1. Randomization;	~~sensitivity will only be explored if the primary analysis of this study is not successful. Assay sensitivity refers to the ability of a clinical study to detect the efficacy of a study intervention. In this Phase 3 study, assay sensitivity will be demonstrated by showing that the efficacy for the infliximab arm is similar to the efficacy shown in a past study of infliximab in the same participant population (C0168T72), thereby demonstrating that the current study has the ability to detect efficacy. Details on how assay sensitivity will be determined are presented in Section 9.4.1.4 and will be included in the Statistical Analysis Plan (SAP). Side-by-side summaries of the infliximab data from this study and the infliximab data from the prior pediatric UC infliximab study (C0168T72) will be provided regardless of the outcome of the primary analysis for this study. No formal comparisons of infliximab to golimumab will be performed.~~ **Prior to Amendment 4, c**~~C~~entral randomization w**as** ~~ill~~ **to** be implemented in this study. Participants ≥30 kg w**ere** ~~ill be~~ randomized in a 3:1 ratio across intervention groups, golimumab and infliximab, respectively. Randomization w**as to** ~~ill~~ be used to minimize bias in the assignment of participants to intervention groups and to increase the likelihood that known and unknown participant attributes (eg, demographic and baseline characteristics) are evenly balanced across intervention groups. Participants <30 kg **were not to** ~~ill not~~ be randomized and offered only golimumab. This **was implemented**~~is~~ to ensure that the Sponsor enroll**ed**~~s~~ at least 5 participants who weigh <30 kg and ~~will~~ receive**d** golimumab as this is a rare subpopulation. **Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.** *Procedures for Randomization and Stratification* **Prior to implementation of Amendment 4, p**~~P~~articipants weighing ≥30 kg **were to**~~ill~~ be randomly assigned to 1 of 2 intervention groups based on a computer-generated randomization schedule prepared before the study by or under the supervision of the sponsor. Participants **were to**~~ill~~ be randomized in a 3:1 ratio to golimumab or infliximab. Based on this randomization 6.3. Measures to Minimize Bias: Randomization and Blinding;	

Section number and Name	Description of Change	Brief Rationale
9.3. Sample Size Determination; 9.4.1. Efficacy Analyses;	code, study intervention w**as**~~ill be~~ assigned and administered to each participant. Permuted block randomization w**as**~~ill be~~ used. The interactive web response system (IWRS) ~~will~~ assign**ed** a unique treatment code, which ~~will~~ dictate**d** the treatment assignment and matching study intervention kit for the participant. The requestor ~~must~~ use**d** his or her own user identification and personal identification number when contacting the IWRS and **gave** ~~will then give~~ the relevant participant details to uniquely identify the participant. Participants <30 kg w**ere not to** ~~ill not~~ be randomized and offered only golimumab. This ~~is to~~ ensure**d** that at least 5 participants who weigh**ed** <30 kg ~~will~~ receive**d** golimumab treatment. **Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.** ~~To ensure that 90 participants are treated with golimumab, at least 90 participants who are at least 30 kg will be randomized into the golimumab arm, and at least 5 additional participants who are less than 30 kg will also be enrolled.~~ **Upon implementation of Amendment 4, no additional participants will be randomized to infliximab; all newly enrolled participants will receive golimumab.** ~~A sample size of 30 participants for infliximab was determined sufficient to serve as a reference arm in demonstrating assay sensitivity. With 30 infliximab-treated participants, the probability of observing a clinical remission rate at Week 6 based on the PUCAI score of ≥25%, given the assumed rate of 32.0% (from Remicade pediatric UC study [C0168T72]), is approximately 80%. Table 7 provides the probability of observing a certain remission rate or higher based on the assumed true remission rate of 32.0%.~~ Deleted Table 7. A formal comparison is planned for the primary endpoint. Summary statistics will be provided for all efficacy endpoints **for golimumab and infliximab**. Unless otherwise specified, all endpoints that involve the Mayo endoscopy subscore will be based on the subscore assigned by the local endoscopists.	

Section number and Name	Description of Change	Brief Rationale
9.4.1.4. Analyses to Assess for Assay Sensitivity	~~In addition, as a response to a request from health authorities, an infliximab reference arm is included in this study to assess assay sensitivity. The determination of assay sensitivity will only be explored if the primary analysis of this study is not successful.~~ No comparisons of infliximab to golimumab will be performed. ~~Side-by-side summaries of the infliximab data from this study and the infliximab data from the prior pediatric UC infliximab study (C0168T72) will be provided regardless of the outcome of the primary analysis for this study.~~ **Upon implementation of Amendment 4, participants will not be randomized to the infliximab arm. However, summary statistics will still be provided for the infliximab group.** Section 9.4.1.4 was deleted, and cascading sections were renumbered**.** ~~The determination of assay sensitivity will only be explored if the primary analysis of this study is not successful.~~ ~~To demonstrate assay sensitivity in this trial, efficacy measures based on the PUCAI score and partial Mayo score will be examined for all participants who received infliximab during the short-term phase, for side-by-side evaluation with the prior pediatric UC infliximab study (C0168T72). No formal testing will be performed.~~ ~~Summaries for the following endpoints will be provided:~~ ~~Clinical remission at Week 6 as assessed by the PUCAI score~~ ~~Change from baseline in the PUCAI and the Partial Mayo score at Week 6~~ ~~Details will be provided in the SAP.~~	

Section number and Name	Description of Change	Brief Rationale
Synopsis Intervention Groups and Duration;	**Infliximab** **After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have the Week 54 or Early Termination visit.** Finally, while dose escalation should be based on clinical criteria as described above, investigators at their discretion may utilize infliximab serum levels to assist their decision making. This approach was chosen as it most closely mimics clinical practice in treatment of pediatric UC, allowing investigators some flexibility in dosing to treat their patients. **Also, if an investigator wants to dose-escalate using a different regimen than listed above, discuss the plan with the medical monitor.** After the Week 54 evaluations, participants receiving infliximab will be transitioned off the study to standard medical care.	Clarified study procedure to indicate that participants in the infliximab arm only require study visits on treatment days.
1.3. Schedule of Activities (SoA), Table 1, footnotes cc and dd;	Added footnote **"cc"** to "Administer IV infliximab" and Weeks 10, 18, 26, 34, 36, 42, 50 **cc. For infliximab patients only: Visits at Week 10, 18, 26, 34, 36, 42, 50 and associated study procedures are optional, and only required if investigator implements flexible dosing and is administering infliximab at these time points.** Added footnote "**dd**" to "Hematology, Chemistry" and "ANA and anti-dsDNA antibodies," Week 26 **dd. Infliximab participants who do not have a dosing visit at Week 26 should have hematology, chemistry, ANA, and anti-dsDNA antibodies performed at Week 22 visit.**	
4.1. Overall Design;	**After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have the Week 54 or Early Termination visit.**	
4.2.2. Infliximab;	Participants who experience a flare in their UC disease (defined in Section 6.5.3) after Week 6 may initiate this step-wise dose escalation at any time to the maximum of 10 mg/kg (capped at 1 gm) q4w. Participants who dose-escalate in response to a UC flare will be reassessed after 2 administrations at the final new higher dose.	

Section number and Name	Description of Change	Brief Rationale
6.1. Study Interventions Administered	Participants in partial Mayo response (ie, a decrease from flare baseline of ≥2 in the partial Mayo score) will continue receiving open-label infliximab through Week 46 at the escalated dosage. Participants who have not achieved a partial Mayo response will be discontinued from study intervention administration and should return for a final safety visit at least 8 weeks after their last infliximab administration. **After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have Week 54 or Early Termination visit.** Importantly, while escalation should be based on clinical criteria as described above, investigators, may utilize infliximab serum levels to assist their decision making in this flexible dosing approach. Additionally, a step-wise flexible dose escalation approach (to a maximum dose of 10 mg/kg [capped at 1 gm] at an interval of q4w) will be permitted in the infliximab arm, at the investigator's discretion, for those participants not in clinical response at Week 6 (defined by the Mayo score), or participants who were in response at Week 6 but have a worsening of their UC signs and symptoms during the study period. This approach was chosen as it most closely mimics clinical practice in treatment of pediatric UC, allowing investigators some flexibility in dosing to treat their patients. **Also, if an investigator wants to dose-escalate using a different regimen than listed above, discuss the plan with the medical monitor.** After the Week 54 efficacy and safety evaluations, participants receiving infliximab will be transitioned to standard medical care. At the investigator's discretion a separate blood sample may be obtained and submitted to the central laboratory to evaluate infliximab dose levels and anti-infliximab antibodies (at a maximum of 2 timepoints at Week 6 or later) to inform dose escalations. Infliximab will be supplied in a 20 mL disposable glass vial. Infliximab will be administered as an IV infusion by qualified study site personnel and the details of each administration will be recorded in the source notes and in the eCRF (including date, start and stop times of the IV infusion, and volume infused).	

Section number and Name	Description of Change	Brief Rationale
	After the Week 8 visit and before the Week 54 visit, participants in the infliximab arm will only require study visits on treatment days. All other nontreatment visits during this time period will be optional. All participants must have Week 54 or Early Termination visit.	
Synopsis Objectives, Overall Design; 1.3. Schedule of Activities (SoA), Table 2, footnote l;	*Additional Objective (Usability Assessment Substudy)* To evaluate the potential for at home use of golimumab in the participant population ~~≥45kg~~ during the Usability Assessment Substudy. **OVERALL DESIGN** Beginning at Week 58, participants who are eligible to continue receiving golimumab in the study extension will be offered the option for self-administration (at least 12 years old ~~and body weight ≥45 kg~~) or caregiver administration (any age ~~but body weight ≥45 kg~~). **At home administration (AHA)** ~~This~~ is optional; if a pediatric participant or caregiver elects against self- or caregiver administration, the health care professional will continue to administer injections in this study. At select sites, participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in a Usability Assessment Substudy. Approximately 15-20 participants will be enrolled in the Usability Assessment Substudy at Week 58. The objective of the Substudy is to provide supportive data that the **P**~~p~~refilled **S**~~s~~yringe with UltraSafe **(PFS-U) and Prefilled Pen (PFP-V)** as designed, together with the appropriate training and written Instructions for Use, ~~is~~**are** suitable for AHA by pediatric participants or their caregivers. l. At Week 58, all participants ~~who are ≥12 years of age and are ≥45 kg~~ are eligible for AHA~~s~~ of study intervention. Participants who are <12 years of age ~~but are ≥45 kg~~ are eligible for AHA~~s~~ of study intervention by parent(s)/caregivers**; participants**	Updates made to include at home administration for all participants during the study extension.

Section number and Name	Description of Change	Brief Rationale
	>12 years of age are eligible for AHA by self or parent(s)/caregivers.	
1.3. Schedule of Activities (SoA), Table 3;	Completion of the ~~Prefilled Syringe~~ Injection **Device** Assessment Questionnaire after completion of the second and third self- or caregiver administration visits by Substudy participants (Appendix 11 [Section 10.11])	
2.1. Study Rationale;	CNTO148UCO3003 (this study): A multicenter, randomized, open-label study to assess the efficacy, safety, and PK of golimumab treatment in pediatric participants from 2 to 17 years of age with moderately to severely active UC. In this study, the remission rate on golimumab in these pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints. ~~Additionally, open-label infliximab will serve as a reference arm to demonstrate assay sensitivity if the formal comparison for the primary endpoint of this study is not successful; no formal comparisons between golimumab and infliximab will be performed.~~ A study extension is included for eligible golimumab-treated participants. In this study extension, participants ~~≥45 kg~~ will be eligible for at home administration (AHA). Participants entering the study extension who elect to administer the study intervention at home will have the option to be enrolled in a Usability Assessment Substudy (Appendix 18 [Section 10.18]).	
3. Objectives and Endpoints;	**Additional Objective (Usability Assessment Substudy)** To evaluate the potential for at home use of golimumab in the participant population ~~≥45kg~~ during the Usability Assessment Substudy.	
4.1. Overall Design;	**At Home Administration** At any time after Week 54 (Week 58 at the earliest), participants who are eligible to continue receiving golimumab in the study extension will be offered the option for self-administration (at least 12 years old ~~and body weight ≥45 kg~~) or caregiver administration (any age ~~but body weight ≥45 kg~~; Appendix 18 [Section 10.18]). This is optional; if a pediatric participant or caregiver elects against self- or caregiver administration, the health care professional (HCP) will continue to administer injections in this study.	

Section number and Name	Description of Change	Brief Rationale
6.1. Study Interventions Administered;	All participants who elect AHA of the study intervention will receive a face-to-face training from study site staff on the use of the **P~~p~~refilled **S~~s~~yringe with UltraSafe (PFS-U) **or the Prefilled Pen (PFP-V)**. Training for AHA will occur over 3 q4w administration visits beginning as early as Week 58. Participants will complete a training administration at the first visit, using the PFS**-U or the PFP-V** device at the clinic under the observation/supervision of site staff. Site staff will complete an observer checklist (Appendix 10 [Section 10.10]). An HCP will determine whether a participant (≥12 years of age ~~and ≥45 kg~~) or their caregiver (participant may be any age ~~but must be ≥45 kg~~) can perform the injections. The 2 remaining self- or caregiver-dose administrations will be performed in the clinic by the participants or their caregivers, with site staff available for any questions, and should be performed by the person who received the appropriate training. Participants may elect at any time during the study extension to have golimumab administered by an HCP or return entirely to HCP administration of study intervention. ~~If a participant is <45 kg during a visit (ie, and requires a dose less than 100 mg), that participant will no longer qualify to receive AHA, unless the participant weight is ≥45 kg at a follow-up visit.~~ **Golimumab** In the study extension beginning at Week 58 participants ~~≥45 kg~~ will have the option of AHA of golimumab by participants and/or their caregivers after being properly trained. **At Home Administration** Beginning at Week 58, for eligible participants ~~≥45 kg~~ in the golimumab treatment arm, participants/caregivers will have the option to receive training to administer golimumab at home; the training must be documented. Training of the participants/caregivers will occur at the investigative site under the supervision of a health care professional. Participants/caregivers who are unable or unwilling to administer golimumab at home will return to the investigative site for each administration of golimumab. ~~If a participant is <45 kg during a visit, that participant will no longer qualify to receive AHA, unless the participant weight is ≥45 kg at a subsequent visit.~~	

Section number and Name	Description of Change	Brief Rationale
10.9. Appendix 9: PFS-U and PFP-V Actual Use Data Collection;	10.9. Appendix 9: ~~Prefilled Syringe with UltraSafe (~~PFS**-U~~)~~ **and PFP-V** Actual Use Data Collection **Introduction** The PFS**-U and PFP-V** Actual Use Data Collection is designed to capture and document real-life ~~PFS~~ handling and use experience data from injections administered by pediatric participants or caregivers in a home-like setting, including complaints and failures in use. The actual use data to be collected is intended as additional support of the human factors and labeling comprehension data obtained during Summative Human Factors Studies but is not itself considered a human factors study. Following the second independent self- or caregiver-administration by appropriately trained pediatric participants capable of self-administration or their caregivers, all study participants performing the injection will be asked to complete a questionnaire (provided below) regarding their experience using **either** the PFS**-U or the PFP-V**. Evaluation of the user experience after the second independent administration is considered adequate to evaluate how well participants can understand and recall the dosage instructions, and to assess for any common difficulties with injections. The Schedule of Activities (Table 2) summarizes the setup of data collection. Pediatric participants aged 12 and older~~ and who weigh at least 45 kg~~, or caregivers of participants of any age~~ who weigh at least 45 kg~~ will be offered the option for self- or caregiver administration after the Week 54 study evaluations. This is optional; if a pediatric participant or caregiver elects against self- or caregiver administration, the HCP will administer injections in this study. If a pediatric participant or caregiver does elect self- or caregiver administration, the pediatric participant or caregiver will perform a training administration no earlier than Week 58. Pediatric participants or caregivers will receive face-to-face training by study site staff on the use of the ~~PFS~~**injection device**. The training will include a review of the IFU with site staff, a demonstration with ~~the PFS~~ **a device** Trainer **(when available)** performed by the site staff, and 'hands-on' practice injections performed by the pediatric participants and/or their caregivers using the ~~PFS~~**device** Trainer. An Observer Checklist will be completed by the trainer in order to determine that the user is able to correctly administer the injection. Based on this information, the HCP will determine whether the pediatric participant, or their caregiver, is able to	

Section number and Name	Description of Change	Brief Rationale
10.10. Appendix 10: Injection Device Observer Injection Checklist; 10.11. Appendix 11: Injection Device Assessment Questionnaire;	administer the injection in a home-like setting at the site. Self- or caregiver training injections will occur in 2 subsequent study intervention administrations, the second and third self- or caregiver administration visits. Injections will be performed independently in a home-like setting in the clinic, with the IFU available for reference. Approximately the first 15-20 participants from Sponsor identified sites who choose AHA will enter the Usability Assessment Substudy at Week 58 and complete a**n injection device** ~~PFS~~ Usability Questionnaire at Weeks 62 and 66 after completion of the second and third self- or caregiver administration visits (Sections 4.1 and 6.1). Appendix 10: ~~Prefilled Syringe~~ **Injection Device** Observer Injection Checklist ~~Prefilled Syringe~~ **Injection Device** Observer Injection Checklist **Type of Injection Device: PFS-U PFP-V** Appendix 11: ~~Prefilled Syringe~~ Injection **Device** Assessment Questionnaire Added a question to the form: **Which type of injection device did you use for this injection?** Were you able to successfully inject using the **injection device (PFS-U or PFP-V)** ~~Prefilled Syringe~~? Ease of Use of the ~~Prefilled Syringe~~**Injection Device** The following questions ask about the ease of use of the **injection device (PFS-U or PFP-V)**~~Prefilled Syringe~~. How difficult or easy was it to: position the ~~Prefilled Syringe~~**injection device** at the injection-site? press the plunger on the ~~Prefilled Syringe~~**injection device** to inject the liquid? hold the ~~Prefilled Syringe~~**injection device** during the injection? Appendix 18: Usability Assessment Substudy The objective of the Substudy is to provide supportive data that the PFS**-U or PFP-V** as	

Section number and Name	Description of Change	Brief Rationale
10.18. Appendix 18: Usability Assessment Substudy	designed, together with the appropriate training and written Instructions for Use, ~~is~~**are** suitable for at home administration (AHA) by pediatric participants or their caregivers. Similar for all AHA participants, pediatric participants or their caregivers in CNTO148UCO3003 will be trained in safe AHA the first week, and their self- or caregiver administration observed over 2 subsequent q4w visits. Participants or their caregivers will receive face-to-face training by study site staff on the use of the PFS**-U or the PFP-V** at the first training visit (at the Week 58 study visit for Usability Assessment Substudy participants). Participants will perform a training administration using the PFS**-U or the PFP-V** at the clinic under the observation/supervision of site staff. Site staff will complete an Observer Checklist at the Week 58 visit. The health care professional will determine whether a pediatric participant or their caregiver can perform the injections. During the 2 subsequent q4w clinic visits, administrations will be performed in a home-like setting in the clinic by pediatric participants or caregivers and should be performed by the same person (ie, pediatric participant or caregiver) and not switched unless participants opt to return to the HCP administration. Participants or caregivers performing the injection who are enrolled in the Usability Assessment Substudy will be asked to complete a**n** ~~Prefilled Syringe~~ Injection **Device** Assessment Questionnaire (Section 10.11) regarding their experience using the PFS**-U or the PFP-V** at Weeks 62 and 66 after completion of the second and third self- or caregiver administration visits. If the injections have been performed by the caregiver, the questionnaire will be completed by the caregiver. If the self-injections have been performed by the pediatric participant, the participant will complete the questionnaire with parent or caregiver assistance, if needed. Evaluation of the user experience after the second independent self- or caregiver administration is considered adequate to evaluate how well participants can understand and recall the dosage instructions, and to assess for any common difficulties with injections. **Participant Population** This Substudy population will include pediatric participants ~~≥45 kg~~ who are enrolled in the study	

Section number and Name	Description of Change	Brief Rationale
	extension. The inclusion and exclusion criteria of the Substudy are described below. Exclusion Criteria 1. **Unable to demonstrate the ability to complete a study intervention administration by self or parent/caregiver.** ~~Participants weighing <45kg will not be eligible for AHA or this Substudy.~~ For self-administration, participants must be ≥12 years of age**.** ~~**AND** weigh ≥45 kg. However, p~~**P**articipants <12 years of age ~~but who weigh ≥45 kg may receive~~ **must have** study intervention administrations by the parents or caregiver ~~and be eligible for this Substudy~~. **Schedule** Participants in this study will follow the schedule of events as outlined in Table 3 for collection of actual use data for the PFS**-U and PFP-V** (~~Prefilled Syringe~~ Injection **Device** Assessment Questionnaire).	
Synopsis Statistical Methods;	Criteria for Success **The success of the study will ultimately be based on the totality of evidence.** The primary analysis will be based on the proportion of golimumab pediatric participants in clinical remission at Week 6 based on the Mayo score and its associated 90% confidence interval (CI). ~~The study will be considered successful and the~~ criteri**a**~~on~~ **for the primary analysis** ~~for determining that golimumab is effective in the treatment of UC in pediatric participants~~ will have been met if the lower limit of the two-sided 90% CI for the proportion of golimumab participants in clinical remission at Week 6 is >10.0% (ie, the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 derived from a meta-analysis of 7 adult UC studies including 2 adult Phase 2/3 studies of golimumab and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints). *Primary Efficacy Analysis* The primary analysis population includes all participants (including the youngest weight cohort [<30 kg]) who were treated with golimumab. The primary analysis will be based on the proportion of pediatric participants who received golimumab and who were in clinical remission at Week 6 based on the Mayo score (endoscopy subscore assigned by local endoscopist) and its associated 90% CI. ~~The~~	Clarification has been made that the success of the study will be based on the totality of evidence.

Section number and Name	Description of Change	Brief Rationale
	~~study will be considered successful and the criterion for determining that golimumab is effective in the treatment of UC in pediatric participants~~ T**he criteria for the primary analysis** will have been met if the lower limit of the two-sided 90% CI for the proportion of pediatric golimumab participants in clinical remission at Week 6 is greater than the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 (ie, >10.0%) derived from a meta-analysis of 7 adult UC studies including 2 Phase 2/3 studies of golimumab and 5 Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints.	
9.2. Criteria for Success;	**The success of the study will ultimately be based on the totality of evidence.** The primary analysis will be based on the proportion of golimumab pediatric participants in clinical remission at Week 6 based on the Mayo score and its associated 90% CI. The ~~study will be considered successful and the~~ criteri**a**~~on~~ for **the primary analysis** ~~determining that golimumab is effective in the treatment of UC in pediatric participants~~ will have been met if the lower limit of the two-sided 90% CI for the proportion of golimumab participants in clinical remission at Week 6 is >10.0% (ie, the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 derived from a meta-analysis of 7 adult UC studies including 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints).	
9.4.1.1. Primary Endpoint	The primary analysis population includes all participants (including the youngest weight cohort [<30 kg]) who were treated with golimumab. **The success of the study will ultimately be based on the totality of evidence.** The primary analysis will be based on the proportion of pediatric participants who received golimumab and who were in clinical remission at Week 6 based on the Mayo score (endoscopy subscore assigned by local endoscopist) and its associated 90% CI. ~~The study will be considered successful and t~~**T**he criteri**a**~~on~~ for **the primary analysis** ~~determining that golimumab is effective in the treatment of UC in pediatric participants~~ will have been met if the lower limit of the two-sided 90% CI for the proportion of pediatric golimumab participants in clinical remission at Week 6 is greater than the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 (ie, >10.0%) derived from a meta-analysis	

Section number and Name	Description of Change	Brief Rationale
	of 7 adult UC studies (2 adult Phase 2/3 UC studies of golimumab and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints).	
1.3. Schedule of Activities (SoA), Table 1, TB test row and footnotes i and j; 1.3. Schedule of Activities (SoA), Table 2, footnote g; 5.1. Inclusion Criteria, Criterion #17; 5.2. Exclusion Criteria, Criterion #44; 7.1. Discontinuation of Study Intervention, #11;	QuantiFERON®-TB **or T-Spot®** test[i] i. A tuberculin skin test is required if the QuantiFERON-TB **or T-Spot** test is not approved/registered in that country, OR the tuberculin skin test is mandated by local health authorities. j. Chest radiograph should be obtained during the screening period unless one was obtained within 6 months before screening and the findings recorded in the study source documents. Chest radiographs should be reviewed to assess for potential undiagnosed pulmonary pathologies that may include manifestations of IBD, malignancies, and prior or current infection (eg, latent TB). Chest radiographs must be obtained in all cases when the QuantiFERON-TB **or T-Spot** test and/or the tuberculin skin test for TB is positive or repeatedly indeterminate. g. See Section 8.3.6 for TB evaluations. If TB is suspected at any time, a chest x-ray and QuantiFERON-TB **or T-Spot** test**,** or ~~TST~~ **tuberculin skin test** should be performed. During the screening period have a negative QuantiFERON®-TB test **or T-Spot® test** result. Within 1 month, prior to the first study intervention administration, a negative tuberculin skin test is additionally required if the QuantiFERON-TB test **or T-Spot test** is not approved/registered in that country or the tuberculin skin test (Appendix 3 [Section 10.3]) is mandated by local health authorities. **The results of the T-Spot test will be acceptable in place of the QuantiFERON-TB test. If the QuantiFERON-TB or T-Spot test cannot be obtained, the tuberculin skin test can be performed instead after discussion with the medical monitor.** Have persistently indeterminate (indeterminate on repeat sampling) QuantiFERON-TB **or T-Spot** test results. Indeterminate results should be handled as outlined in Section 8.3.6. A participant undergoing evaluation has a chest radiograph with evidence of current active TB and/or a positive QuantiFERON-TB **or T-Spot** test result (and/or a positive tuberculin skin test result in countries in which the QuantiFERON-TB **or T-Spot** test is not approved/registered or the	Clarifications regarding the use of the T-Spot test have been made.

Section number and Name	Description of Change	Brief Rationale
8.3.6.1. Initial Tuberculosis Evaluation;	tuberculin skin test is mandated by local health authorities), unless active TB can be ruled out and appropriate treatment for latent TB can be initiated prior to the next study intervention administration and continued to completion (see also Section 8.3.6, and Appendix 3 [Section 10.3]). Indeterminate QuantiFERON-TB test **or T-Spot test** results should be handled as in Section 8.3.6. A participant whose first QuantiFERON-TB test result **or T-Spot test result** is indeterminate should have the test repeated. In the event that the second QuantiFERON-TB **or T-Spot** test result is also indeterminate, the participant should be excluded from the study. Participants with a negative QuantiFERON-TB **or T-Spot** test result (and/or a negative tuberculin skin test result in countries in which the QuantiFERON-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities) are eligible to continue with prerandomization procedures. Participants with a newly identified positive QuantiFERON-TB **or T-Spot** ~~(~~or tuberculin skin~~)~~ test result must be excluded from the study (see Appendix 3 [Section 10.3]). **If the QuantiFERON-TB or T-Spot cannot be obtained, the tuberculin skin test can be performed instead after discussion with the medical monitor. The tuberculin skin test will be required in addition to the QuantiFERON-TB or T-Spot in countries where QuantiFERON-TB or T-Spot is not registered/approved or if the tuberculin skin test is mandated by local health authorities.** Investigators have the option to use ~~both~~ **2 TB screening tests (selecting from** the QuantiFERON-TB test**, the T-Spot test,** and the tuberculin skin test**)** to screen for latent TB if they believe, based on their judgment, that the use of ~~both~~ **2** tests is clinically indicated in order to evaluate a participant who has high risk of having latent TB. If **a single test** ~~either the QuantiFERON-TB test or the tuberculin skin test~~ is positive, the participant is considered to have latent TB infection for the purposes of eligibility for this study and must be excluded from the study. A participant whose first QuantiFERON-TB **or T-Spot or tuberculin skin** test result is indeterminate should have the test repeated. In the event that the second QuantiFERON-TB **or T-Spot or tuberculin skin** test result is also	

Section number and Name	Description of Change	Brief Rationale
8.3.6.2. Ongoing Tuberculosis Evaluation	indeterminate, the participant should be excluded from the study. In select circumstances as approved by the Sponsor, a local laboratory may be used to perform the QuantiFERON-TB **or T-Spot** test. Participants who experience close contact with an individual with active TB during the conduct of the study must have a chest radiograph, a repeat QuantiFERON-TB **or T-Spot** test, a repeat tuberculin skin test in countries in which the QuantiFERON-TB **or T-Spot** test is not approved/registered or the tuberculin skin test is mandated by local health authorities, and if possible, referral to a physician specializing in TB to determine the participant's risk of developing active TB and whether treatment for latent TB is warranted. If the QuantiFERON-TB **or T-Spot** test result is indeterminate, the test should be repeated. In the event that the second QuantiFERON-TB **or T-Spot** test result is also indeterminate, the participant **must immediately discontinue further administration of study intervention and** ~~should be discussed with the Sponsor. Participants should~~ be encouraged to return for all subsequent scheduled study visits according to the protocol.	
1.3. Schedule of Activities (SoA), Table 1, immunization screening row and footnote l; 5.1. Inclusion Criteria, Criterion #19	Screening for **up-to-date immunizations per local guidelines**~~acceptable evidence of immunity to measles, mumps, rubella, and varicella~~[l] l. **Refer to local immunization guidelines for immunosuppressed participants prior to Week 0.**~~Titers for measles and varicella only required if adequate documentation of complete vaccination schedule or healthcare provider verification of previous infection is unavailable.~~ **Participants must be up to date with all immunizations (ie, measles, mumps, rubella, and varicella) in agreement with current local immunization guidelines for immunosuppressed participants before Week 0.** ~~Participants must have acceptable evidence of immunity to measles, mumps, rubella, and varicella, which includes any one of the following:~~ ~~a. Healthcare provider documentation of age-appropriate vaccination for varicella* and measles, mumps, and rubella that includes both doses of each vaccine;~~ ~~OR~~	Varicella and measles titers are no longer required in the absence of documented infection or vaccination for the following reasons: 1) the serology titers are not reliable predictors of protective immunity especially in vaccinated individuals; 2) there is wide variability among laboratory procedures, results, and interpretation of antibody levels across the literature; 3) follows current practice of bringing patients up to date with all vaccinations prior to initiating anti-TNF therapy; and 4) accurately reflects golimumab and infliximab product label vaccination language. Participants will be required to be up to date with all immunizations per local immunization guidelines for immunocompromised participants.

Section number and Name	Description of Change	Brief Rationale
	~~b. Documentation of past varicella and measles infection by a healthcare provider;~~ ~~OR~~ ~~c. In the absence of (a) or (b) above, must have positive protective antibody titers to varicella and measles prior to the first administration of study intervention. If antibody titers are checked for any reason and are negative, the participant must be excluded from the study until they have been re-vaccinated and can demonstrate positive antibody titers.~~ ~~*If required or recommended in the country in which the participant is receiving study treatments.~~	
1.3. Schedule of Activities (SoA), Table 1, footnote r	r. ~~Optional at the discretion of the investigator.~~ Only if decision is made to escalate the dose of infliximab to 10 mg/kg q8w, and only if participant was given 5 mg/kg Week 6, may the participant receive a dose at Week 8 of infliximab at 5 mg/kg, with subsequent doses of 10 mg/kg starting at Week 14. Infliximab infusions are capped at 1 gm maximum per administration. Additional details are available in Section 4, Study Design. If participant receives infliximab infusion at Week 8, they will need a urine pregnancy test in addition to the other assessments collected from all study participants.	Clarification regarding the administration of infliximab has been made.
1.3. Schedule of Activities (SoA), Table 2; 6.5. Concomitant Therapy; 8.2.4. Concomitant Medication Review	Every **6 months** ~~12 weeks~~ starting Week 66 for all participants Added footnote k to Table 2 and changed cascading footnotes accordingly: **k. After Week 54, only include concomitant medications in eCRF that are associated with AE and SAEs (ie, used to treat event or suspected in causing event) and/or with the treatment of UC.** **All concomitant medications will be recorded in the eCRF through Week 54. After Week 54, only concomitant medications associated with AEs and SAEs (ie, used to treat event or suspected in causing event) and/or with the treatment of UC will be recorded in the eCRF.** **All concomitant medications will be recorded in the eCRF through Week 54. After Week 54, only concomitant medications associated with AEs and SAEs (ie, used to treat event or suspected in causing event) and/or with the treatment of UC will be recorded in the eCRF.**	Minor edits made to streamline the study extension.

Section number and Name	Description of Change	Brief Rationale
5. Study Population; 5.4. Screen Failures 10.12 Appendix 12: Regulatory, Ethical, and Study Oversight Considerations	Screening for eligible participants ~~will~~ **should** be performed within 6 weeks before administration of the study intervention. Refer to Section 5.4 Screen Failures for conditions under which the repeat of any screening procedures is allowed. On a case-by-case basis, **and after consultation with the medical monitor,** ~~retesting~~ procedures may exceed the 6-week window and will not be considered protocol deviations. ~~Completion of s~~**S**creening and ~~randomization~~ **enrollment** procedures **should typically be completed** within the specified screening window of within 6 weeks~~.~~**; extensions can be discussed with the medical monitor.** Rescreening Participants who do not meet the criteria for participation in this study (screen failure) may be rescreened 1 time. **In rare cases, a participant may be screened a third time after discussion with the medical monitor.** Participants who are rescreened will be assigned a new participant number, undergo the informed consent/assent process, and then start a new screening phase. On a case-by-case basis, **after consultation with the medical monitor,** rescreening procedures may exceed the 6-week window and will not be considered protocol deviations. INFORMED CONSENT PROCESS A participant may be rescreened 1 time. Participants who are rescreened are required to sign a new ICF. **In rare cases, a participant may be screened a third time after discussion with the medical monitor.**	Clarification added to indicate that extensions to the typical screening window can be discussed with the medical monitor.
5.1. Inclusion Criteria Criterion #12; Criterion #20	Before **enrollment** ~~randomization~~, a girl must be either: a. Not of childbearing potential defined as: 1) Premenarchal a) A premenarchal state is one in which menarche has not yet occurred. 2) Permanently sterile a) Permanent sterilization methods include hysterectomy, bilateral salpingectomy, bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy. For participants who have not completed the recommended vaccination schedule for varicella,	Clarifications of inclusion criteria have been made.

Section number and Name	Description of Change	Brief Rationale
	measles, mumps, and rubella, and the subsequent vaccination falls within the next 4 years, an accelerated vaccination schedule must be completed prior to study enrollment, **per local or professional guidelines.** ~~if available and required or strongly recommended for the country.~~ If live, attenuated viral vaccine is utilized, it is necessary for **at least 4 weeks (or longer as indicated on the package insert of the relevant vaccine)** ~~8 weeks~~ to elapse between the vaccination and receipt of study intervention. **Once study intervention has been initiated, at least a 16-week period must elapse after last dose before a live vaccine is utilized. For additional restrictions regarding Bacille Calmette-Guerin (BCG) vaccination, see Exclusion Criterion 41 in Section 5.2.**	
5.2. Exclusion Criteria Criterion #8; Criterion #34, added note to exclusion criterion; Criterion #46; Criterion #47	Received an investigational vaccine or used an invasive investigational medical device within 3 months before the planned first dose of study intervention or is currently enrolled in an investigational study. **Receipt of an investigational vaccine for COVID-19 is not an automatic exclusion criterion, discuss with the medical monitor.** Has a stool culture or other examination positive for an enteric pathogen, including *Clostridium difficile* toxin in the previous 4 months, unless a repeat examination is negative and there are no signs of ongoing infection with that pathogen. **Note: For participants who have a positive *C. difficile* test during the screening period, participant may be treated and retested during the screening period (extensions of the screening period can be discussed with the medical monitor). If repeat test is negative and there are no signs of ongoing infection, participant can be considered for enrollment. If repeat *C. difficile* test remains positive during the screening period, the participant must be a screen failure and may be treated and rescreened.** Have had 2 or more serious infections requiring hospitalization or treatment with parenteral antibiotics within the past year. Less serious infections (eg, acute upper respiratory tract infection, simple urinary tract infection) need not be considered exclusionary at the discretion of the investigator. **Prior parenteral antibiotics administered for the indication of UC are acceptable and not a reason for exclusion.** Must not have received, or are expected to receive, any live ~~virus or bacterial~~ vaccination within	Clarifications of exclusion criteria have been made.

Section number and Name	Description of Change	Brief Rationale
	8 weeks (or longer as indicated in the package insert of the relevant vaccine) prior to the first administration of study intervention, during the study, or within 16 weeks (more than 5.5 half-lives of SC golimumab) after the last administration of study intervention. **Receipt of a live SARS-CoV-2 vaccine (against the virus that causes COVID-19) is *not* automatically an exclusion criterion and must be discussed with the medical monitor.**	
5.2. Exclusion Criteria New exclusion criterion added (Criterion #61)	**Infections or predisposition to infections** **During the 6 weeks prior to baseline, have had ANY of:** **a. Confirmed SARS-CoV-2 (COVID-19) infection (test positive);** **OR** **b. Suspected SARS-CoV-2 infection (clinical features without documented test results);** **OR** **c. Close contact with a person with known or suspected SARS-CoV-2 infection.** **•Exception: may be included with a documented negative result for a validated SARS-CoV-2 test:** **1) obtained at least 2 weeks after conditions (a), (b), (c) above (timed from resolution of key clinical features if present, eg, fever, cough, dyspnea);** **AND** **2) with absence of ALL conditions (a), (b), (c) above during the period between the negative test result and the baseline study visit.** **NOTES on COVID-19-related exclusion:** **•The field of COVID-19-related testing (for presence of, and immunity to, the SARS-CoV-2 virus) is rapidly evolving. Additional testing may be performed as part of screening and/or during the study, if deemed necessary by the investigator and in accordance with current regulations/guidance from authorities/standards of care.**	Additional exclusion criterion regarding SARS-CoV-2 has been added.

Section number and Name	Description of Change	Brief Rationale
	•Precaution: for those who may carry a higher risk for severe COVID-19 illness, follow guidance from local health authorities when weighing the potential benefits and risks of enrolling in the study, and during participation in the study.	
8. Study Assessments and Procedures	~~Details about who will perform and/or complete the assessments/data and the order of completion are provided in Section 8.1.~~ Information about how and when data are filed, stored, and transmitted to or from the study site is provided in the electronic patient-reported outcome (ePRO) electronic tablet device and User Manual.	Sentence deleted to align with Section 8.1.
10.19. Appendix 19: Guidance on Study Conduct during the COVID-19 Pandemic	An appendix for guidance on study conduct during the Coronavirus Disease of 2019 (COVID-19) pandemic was added.	COVID-19-related guidance on study conduct during the pandemic was added.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted.

Amendment 3 (8 Jul 2019)

Overall Rationale for the Amendment: To incorporate the following changes: 1) changed the allowable timeframe for a chest radiograph prior to screening for assessment of undiagnosed medical conditions in the exclusion criteria and clarified the rationale for having a chest radiograph; and 2) clarified permitted allowable nutrition in the inclusion criteria for participants with UC who may enroll in the study.

Section number and Name	Description of Change	Brief Rationale
Section 1.3 Schedule of Activities Table 1	Serum pregnancy test added back in to Schedule of Activities (SoA) at screening.	Serum pregnancy test was deleted in error.
Section 1.3 Schedule of Activities Table 1, footnote j	Revised SoA footnote text to read: "Chest radiograph should be obtained **during the screening period unless one was obtained** within **6 months** before screening **and the findings recorded in the study source documents. Chest radiographs should be reviewed** to assess for potential undiagnosed pulmonary pathologies that may include manifestations of IBD, malignancies, and prior or current infection (eg, latent TB). Chest radiographs must be obtained in all cases when the QuantiFERON-TB test and/or the tuberculin skin test for TB is positive or repeatedly indeterminate."	Clarified the chest radiograph requirements at screening.
Section 1.3 Schedule of Activities Table 1, footnote n	Revised SoA footnote to read: "HIV testing in study participants who ~~weigh less than 30 kg~~ **are less than 6 years of age** is not universally required. It is required in those study participants who ~~weigh <30 kg~~ **are less than 6 years of age** and the birth history is unknown (ie adopted) or has	Changed testing for HIV from a weight-based to an age-based requirement depending on birth history, exposure risks, or at discretion of the study investigator.

Section number and Name	Description of Change	Brief Rationale
	exposure risks (parents with HIV or with risk factors) or at the discretion of the study investigator. In subjects who ~~weigh <30 kg~~ **are less than 6 years of age** where testing would be required, if there is a record of a negative HIV test at birth this is acceptable at the discretion of the study physician as long as it is entered into the study record."	
Section 5.1. Inclusion criterion #6	Revised text to read: "Criterion modified per Amendment 3. 6.1. Prior or current medication for UC must include at least 1 of the following (Appendix 2 [Section 10.2]): a. Current treatment with at least 1 of the following therapies: oral ~~or intravenous~~ corticosteroids, or the immunomodulators 6-MP, MTX, or AZA."	Deleted intravenous corticosteroids from current treatment for UC.
Section 5.1 Inclusion criterion #7	Revised text to read: "Criterion modified per Amendment 3. 7.1. Must meet concomitant medication dose stability prior to the first administration of study intervention: a. Corticosteroids: 1) If receiving oral ~~or IV~~ corticosteroids, the dose (in prednisone equivalents) must have been stable for at least 2 weeks prior to Week 0."	Deleted intravenous corticosteroids from concomitant medication dose stability prior to the first administration of study intervention.
Section 5.1. Inclusion criterion #8	Deleted the following text: ~~If receiving parenteral nutrition, must have discontinued 2 weeks prior to the first administration of study intervention at Week 0.~~ Revised text to read: "Criterion modified per Amendment 3. 8.1. If receiving enteral nutrition, must have been on a stable regimen for at least 2 weeks prior to the first administration of study intervention at Week 0. **Participants who receive parenteral nutrition are not permitted to enroll in the trial.**"	Changed for allowable nutrition to specify that only enteral nutrition is permitted. Participants with UC who receive parenteral nutrition are no longer permitted to enroll in the trial.
Section 5.1 Inclusion criterion #13	Added the following text: "Criterion modified per Amendment 3. 13.1. Boys must agree not to donate sperm for the purpose of reproduction during the study and for a minimum 6 months after receiving the	Requirements for use of contraception by a boy have been added and specified.

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	last dose of study intervention. "**During the study and for a minimum of 6 months after receiving the last dose of study intervention, in addition to the highly effective method of contraception, a boy:** **a. Who is sexually active with a girl of childbearing potential must agree to use a barrier method of contraception (eg, condom with spermicidal foam/gel/film/cream/suppository).** **b. Who is sexually active with a girl who is pregnant must use a condom."**	
Section 5.2. Exclusion criterion #42	Deleted the following text: ~~Have a chest radiograph within 3 months prior to the first study intervention administration that shows an abnormality suggestive of a malignancy or current active infection, including TB.~~ Revised text to read: "Criterion modified per Amendment 3. 42.1. Have a chest radiograph **during screening or 6 months** prior to **screening** that shows an abnormality suggestive of **an undiagnosed pulmonary pathology that may include manifestations of IBD,** malignancy**, prior or** current active infection, including TB."	Changed the allowable timeframe for a previous chest radiograph in exclusion criterion #42 and clarified the rationale for a chest radiograph.
Section 6.5.3. Rescue Medication	Revised the text to read: "**During the long-term phase of the study, participants who meet the following criteria will be considered to be in clinical flare:** • **For study subjects who responded at Week 6-an increase of the partial Mayo score from Week 6 of at least 2 points and an absolute partial Mayo score ≥4; or an absolute partial Mayo score ≥7 points, or** • **For study subjects who did not have a Week 6 response but achieved a response at Week 14 or 22 (after additional discretionary doses of golimumab or infliximab [Section 4.1])-an increase in the partial Mayo score from Weeks 14 or 22 of at least 2 points and an absolute partial Mayo score ≥4; or an absolute partial Mayo score ≥7 points.** However, the basis for this determination should be consistent with **the criteria used in the long-term phase, namely an increase in the partial Mayo score by 2 points and an absolute partial Mayo score ≥4; or an absolute partial Mayo score of** ≥7 and based on the study participant (or	Expanded the criteria used to determine the onset of a UC flare in the study extension. Added the need for use of parenteral (IV) steroids for UC during the study as a reason for discontinuation from further study intervention administration.

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	caregiver)-reported stool frequency and degree of rectal bleeding, as well as a global assessment of UC disease activity made by a study primary- or sub-investigator." Revised last paragraph to read: "However, any participant who uses UC-prohibited medications (Section 6.5.2) or requires more than 2 courses of corticosteroids (including budesonide) **or requires parenteral (IV) steroids f**or UC during the 54-week study will be discontinued from further administration of study intervention."	
Secton 6.5.3. Rescue Medication	Added the following sentence: **"In the study extension, the determination that a subject is in clinical flare will be at the discretion of the investigator."**	Added sentence regarding clinical flare determination for study extension.
Section 7.1. Discontinuation of Study Intervention	Discontinuation of a participant's study intervention must be <u>strongly considered</u> under the following conditions: 1. Persistent inadequate response or worsening of UC: f. Revised the text to read: "**Participants in the long-term or study extension phases of the study who meet the criteria as defined Section 6.5.3 will be considered to be in clinical flare. A sigmoidoscopy (or colonoscopy) can be considered to aid clinical judgment and should be performed using study software and submitted for central review.**" Revised last paragraph to read: "If a participant discontinues study intervention for any reason before Week 6, they should return for all scheduled visits through Week **14 (**including endoscopy at Week **6**) and a final safety visit, 16 weeks after the last dose of golimumab or 8 weeks after the last dose of infliximab."	Revised to be consistent with Section 6.5.3. Clarified time points when participant needs to return for visits after discontinuation including for an endoscopy.
Section 7.1 Discontinuation of Study Intervention	Revised the following text: "3. The participant requires the addition of ~~parenteral (IV) steroids immunomodulators (ie, 6-MP, AZA, or MTX) or~~ more than 2 courses of corticosteroids (including budesonide) for UC flares during the 54-week study."	Modified the statement to exclude IV steroids and other immunomodulators.
Section 8.1.7.1. TUMMY-UC and Observer TUMMY-UC	Revised sentence text to read: "It includes 6 components similar to the PUCAI index and ranges from 0 to ~~56~~**114."**	The scoring range for the TUMMY-UC and Observer TUMMY-UC has been changed.
Section 8.2.3.	• Revised text to read: "Serology for HIV at screening: HIV testing in study participants who ~~weigh less than 30 kg is~~ **are less than 6 years of**	Changed serology for HIV from a weight-based to an age-based requirement depending on birth

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Clinical Safety Laboratory Assessments	**age** is not universally required. It is required in those study participants who ~~weigh <30 kg~~ **are less than 6 years of age** and the birth history is unknown (ie adopted) or has exposure risks (parents with HIV or with risk factors) or at the discretion of the study investigator. In subjects who ~~weigh <30 kg~~ **are less than 6 years of age** where testing would be required, if there is a record of a negative HIV test at birth this is acceptable at the discretion of the study physician as long as it is entered into the study record."	history, exposure risks, or at discretion of the study investigator.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted.

Amendment 2 (13 May 2019)

Overall Rationale for the Amendment: To incorporate the following changes: 1) expansion of the Usability Assessment Substudy to additional countries instead of US only; 2) added a major secondary endpoint and modified the order of the major secondary endpoints per FDA request; and 3) updated the blood sampling scheme to comply with allowable blood sample volumes with the EU guideline on clinical trials conducted with minors. Clarification of wording and editorial updates were made to improve readability.

Section number and Name	Description of Change	Brief Rationale
1.1 Synopsis Overall Design	Revised the following text: "In this study, the remission rate of golimumab in pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of **2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints**."	Phases of the studies that contribute to the meta-analysis were updated.
1.1 Synopsis Overall Design	Revised the following text: "**At select sites, participants** ~~from North American~~ **entering the study extension** ~~at select sites~~ who elect to administer the study intervention at home will have the option to be enrolled in an Usability Assessment Substudy."	Specification for North American sites removed to allow for possibility of participants from other countries to join the substudy.
1.1 Synopsis Number of Participants	Revised the following text: "Approximately 125 participants who satisfy the inclusion/exclusion criteria will be included in the study at sites located globally, including in North **and South** America, Asia, and Europe. In order to **ensure** at least 5 participants **with body weight <30 kg receive golimumab,** participants who weigh <30 kg will only be allocated to the golimumab treatment arm."	Included South America for global protocol. Revised sentence regarding enrollment of participants with body weight <30 kg.
1.1 Synopsis Efficacy Evaluations	Modified the following bullet: • TUMMY-UC **and Observer TUMMY-UC**	Added the terminology for "Observer" TUMMY-UC questionnaire for

Section number and Name	Description of Change	Brief Rationale
		efficacy/exploratory measurements for participants less than 8 years old.
1.1 Synopsis Endpoints *Major secondary endpoints*	Modified the following bulleted list: • **Symptomatic remission at Week 54** • **Clinical remission at Week 54 as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).** • **Clinical remission at Week 54 as assessed by the PUCAI score.** • **Clinical remission at Week 6 as assessed by the PUCAI score.** • **Clinical response at Week 6 as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).** • **Endoscopic healing at Week 6 (based on the Mayo endoscopy subscore assigned by the local endoscopist).** • **Endoscopic healing at Week 54 (based on the Mayo endoscopy subscore assigned by the local endoscopist).** Added the definition of symptomatic remission: "The definitions of the major secondary endpoints are provided below: • **Symptomatic remission: Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0."**	Added symptomatic remission and clinical remission (Mayo) at Week 54 as major secondary endpoints and revised the order and description of all major secondary endpoints to align with the SAP. Added definition for "symptomatic remission."
1.1 Synopsis STATISTICAL METHODS Statistical Hypothesis	Revised the following text: "The historical placebo control is based on a meta-analysis of 7 adult UC studies including infliximab **Phase 3 (C0168T37** and C0168T46), golimumab **Phase 2/3** (C0524T16 and C0524T17), adalimumab **Phase 3** (ULTRA 1 and ULTRA 2), and vedolizumab **Phase 3** (GEMINI 1)."	Phases of the studies that contribute to the meta-analysis were updated.
1.1 Synopsis STATISTICAL METHODS Criteria for Success	Revised the following text: "The study will be considered successful and the criterion for determining that golimumab is effective in the treatment of UC in pediatric participants will have been met if the lower limit of the two-sided 90% CI for the proportion of golimumab participants in clinical remission at Week 6 is >10.0% (ie, the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 derived from a meta-analysis of 7 adult UC **studies including 2 adult Phase 2/3 studies of golimumab and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints)."**	Phases of the studies that contribute to the meta-analysis were updated.
1.1 Synopsis STATISTICAL METHODS Sample Size Calculation *Primary Efficacy Analysis*	Revised the following text: "The study will be considered successful and the criterion for determining that golimumab is effective in the treatment of UC in pediatric participants will have been met if the lower limit of the two-sided 90% CI for the proportion of pediatric golimumab participants in clinical remission at Week 6 is greater than the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 (ie, >10.0%) derived from a meta-analysis of 7 adult UC studies **including 2 Phase 2/3 studies of golimumab and 5 Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints**."	Phases of the studies that contribute to the meta-analysis were updated.

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1.1 Synopsis STATISTICAL METHODS Sample Size Calculation *Major Secondary Efficacy Analyses*	Deleted the following 2 sentences: "~~A formal comparison is only planned for the primary endpoint. No comparisons are planned for any other efficacy endpoints.~~"	Deleted first 2 sentences of the paragraph.
1.3 Schedule of Activities Table 1, Screening/Administrative	Revised the following text, "**Confirmation of prestudy diagnostic UC biopsy results**" in list of Screening/Administrative activities.	Clarification of prestudy biopsy assessment for UC.
1.3 Schedule of Activities Table 1, Efficacy assessments, Footnote bb added	Added "**Mayo Patient Diary completed**" to list of Efficacy assessements. Added footnote "**bb: Mayo Patient Diary is completed for 7 continuous days within the 14 days prior to the screening visit. For the screening visit, the Mayo diary will be provided at screening and collected at the Week 0 visit."**	Mayo Patient Diary had been omitted in error to the SoA list of efficacy evaluations; an explanatory footnote has been added.
1.3 Schedule of Activities Table 1, Study procedures, HIV testing Footnote cc added	Added footnote for HIV testing: **"cc. HIV testing in study participants who weigh less than 30 kg is not universally required. It is required in those study participants who weigh <30 kg and the birth history is unknown (ie adopted) or has exposure risks (parents with HIV or with risk factors) or at the discretion of the study investigator. In subjects who weigh <30 kg where testing would be required, if there is a record of a negative HIV test at birth this is acceptable at the discretion of the study physician as long as it is entered into the study record."**	Added limits on testing for HIV in the smallest or youngest children.
1.3 Schedule of Activities Table 1 Footnote e	Revised the following text: "**Should be performed within 2 weeks prior to the administration of study intervention at Week 0, within 2 weeks <u>prior to</u> Week 54, and within 7 days <u>prior to</u> study intervention for Week 6. All study endoscopies (sigmoidoscopy preferred unless colonoscopy clinically indicated) must be performed with study software to permit central reads and scoring in addition to local study scoring. A colonoscopy will replace a sigmoidoscopy if screening for dysplasia is required. The Sponsor suggests that at least 48 hours must elapse between a colonoscopy with polypectomy or multiple biopsies and the study intervention administration (Week 0) visit.**"	Clarification to include "prior to" for Week 54 and Week 6.
1.3 Schedule of Activities Table 1 Footnote f	Changed footnote f to read: "**Previous assessment must be consistent with a diagnosis of UC (eg, crypt distortion, crypt abscess, goblet cell depletion, and continuous distribution).**"	Clarification of screening biopsy requirements.
1.3 Schedule of Activities Table 1 Footnote k	Removed indication for footnote k next to serum pregnancy test (footnote k is correctly listed for urine pregnancy test).	<u>Editorial correction</u>: Footnote k was indicated next to serum pregnancy sample in error.

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1.3 Schedule of Activities Table 1 Footnote n clarified with updated information	Revised the following text: "Blood sampling in participants with a body weight of 10 kg to **24 kg** must be divided between visits during the screening period. **Contact Sponsor for details of recommended sampling sequence."**	Update in blood sampling scheme to comply for allowable blood sample volumes with the EU guideline on clinical trials conducted with minors (see ref 12).
1.3 Schedule of Activities Table 1 Footnote v added for "Blood RNA"	Updated the following text: "**The RNA blood sample should not be collected at any time point for any participant who at Screening has a body weight of 10 kg to <12.3 kg, even if the weight increases to above 12.3 kg during the study. For participants who weighed more at Screening but whose body weight falls to between 10 kg to <12.3 kg, the RNA blood sample should not be collected, and blood draws are not to exceed 8.0 mL at any one visit for this weight group."**	Update in blood sampling scheme to comply for allowable blood sample volumes with the EU guideline on clinical trials conducted with minors (see ref 12).
1.3 Schedule of Activities Table 1 Footnote x	Updated the following text: "x. For additional details, refer to **Appendix 8 (Section 10.8)**."	Added updated examples of the TUMMY-UC and the Observer TUMMY-UC questionnaires in the appendix.
1.3 Schedule of Activities Table 3, Events	Revised the following text: "**Administration of golimumab** by self or caregiver; or continued administration at the site, if desired"	Clarification of study agent to be administered.
2. Introduction	Modified the following text: "The remission rate of golimumab in these pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of **2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved for this indication** utilizing similar populations and endpoints."	Phases of the studies that contribute to the meta-analysis were updated.
2.1 Study Rationale	Modified the following text: "The second study is: • CNTO148UCO3003 (this study): A multicenter, randomized, open-label study to assess the efficacy, safety, and pharmacokinetics of golimumab treatment in pediatric participants from 2 to 17 years of age with moderately to severely active UC. In this study, the remission rate on golimumab in these pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of **2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication** utilizing similar populations and endpoints."	Phases of the studies that contribute to the meta-analysis were updated.
3.1 Endpoints Major Secondary Endpoints	Modified the following bulleted list: **1. Symptomatic remission at Week 54** **2. Clinical remission at Week 54 as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).** **3. Clinical remission at Week 54 as assessed by the PUCAI score.**	Added symptomatic remission and clinical remission (Mayo) at Week 54 as major secondary endpoints and revised the order and description of all

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	4. Clinical remission at Week 6 as assessed by the PUCAI score. **5. Clinical response at Week 6 as assessed by the Mayo score (based on the Mayo endoscopy subscore assigned by the local endoscopist).** **6. Endoscopic healing at Week 6 (based on the Mayo endoscopy subscore assigned by the local endoscopist).** **7. Endoscopic healing at Week 54 (based on the Mayo endoscopy subscore assigned by the local endoscopist).** Added the definition of symptomatic remission: "The efficacy endpoint definitions are as follows: • **Symptomatic remission: Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0."**	major secondary endpoints to align with the SAP. Added definition for "symptomatic remission."
4.1 Overall Design	Revised the following text: "In this study, the remission rate on golimumab in pediatric participants will be formally compared with a historical placebo remission rate derived from a meta-analysis of **2 adult Phase 2/3 UC studies of golimumab and 5 adult Phase 3 studies of** other biologic products approved in this indication utilizing similar populations and endpoints. For additional details see Sections 4.2.1, 9.1, and 9.2." Added the following text regarding participant body weight limit: **"If a study participant's weight is not at least 10 kg at Week 0, or falls below 10 kg after Week 10, the study intervention must be withheld until their body weight is ≥10 kg. If they miss 2 consecutive doses of golimumab because of body weight below this 10 kg limit, the study participant should be withdrawn from the study."** Added the following text: "For participants receiving 5-ASAs at Week 0, the dose must remain stable through Week 54 (except for weight-based adjustments**, as treatment for a documented UC flare after Week 6, or if investigator judgment requires dose reduction or cessation because of toxicity or medical necessity (Section 6.5.3)**. For participants receiving immunomodulators at Week 0, the dose should not be increased (except for weight-based adjustments) **through Week 6**. Although immunomodulators may be discontinued or the dose reduced at any time during the study, it is preferred, at the discretion of the investigator, that they be continued at least through Week 14. **For participants receiving corticosteroids, the steroids may be tapered beginning at Week 0, although it would be preferable to delay the stopping of steroids until after the Week 6 evaluation if clinically reasonable. UC-specific medical therapies (ie, oral/rectal corticosteroids, oral/rectal 5-aminosalicylate [5-ASA] compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX])** may not be initiated **or their dose increased** at any	Phases of the studies that contribute to the meta-analysis were updated. Addressed issue of withholding study intervention from subjects whose body weight is NOT at least 10 kg. Added information regarding the use of UC-specific therapies during the study or as rescue medications.

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	time **after** Week **6** to Week **54 except for weight-based dose adjustments or unless there is a documented UC flare and loss of response that makes the subject eligible for rescue medication (Section 6.5.3). For additional details regarding UC-specific allowed concomitant therapies, see Section 6.5.1.**"	
4.2.1 Historical Placebo	Revised the following text: "The primary analysis will involve a formal statistical comparison to a historical **adult** placebo remission rate derived from a meta-analysis of ~~adult~~ **2 adult Phase 2/3 UC studies of golimumab and 5 adult Phase 3 studies of other products approved in this indication** (for additional details see 9.1 and 9.2) utilizing similar endpoints (clinical remission as assessed by the Mayo Score), populations, and methodologies for endpoint determination (clinical remission as determined by the local endoscopy)." "To ensure a robust estimate of the placebo remission rate, the Sponsor has derived a **historical adult** placebo remission rate from a meta-analysis of placebo controlled ~~2 Phase 2/3 adult UC~~ studies ~~of golimumab and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints~~ studies that met the following criteria:"	Phases of the studies that contribute to the meta-analysis were updated.
4.2.3 Biomarker Collection	Added sentence at end of section: "**The RNA blood sample should not be collected at any time point for any participant who at Screening has a body weight of 10 kg to <12.3 kg, even if the weight increases to above 12.3 kg during the study. For participants who weighed more at Screening but whose body weight falls to between 10 kg to <12.3 kg, the RNA blood sample should not be collected.**"	Update in blood sampling scheme to comply for allowable blood sample volumes with the EU guideline on clinical trials conducted with minors (see ref 12).
4.2.4 Study-Specific Ethical Design Considerations	Updated the following text: "**For each participant, his or her parent(s) (preferably both parents, if available) or legally acceptable representative(s), as required by local regulations, must give written consent (permission) according to local requirements after the nature of the study has been fully explained and before the performance of any study-related assessments. Assent must be obtained from children (minors) capable of understanding the nature of the study, typically participants 7 years of age and older, depending on the institutional policies and national/local guidelines."**	Update of text regarding how informed consent is to be obtained from pediatric participants.
4.2.4 Study-Specific Ethical Design Considerations	Revised the following text: "The total blood volume to be collected is considered to be an acceptable amount of blood to be collected over this time period from the population in this study ~~based upon the standard of the American Red Cross and EU guidelines~~. **Total blood volume to be collected in this study is in line with the allowable blood sample volumes described in the EU guideline on clinical trials conducted with minors (EU Guideline Ethical**	Updated reference to EU guideline on clinical trials conducted with minors (see ref 12).

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	considerations for clinical trials on medicinal products conducted with minors (Rev 1; 18 Sep 2017)).[12]"	
5. Study Population	Revised the following text: "On a case-by-case basis, ~~rescreening~~ **retesting** procedures may exceed the 6-week window and will not be considered protocol deviations."	Correction from "rescreening" to "retesting".
5.1 Inclusion Criteria Criterion 7b, 3)	Revised the following text: "3) If receiving MTX, 6-MP, or AZA compounds, **the participant must have been taking them for ≥12 weeks and on a stable dose for 2 weeks prior to Week 0.** If the MTX, 6-MP, or AZA have been recently discontinued, they must have been stopped for at least 2 weeks prior to Week 0."	Updated the duration that a participant must have been taking MTX, 6-MP, or AZA compounds prior to Week 0 based on expert advice for pediatric studies.
5.2 Exclusion Criteria Criterion 25	Have received vedolizumab within **12 weeks** ~~4 months (16 weeks)~~ of the first study intervention.	Changed the time period for exclusion if a participant has received vedolizumab.
5.4 Screen Failures Retesting	Modified the following text: "Retesting can occur at an unscheduled visit during the screening phase, as long as this is done within the specified screening window of within 6 weeks **(6 weeks may be exceeded on a case-by-case basis)**."	Clarified whether specified screening window can be exceeded.
6.1 Study Interventions Administered Infliximab	Second paragraph of subsection beginning "Additionally…" Added a sentence that reads: "**At the investigator's discretion a separate blood sample may be obtained and submitted to the central laboratory to evaluate infliximab dose levels and anti-infliximab antibodies (at a maximum of 2 timepoints at Week 6 or later) to inform dose escalations**."	Information omitted in error from protocol Amendment 1.
6.1 Study Interventions Administered Usability Assessment Substudy	Revised the following text: "At the ~~North American~~ **Sponsor identified** sites, the participant and/or caregiver will have the option to be enrolled in an Usability Assessment Substudy at Week 58. At Weeks 62 and 66, after self-dosing, the sponsor will collect data on their experience using PFS for administrations of golimumab. For additional details see Appendix 18 (Section 10.18)."	Specification for North American sites removed to allow for possibility of participants from other countries joining the substudy.
6.5.1 Concomitant Therapy	Added the following text: "For participants receiving 5-ASAs at Week 0, the dose must remain stable through Week 54 (except for weight-based adjustments**, as treatment of a documented UC flare after Week 6, or if investigator judgment requires dose reduction or cessation because of toxicity or medical necessity**)." Added the following text: "Immunomodulators (ie, 6-MP, AZA, or MTX) should not be initiated between Week 0 and Week **6**. For participants receiving immunomodulators at Week 0, the dose should not be increased (except for weight-based adjustments) **through Week 6."** Added the following text: "**UC-specific medical therapies (ie, oral/rectal corticosteroids, oral/rectal 5-aminosalicylate (5-ASA) compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX]) may not be initiated or their dose increased at**	Added information regarding the use of UC-specific therapies during the study or as rescue medications.

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	any time from Week 6 to Week 54 except for weight-based dose adjustments or unless there is a documented UC flare and loss of response that makes the subject eligible for rescue medication (Section 6.5.3)."	
6.5.3 Rescue Medication	Added the following text: "**In the study extension, the determination that a subject is in clinical flare will be at the discretion of the investigator. However, the basis for this determination should be consistent with a partial Mayo score of ≥7 and based on the study participant (or caregiver)-reported stool frequency and degree of rectal bleeding, as well as a global assessment of UC disease activity made by a study primary- or sub-investigator. These findings supporting a determination of UC disease flare in the study extension should be recorded in the study source documents**."	Inserted text clarifying the basis for the determination by the investigator of when a participant is experiencing a clinical flare that requires rescue medication.
6.5.3 Rescue Medication	Added the following text: "**UC-specific medical therapies (ie, oral/rectal corticosteroids, oral/rectal 5-aminosalicylate (5ASA) compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX]) may not be initiated or their dose increased at any time from Week 6 to Week 54 except for weight-based dose adjustments or unless there is a documented UC flare and loss of response that makes the subject eligible for rescue medication (Section 6.5.1)."** Added the following text: "Participants who flare while enrolled in the study will be eligible to receive rescue medication (**ie, corticosteroids, 6-MP, AZA, MTX, and/or 5-ASAs**) while continuing to receive study intervention administration as scheduled." Added the following text: "**Other UC-specific rescue therapies (ie, rectal corticosteroids, oral/rectal 5-aminosalicylate (5-ASA) compounds, or the immunomodulators 6-MP, AZA, or methotrexate [MTX]) may be initiated or their dose increased at the discretion of the investigator to manage symptoms in the setting of a documented UC flare. The use of rectal steroids does not count toward the permitted steroid courses.**" Added the following text: "However, any participant who **uses UC-prohibited medications (Section 6.5.2) or** requires more than 2 courses of corticosteroids (including budesonide) for UC during the 54-week study will be discontinued from further administration of study intervention."	Added information regarding the use of UC-specific therapies during the study or as rescue medications.
7.1 Discontinuation of Study Intervention	Added criterion #10 to list for discontinuation: **10. The participant misses 2 consecutive doses of golimumab because of body weight below the 10 kg limit.**	Addressed the issue of discontinuing study intervention in subjects whose body weight is below the 10 kg limit.

Section number and Name	Description of Change	Brief Rationale
7.1 Discontinuation of Study Intervention **Discontinuation of a participant's study intervention must be strongly considered under the following conditions:**	Added the following text: 1. Persistent inadequate response or worsening of UC: a. **In the study extension, the determination that a subject is in clinical flare will be at the discretion of the investigator. However, the basis for this determination should be consistent with a partial Mayo score of ≥7 (as defined in Section 6.5.3) and recorded in the study source documents.** b. Participants in clinical flare will be eligible to receive rescue medication (ie, corticosteroids, **5-ASA, 6-MP, AZA, MTX**, Section 6.5.3 or infliximab dose escalation Section 6.6) while continuing to receive study intervention administration as scheduled. c. **For participants in the study extension, a clinical response to rescue therapy will be at the discretion of the study investigator but should be consistent with a partial Mayo score of ≤4 based on participant (or caregiver)-reported stool frequency and degree of rectal bleeding, as well as a global assessment of UC disease activity determined by a study primary- or sub-investigator. These findings demonstrating a clinical response should be recorded in the study source documents. Participants in the study extension who do not achieve a clinical response despite rescue medications will be discontinued from the study interventions and should return for a final safety visit 16 weeks after the last administration of study drug.** **Participants who are assessed as having responded to rescue therapy will continue in the study.** d. After the clinical flare, participants who remain in the study will continue to be assessed for clinical flare ~~using the criteria based on the partial Mayo score~~. Participants who subsequently meet the criteria for clinical flare again may receive rescue medication a second time and be assessed for ~~partial Mayo~~ an adequate response and managed as described above.	Inserted text in 1(a) to describe the basis for the determination by the investigator of a clinical flare that requires rescue medication. Added information in 1(b) regarding the use of UC-specific therapies during the study or as rescue medications. Inserted text in 1(c) to describe the basis for the determination by the investigator of a clinical response use of rescue medication. Deleted text in 1(d) to improve readability.

Section number and Name	Description of Change	Brief Rationale
8. STUDY ASSESSMENTS AND PROCEDURES Overview	Modified/updated the following text: "All visit-specific patient-reported outcomes (PRO) assessments should be conducted/completed **after the PUCAI is administered but before** any other tests, procedures, or other consultations for that visit to prevent influencing participant perceptions." Added sentence that reads: "**Participants with body weight of 10 kg to <12.3 kg will not have the RNA blood sample collected and will have lesser total volume**."	Clarifies when PRO assessments are to be conducted/completed. Update in blood sampling scheme to comply with allowable blood sample volumes with the EU guideline on clinical trials conducted with minors (see ref 12).
8. STUDY ASSESSMENTS AND PROCEDURES Study-Specific materials	The following additions/changes were made to the list in-text: "The investigator will be provided with the **following**: • IFU**s** • **Retesting and rescreening plan** • **eCRF guidelines** • Sample ICF/assent form**s** • Imaging **kit (laptop) and** manual"	Clarification of study-specific materials to be supplied to the sites.
8.1 Efficacy Assessments	The following changes were made to the bullet in-text: • Tummy-UC and **Observer TUMMY-UC**	Added the terminology for "Observer TUMMY-UC" questionnaire for efficacy assessments listed.
8.1.1. Mayo Score	Revised the following text: Mayo scores are calculated using the following: "1. The stool frequency and rectal bleeding data **collected in a study diary over 7 consecutive days** within the **14 days** prior to the visit. **Stool frequency and rectal bleeding subscores will be calculated using the average of the 3 consecutive day period in the diary closest to the study visit.** Refer to the study reference study binder on how to proceed when a consecutive 3-day period is not available." "3. The results of a sigmoidoscopy or colonoscopy. Endoscopies are to be performed using study software and submitted for central review. Scoring for disease activity based on endoscopic appearance is to be performed both by the local endoscopist and the central reviewer. All decisions to initiate (Week 0) or continue therapy (Weeks 6 and 54) based on mucosal disease activity will be based on local reads. **Approaches to calculating Mayo and partial Mayo scores in participants who have missing subscores will be detailed in the SAP.**"	Definitions and use of Mayo scores and subscores in assessments (including participants with missing subscores) are provided to align with the SAP.

Section number and Name	Description of Change	Brief Rationale
8.1.7.1. TUMMY-UC and Observer TUMMY-UC	Revised the following text: "**The** TUMMY-UC is an **exploratory** noninvasive **patient**-reported outcome (PRO) for the **measurement** of signs and symptoms for pediatric UC which is undergoing validation.[32] It is calculated using variables listed in Appendix 8 (Section 10.8). It includes 6 components similar to the PUCAI index and ranges from 0 to 56. **The Observer TUMMY-UC** is for participants under age 8 and is completed by caregivers."	Clarification that TUMMY-UC is a "patient-reported" outcome measure. Added the terminology "Observer" TUMMY-UC as an exploratory evaluation.
8.2.3. Clinical Safety Laboratory Assessments	Added "**gamma glutamyl transferase (GGT)**" to list in-text for serum chemistry panel.	Information omitted from section 8.2.3. in error from protocol Amendment 1.
8.2.3 Clinical Safety Laboratory Assessments	Added bullet to list that reads: "**HBV DNA detection will only be performed for participants who test positive for core antibody and negative for surface antibody.**" Added the following text to the bullet list that reads: "**Serology for HIV at screening. HIV testing in study participants who weigh less than 30 kg is not universally required. It is required in those study participants who weigh <30 kg and the birth history is unknown (ie adopted) or has exposure risks (parents with HIV or with risk factors) or at the discretion of the study investigator. In subjects who weigh <30 kg where testing would be required, if there is a record of a negative HIV test at birth this is acceptable at the discretion of the study physician as long as it is entered into the study record."**	Information omitted from section 8.2.3. in error from protocol Amendment 1. Added information regarding considerations for HIV screening in the smallest or youngest of participants.
9.2 Criteria for Success	Revised the following text: "The study will be considered successful and the criterion for determining that golimumab is effective in the treatment of UC in pediatric participants will have been met if the lower limit of the two-sided 90% CI for the proportion of golimumab participants in clinical remission at Week 6 is >10.0% (ie, the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 derived from a meta-analysis of 7 adult UC studies **including 2 adult Phase 2/3 studies of golimumab for UC and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints."**	Phases of the studies that contribute to the meta-analysis were updated.

Section number and Name	Description of Change	Brief Rationale
9.4.1 Efficacy Analyses	Revised the following text: "A formal comparison is ~~only~~ planned for the primary endpoint. Summary statistics will be provided for all efficacy endpoints. Unless otherwise specified, all endpoints that involve the Mayo endoscopy subscore will be based on the subscore assigned by the local **endoscopists**."	Deleted "only" in first sentence. Typographical error: Correction of "endocopists" to "endoscopists" in last sentence.
9.4.1.1 Primary Endpoint	Added information to a bullet in the text: • Had protocol prohibited medication changes **including increase above the baseline corticosteroid dose due to worsening UC** (detailed in SAP) Modified the following text: "The study will be considered successful and the criterion for determining that golimumab is effective in the treatment of UC in pediatric participants will have been met if the lower limit of the two-sided 90% CI for the proportion of pediatric golimumab participants in clinical remission at Week 6 is greater than the upper limit of the 95% CI for the proportion of placebo participants in clinical remission at Week 6 (ie, >10.0%) derived from a meta-analysis of 7 adult UC studies **(2 adult Phase 2/3 UC studies of golimumab and 5 adult Phase 3 studies of other products approved in this indication utilizing similar populations and endpoints)**."	Revised the bullet to make it explicit that steroid doses above the baseline dose due to worsening UC are considered treatment failure. Phases of the studies that contribute to the meta-analysis were updated.
9.4.1.2 Major Secondary Endpoints	Modified the following bulleted list: **1. Symptomatic remission at Week 54** **2. Clinical remission at Week 54, as assessed by the Mayo score (based on the Mayo endoscopy subscore assigned by the local endoscopist).** **3. Clinical remission at Week 54 as assessed by the PUCAI score** **4. Clinical remission at Week 6 as assessed by the PUCAI score.** **5. Clinical response at Week 6 as assessed by the Mayo score (based on the Mayo endoscopy subscore assigned by the local endoscopist).** **6. Endoscopic healing at Week 6 (based on the Mayo endoscopy subscore assigned by the local endoscopist).** **7. Endoscopic healing at Week 54 (based on the Mayo endoscopy subscore assigned by the local endoscopist).** Revised the following text: "Treatment failure rules will be applied as specified in the primary efficacy analysis. **In addition, participants who use rescue medication for a clinical flare after Week 6 will be considered a treatment failure for endpoints after Week 6 (detailed in the SAP).** Participants who have any treatment failure events prior to the timepoint of interest will be considered to not have achieved the endpoints at that timepoint. These rules will override the response status based on the Mayo, PUCAI, and endoscopy score. Participants who do not return for evaluation or have insufficient data to calculate their **Mayo score or** PUCAI Score at Week 6 or Week 54 **will be considered not to be in**	Added symptomatic remission and clinical remission (Mayo) at Week 54 as major secondary endpoints and revised the order and description of all major secondary endpoints to align with the SAP. Added a sentence for a reason for treatment failure which had been inadvertently omitted from the original protocol. Revised sentence to align with SAP for how participants with

Section number and Name	Description of Change	Brief Rationale
	clinical response or clinical remission, and not to have endoscopic healing at these timepoints. Participants who do not have sufficient data to calculate their stool frequency and rectal bleeding subscores at Week 54 will be considered to not have achieved symptomatic remission at these timepoints. Approaches to participants with missing subscores, including those missing an endoscopy subscore at Week 6 or Week 54, will be detailed in the SAP."	missing evaluations or who have a missing endoscopy subscore at Week 6 or Week 54 will be handled.
9.4.1.3 Other Endpoints *~~Clinical~~ Remission*	Modified the following bulleted list: *~~Clinical~~ Remission* 1. **Symptomatic remission at Week 6.** **2. Clinical remission at Week 30, as assessed by the PUCAI score, for participants who are in clinical remission at Week 6.** **3. Clinical remission at Week 54, as assessed by the PUCAI score, for participants who are in clinical remission at Week 6.** **4. Clinical remission at Week 54, as assessed by the Mayo score, for participants who are in clinical remission at Week 6 (based on Mayo endoscopy subscore assigned by the local endoscopist).** **5. Symptomatic remission at Week 54 for participants who are in symptomatic remission at Week 6.** **6. Corticosteroid-free clinical remission at Week 54, as assessed by the PUCAI score.** **7. Corticosteroid-free clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).** **8. Corticosteroid-free symptomatic remission at Week 54.** **9. Remission at Week 6 based on Mayo score less than or equal to 2, with no individual subsore greater than 1, a stool frequency subscore of 0, and a rectal bleeding subscore of 0.** **10. Partial Mayo remission at Week 6.** **11. Partial Mayo remission at Week 54.** **12. Participants who were not receiving corticosteroids for at least 12 weeks prior to Week 54 and in symptomatic remission at Week 54.** **13. Participants who were not receiving corticosteroids for at least 12 weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).** **14. Participants who were not receiving corticosteroids for at least 12 weeks prior to Week 54 and in clinical remission at Week 54, as assessed by the PUCAI score.** **Partial Mayo remission is defined as a Partial Mayo score ≤2.**	Added additional remission endpoints to the list. Revised the order and description of the remission endpoints to align with the SAP. Added definition for Partial Mayo remission.

Section number and Name	Description of Change	Brief Rationale
9.4.1.3 Other Endpoints *Other Clinical Efficacy Endpoints*	Modified the following bulleted list: *Other Clinical Efficacy Endpoints* **1. Clinical response at Week 54, as assessed by the Mayo score (based on Mayo endoscopy subscore assigned by the local endoscopist).** **2. Baseline and postbaseline values and the change from baseline in the Mayo score at Week 6 and at Week 54 (based on Mayo endoscopy subscore assigned by the local endoscopist).** **3. Baseline and postbaseline values in the Mayo subscores at Week 6 and at Week 54 (based on Mayo endoscopy subscore assigned by the local endoscopist).** **4. Baseline and postbaseline values and the change from baseline in the PUCAI score through Week 6 and during the long-term phase through Week 54.** **5. Baseline and postbaseline values and the change from baseline in the Partial Mayo score through Week 6 and during the long-term phase through Week 54.** **6. Clinically important change at Week 6 as assessed by the PUCAI score.** **7. Clinically important change at Week 30 as assessed by the PUCAI score.** 8. **Clinically important change at Week 54 as assessed by the PUCAI score.**	Revised order and description of other clinical efficacy endpoints to align with the SAP.
9.4.1.3 Other Endpoints	Modified the following text: **"Additional sensitivity analyses in which subjects with friability present on endoscopy are considered nonresponders in the analysis are detailed in the SAP."** Exploratory analyses of the TUMMY-UC and the **Observer TUMMY-UC** scores **and analyses based on different approaches to handling missing endoscopies** at Week 54 will also be performed. Details will be provided in the SAP. **Treatment failure rules** will be applied as specified in the primary efficacy analysis. **Participants who use rescue medication for a clinical flare after Week 6 will be considered a treatment failure for endpoints after Week 6 (detailed in the SAP).** For continuous endpoints (ie, PUCAI score, Mayo score, partial Mayo score, fecal markers and CRP), the same treatment failure rules that will be applied for the dichotomous efficacy endpoints will also be applied to these endpoints. The baseline value will be carried forward from the time the treatment failure occurs onward.	Additional analyses were added and are detailed in the SAP. Added terminology "Observer" for participants less than 8 years old who use the TUMMY-UC questionnaire. Also, added analyses based on different approaches to missing endoscopies at Week 54. Added a sentence for a reason for treatment failure which had been inadvertently omitted from the original protocol. Removed repetition in the paragraph.

Section number and Name	Description of Change	Brief Rationale
9.4.1.3 Other Endpoints	Modified the following text: "For endpoints beyond Week 6, analyses will also **be conducted on all golimumab participants including partial Mayo responders at Week 14 and separately for all infliximab participants including partial Mayo responders at Week 14 or Week 22**. ~~be conducted for participants who are in clinical response at Week 6 and also for nonresponders at Week 6, who are in partial Mayo response at Week 14~~."	Revised text to clarify which study intervention treated participants will be included in analyses to be conducted beyond Week 6.
9.4.1.5 Analyses of Study Extension	Modified the following text: "The change from **study extension** baseline in the PUCAI score, fecal calprotectin, CRP, **and IMPACT III** will be summarized over time."	Revised text to specify which assessments compared to baseline in the study extension will be summarized.
10.2 Appendix 2: Definitions of Inadequate Response to or Intolerance of Corticosteroids, MTX, or AZA/6 MP and Corticosteroid Dependence	Added text to the following bullets: "METHOTREXATE, 6-MERCAPTOPURINE (6-MP) OR AZATHIOPRINE (AZA) Participants have failed to respond to MTX, 6-MP or AZA if they have had evidence of an initial inadequate response, recurrent disease, or a relapse despite receiving: • At least 3 months of therapy **before screening** on MTX or at least 3 months of therapy **before screening** with 1 mg/kg/day of 6-MP or 2 mg/kg/day of AZA. OR • **At least 3 months before screening at** lower dosage of 6-MP or AZA when country or local guidelines specify a different treatment regimen. (In such an event, the country or local guidelines needs to be included in the source document). OR • **At least 3 months before screening** at a dosage of 6-MP or AZA confirmed to be therapeutic for the participant with whole blood thioguanine nucleotide levels >200 pmol/8 x 10^8 red blood cells. OR • **At least 3 months before screening at the** highest tolerated dosage due to leukopenia, elevated liver enzymes, or nausea."	Added text to clarify criteria for determination of participant failure of response to MTX, 6-MP, or AZA therapies prior to study screening.
10.5 Appendix .5: Pediatric Ulcerative Colitis Activity Index (PUCAI)	Minor typographical corrections were made for consistency with the copyrighted version.	Minor typographical errors were corrected.
10.8 Appendix 8: Examples of the TUMMY-UC and Observer TUMMY-UC Questionnaires	Added updated examples of the TUMMY-UC and the Observer TUMMY-UC Questionnaires **(Version 1.9 23.3.2019)**.	Added updated version of 2 pediatric ulcerative colitis assessment questionnaires.
10.9 Appendix 9: Prefilled Syringe with UltraSafe (PFS) Actual Use Data Collection	Modified the following text: "Approximately the first 15-20 participants from **Sponsor identified** sites who choose AHA will enter the Usability Assessment Substudy at Week 58 and complete a PFS Usability Questionnaire at Weeks 62 and 66 after completion of the second and third self- or caregiver administration visits."	Deleted reference to US or North American sites.

Section number and Name	Description of Change	Brief Rationale
10.12 Appendix 12: Regulatory, Ethical, and Study Oversight Considerations INFORMED CONSENT PROCESS	Updated the following text: "**For each participant, his or her parent(s) (preferably both parents, if available) or legally acceptable representative(s), as required by local regulations, must give written consent (permission) according to local requirements after the nature of the study has been fully explained and before the performance of any study-related assessments. Assent must be obtained from children (minors) capable of understanding the nature of the study, typically participants 7 years of age and older, depending on the institutional policies and national/local guidelines."**	Update of text regarding how informed consent is to be obtained from pediatric participants.
10.18 Appendix 18: Usability Assessment Substudy Overview of Substudy Design	Revised first sentence to read: "The Usability Assessment Substudy will be conducted at ~~US~~ **Sponsor identified** sites."	Specification for US sites has been removed to allow for possibility of participants from other countries joining the substudy.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted.

Amendment 1 (27 June 2018)

Overall Rationale for the Amendment: An important exclusion criterion was inadvertently included as an inclusion criterion. This correction together with other changes to improve structure and readability of the document have been made.

Section number and Name	Description of Change	Brief Rationale
Section 5.1 Inclusion criteria #18	~~Has a stool culture or other examination positive for an enteric pathogen, including *Clostridium difficile* toxin, in the previous 4 months, unless a repeat examination is negative and there are no signs of ongoing infection with that pathogen.~~	This inclusion criterion is an exclusion criterion and so has been deleted from Section 5.1, Inclusion Criteria and moved to Section 5.2, Exclusion Criteria. This criterion is the new exclusion criterion # 34. The numbering for the inclusion and exclusion criteria have been cascaded appropriately.
Section 5.1 Inclusion Criteria #6	Prior or current medication for UC must include at least 1 of the following (Appendix 2 [Section 10.2]): a. Current treatment with at least 1 of the following therapies: oral or intravenous corticosteroids, or the immunomodulators 6-MP, **MTX**, or AZA. OR b. Have a history of failure to respond to or tolerate, or have a medical	MTX had been inadvertently left out of the list of immunomodulators in inclusion criteria #6a and #6b.

Section number and Name	Description of Change	Brief Rationale
	contraindication to, at least 1 of the following therapies: oral or intravenous corticosteroids or the immunomodulators 6-MP, **MTX**, or AZA. OR c. Currently have or have had a history of corticosteroid dependency (ie, an inability to successfully taper corticosteroids without a return of the symptoms of UC). OR d. Have required more than 3 courses of oral or intravenous corticosteroids in the past year.	
Appendix 12 **PUBLICATION POLICY/DISSEMINATION OF CLINICAL STUDY DATA**	The results of the study will be reported in a Clinical Study Report (CSR) generated by the sponsor and will contain eCRF data transmitted from a central laboratory, ePRO, ~~eDiary~~, and IWRS data from all study sites that participated in the study into the sponsor's database, as per protocol. Recruitment performance or specific expertise related to the nature and the key assessment parameters of the study will be used to determine a coordinating investigator for the study. Results of pharmacogenomic and exploratory biomarker analyses performed after the CSR has been issued will be reported in a separate report and will not require a revision of the CSR.	eDiary was deleted from the paragraph as it will not be used.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted

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INVESTIGATOR AGREEMENT

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the study intervention, the conduct of the study, and the obligations of confidentiality.

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Signature: _____ Date: _____
(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Telephone Number: _____

Signature: _____ Date: _____
(Day Month Year)

Sponsor's Responsible Medical Officer:

Name (typed or printed): PPD

Institution: Janssen Research & Development

Signature: electronic signature appended at the end of the protocol Date: _____
(Day Month Year)

Note: If the address or telephone number of the investigator changes during the study, written notification will be provided by the investigator to the sponsor, and a protocol amendment will not be required.

Signature

User	Date	Reason
PPD	13-Nov-2023 17:06:26 (GMT)	Document Approval

Janssen Research & Development *

Clinical Protocol

COVID-19 Appendix

Protocol Title

A Phase 3 Randomized, Open-Label Study to Assess the Efficacy, Safety, and Pharmacokinetics of Golimumab Treatment, a Human anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Pediatric Participants with Moderately to Severely Active Ulcerative Colitis

PURSUIT 2

A Study of the Efficacy and Safety of Golimumab in Pediatric Participants with Moderately to Severely Active Ulcerative Colitis

Protocol CNTO148UCO3003; Phase 3

SIMPONI ® (golimumab)

*Janssen Research & Development is a global organization that operates through different legal entities in various countries. Therefore, the legal entity acting as the sponsor for Janssen Research & Development studies may vary, such as, but not limited to Janssen Biotech, Inc.; Janssen Products, LP; Janssen Biologics, BV; Janssen-Cilag International NV; Janssen, Inc; Janssen Pharmaceutica NV; Janssen Sciences Ireland UC; Janssen Biopharma Inc.; or Janssen Research & Development, LLC. The term "sponsor" is used throughout the protocol to represent these various legal entities; the sponsor is identified on the Contact Information page that accompanies the protocol.

Status: Approved
Date: 20 April 2020
Prepared by: Janssen Research & Development, LLC
EDMS number: EDMS-RIM-36445

THIS APPENDIX APPLIES TO ALL CURRENT APPROVED VERSIONS OF PROTOCOL CNTO148UCO3003 Amendment 3
CNTO148UCO3003 Amendment ITA-3

GCP Compliance: This study will be conducted in compliance with Good Clinical Practice, and applicable regulatory requirements.

COVID-19 APPENDIX

GUIDANCE ON STUDY CONDUCT DURING THE COVID-19 PANDEMIC

It is recognized that the Coronavirus Disease 2019 (COVID-19) pandemic may have an impact on the conduct of this clinical study due to, for example, self-isolation/quarantine by participants and study-site personnel; travel restrictions/limited access to public places, including hospitals; study site personnel being reassigned to critical tasks.

In alignment with recent health authority guidance, the Sponsor is providing options for study related participant management in the event of disruption to the conduct of the study. This guidance does not supersede any local or government requirements or the clinical judgement of the investigator to protect the health and well-being of participants and site staff. If, at any time, a participant's safety is considered to be at risk, study intervention will be discontinued, and study follow-up will be conducted.

Scheduled visits that cannot be conducted in person at the study site will be performed to the extent possible remotely/virtually or delayed until such time that on-site visits can be resumed. At each contact, participants will be interviewed to collect safety data. Key efficacy endpoint assessments should be performed if required and as feasible. Participants will also be questioned regarding general health status to fulfill any physical examination requirement.

Every effort should be made to adhere to protocol-specified assessments for participants on study intervention, including follow up. Modifications to protocol-required assessments may be permitted via COVID-19 Appendix after consultation between the participant and investigator, and with the agreement of the Sponsor (see below).

The Sponsor will continue to monitor the conduct and progress of the clinical study, and any changes will be communicated to the sites and to the health authorities according to local guidance. If a participant has tested positive for COVID 19, the investigator should contact the Sponsor's responsible medical officer to discuss plans for study intervention and follow-up. Modifications made to the study conduct as a result of the COVID-19 pandemic should be summarized in the clinical study report.

ADDITIONAL ELEMENTS, WHERE APPLICABLE:

- Certain protocol-mandated visits to the study site may not be possible during the COVID-19 outbreak. Therefore, temporary measures may be implemented if considered appropriate by the Sponsor and Investigator to maintain continuity of participant care and study integrity. Certain measures, such as those listed below, may be necessary and should be instituted in accordance with applicable (including local) laws, regulations, guidelines, and procedures:

    - remote (eg, by phone / telemedicine) or in-person, off-site (eg, in-home) interactions between site staff (or designees) and participants for study procedures e.g. those related to safety monitoring / efficacy evaluation / study intervention storage and administration (including training where pertinent)

    - procurement of study intervention by participants (or designee) or shipment of study intervention from the study site directly to participants for at home administration (including the potential for self-administration of study intervention)

    - laboratory assessments using a suitably accredited local laboratory; for selected measures (eg, urine pregnancy), home testing may be employed

    - other procedures, eg, imaging, may be conducted at an appropriate facility

- Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented with the prefix "COVID-19-related" in the case report form (CRF).

    - other relevant study data elements impacted by the pandemic should also be documented / labeled as "COVID-19-related" in CRFs and / or other study systems, as directed by detailed Sponsor guidance. These may include missed / delayed / modified study visits / assessments / dosing, and instances where temporary measures such as those above are implemented.

- The Sponsor will evaluate the totality of impact of COVID-19 on collection of key study data and additional data analyses will be outlined in study SAP(s).

- Exclusion: a potential participant with the following features will be excluded from participating in the study protocol:

    - During the 6 weeks prior to baseline, have had ANY of (a) confirmed SARS-CoV-2 (COVID-19) infection (test positive), OR (b) suspected SARS-CoV-2 infection (clinical features without documented test results), OR (c) close contact with a person with known or suspected SARS-CoV-2 infection

- Exception: may be included with a documented negative result for a validated SARS-CoV-2 test

(i) obtained at least 2 weeks after conditions (a), (b), (c) above (timed from resolution of key clinical features if present, e.g. fever, cough, dyspnea)

AND

(ii) with absence of ALL conditions (a), (b), (c) above during the period between the negative test result and the baseline study visit

- NOTES on COVID-related exclusion:

1. If a participant is excluded due to recent COVID-19-related features, the reason for screen failure should be documented in the case report form under the exclusion criterion of having a condition for which participation would not be in the participant's interest or could confound study assessments.

2. The field of COVID-related testing (for presence of, and immunity to, the SARS-CoV-2 virus) is rapidly evolving. Additional testing may be performed as part of screening and/or during the study if deemed necessary by the investigator and in accordance with current regulations / guidance from authorities / standards of care.

- Precaution: for those who may carry a higher risk for severe COVID-19 illness, follow guidance from local health authorities when weighing the potential benefits and risks of enrolling in the study, and during participation in the study.

INVESTIGATOR AGREEMENT

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the study intervention, the conduct of the study, and the obligations of confidentiality.

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Signature: _____ Date: _____
(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Telephone Number: _____

Signature: _____ Date: _____
(Day Month Year)

Sponsor's Responsible Medical Officer:

Name (typed or printed): _____

Institution: Janssen Research & Development

Signature: [electronic signature appended at the end of the protocol] Date: _____
(Day Month Year)

Note: If the address or telephone number of the investigator changes during the course of the study, written notification will be provided by the investigator to the sponsor, and a protocol amendment will not be required.

Signature

User	Date	Reason
PPD	20-Apr-2020 13:42:40 (GMT)	Document Approval