PROTOCOL CIDP04 AMENDMENT 3

AN OPEN-LABEL EXTENSION STUDY TO INVESTIGATE THE LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF ROZANOLIXIZUMAB IN SUBJECTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP)

PHASE 2A

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SERIOUS ADVERSE EVENT REPORTING

Serious adverse event reporting (24h)	
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LIST OF TABLES

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LIST OF ABBREVIATIONS

ADA	antidrug antibody
ADL	activities of daily living
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC	area under the curve from time 0 to infinity
BP	blood pressure
CDMS	clinical data management system
CI	confidence interval
CIDP	chronic inflammatory demyelinating polyradiculoneuropathy
C_{max}	maximum observed plasma concentration
CRO	contract research organization
C-SSRS	Columbia Suicide Severity Rating Scale
CTCAE	Common Terminology Criteria for Adverse Events
DMC	Data Monitoring Committee
ECG	electrocardiogram
eCRF	electronic Case Report form
ES	Enrolled Set
EudraCT	European Union Drug Regulating Authorities Clinical Trials
FAS	Full Analysis Set
FcRn	neonatal Fc receptor
FIH	first-in-human
FV	Final Visit
GCP	Good Clinical Practice
HIV	human immunodeficiency virus
HIV1	human immunodeficiency virus antibody 1
HIV2	human immunodeficiency virus antibody 2
IA	immunoabsorption
IB	Investigator's Brochure
ICF	Informed Consent form

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ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
IgA	immunoglobulin A
IgE	immunoglobulin E
IgG	immunoglobulin G
IgM	immunoglobulin M
IGRA	interferon gamma release assay
IMP	investigational medicinal product
INCAT	Inflammatory Neuropathy Cause and Treatment
IND	Investigational New Drug
IRB	Institutional Review Board
iRODS	inflammatory Rasch-built Overall Disability Scale
IRT	interactive response technology
ITP	immune thrombocytopenia
iv	intravenous(ly)
IVIg	intravenous immunoglobulin
LLOQ	lower limit of quantification
logit	log odds unit
LTBI	latent tuberculosis infection
MCID-SE	minimum clinically important differences-standard error
MedDRA	Medical Dictionary for Regulatory Activities
MG	myasthenia gravis
NF-L	neurofilament light chain
NTMBI	nontuberculosis mycobacterium infection
OLE	open-label extension
PD	pharmacodynamics
PDILI	potential drug-induced liver injury
PD-PPS	Pharmacodynamic Per-Protocol Set
PDS	Protocol Deviation Specification
PEOT	premature end of treatment
PGIC	Patient Global Impressions of Change
PGIS	Patient Global Impressions of Severity

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PK	pharmacokinetic
PK-PPS	Pharmacokinetic Per-Protocol Set
PLEX	plasma exchange
PPS	Per-Protocol Set
PR	pulse rate
PRO	patient-reported outcome
PS	Patient Safety
QTc	QT-interval corrected for heart rate
RT-MRC	Rasch-built, modified interval Medical Research Council scale
SAE	serious adverse event
SAP	Statistical Analysis Plan
sc	subcutaneous(ly)
SCIg	subcutaneous immunoglobulin
SD	standard deviation
SOC	standard of care
SOP	Standard Operating Procedure
SS	Safety Set
TB	tuberculosis
TEAE	treatment-emergent adverse event
ULN	upper limit of normal
WHO	World Health Organization

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1 SUMMARY

Rozanolixizumab (UCB7665) is a humanized anti-neonatal Fc receptor (FcRn) monoclonal antibody that is being developed as an inhibitor of FcRn activity with the aim to reduce the concentration of pathogenic immunoglobulin (IgG) in patients with IgG auto-antibody mediated diseases such as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

CIDP04 is a Phase 2A, multicenter, single-arm, open-label study with the primary objective of evaluating the long-term safety and tolerability of rozanolixizumab when administered as [redacted] subcutaneous (sc) infusion in study participants with CIDP. The secondary objective includes evaluating the long-term clinical efficacy of [redacted] doses of rozanolixizumab in the study participants with CIDP. This open-label study will provide study participants from previous rozanolixizumab studies (eg, CIDP01) the opportunity to have continued access to rozanolixizumab.

Access to CIDP04 for study participants coming from CIPD01: Study participants from CIDP01 who have completed the Treatment Period (ie, all visits up to Visit 17) without a relapse of CIDP will be offered the opportunity to be directly enrolled into this open-label extension (OLE) study. Study participants from CIDP01 who have experienced a relapse of CIDP (during either the Treatment Period or the Observation Period) and have been successfully rescued and stabilized with standard of care (SOC) medication may also be eligible to enroll in CIDP04. The study participants who completed the Treatment Period will be offered the opportunity to enter directly once stabilized. The study participants who relapsed during Treatment Period will be offered entry into CIDP04 only once CIDP01 study results are available, after the blind has been broken at the end of the study, and it is confirmed they received placebo in CIDP01.

In case the study participants have a gap period between the end of the parent study and the start of this open-label study (ie, last visit in the parent study does not take place on the same day as entry of study CIDP04), a Screening Period of 2 to 5 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry in the open-label study and allow for a smooth transition between the treatment used by the study participants during the gap period and initiation of rozanolixizumab. The CIDP04 study includes a 24-week Treatment Period, an optional additional maximum 52-week Treatment Period followed by an 8-week Observation Period. The length of the additional Treatment and Observation Periods may be shortened in case of availability of an Access Program. For the Treatment Periods, study participants will have weekly visits (either on site or at home) during which they will be dosed with an sc infusion of rozanolixizumab, up to [redacted]. The initial dose in the study will be based on the dose the study participant has received at the completion of the parent study (eg, CIDP01). For study participants who were known to be on placebo in the parent study (eg, CIDP01), a starting dose of [redacted] will be used. Dose may be reduced to [redacted] if [redacted] is not tolerable (eg, headache) and/or recurrent low IgG levels (Treatment Period Part 2). The maximum dose of rozanolixizumab in CIDP04 will be [redacted]. For exact doses to be administered, refer to Section 7.2.

The primary safety variable is the occurrence of treatment-emergent adverse events (TEAEs). The other safety variables include TEAEs leading to withdrawal of the investigational medicinal product (IMP); assessment of values and change from Baseline of: vital signs (systolic and diastolic blood pressure [BP], pulse rate [PR], body temperature, and body weight); physical and

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neurological examination findings; 12-lead electrocardiograms (ECGs); clinical laboratory findings (hematology, clinical chemistry, and urinalysis); Tuberculosis Signs and Symptoms Questionnaire; and total protein, albumin, α- and β-globulins. The other variables include the efficacy variables of changes in study participant's score on inflammatory Rasch built Overall Disability Scale (iRODS), Inflammatory Neuropathy Cause and Treatment (INCAT), maximum grip strength (assessed by site personnel), the Rasch-built, modified interval Medical Research Council scale (RT-MRC) sum score, and patient-reported outcomes (PROs); pharmacokinetic (PK) variable of the plasma concentration of rozanolixizumab; pharmacodynamic (PD) variables of changes in concentration of serum IgG, and its subclasses, and neurofilament light chain (NF-L) levels in serum; and immunological variables of changes in concentration of serum IgA, IgE, and IgM, serum complement levels (C3 and C4) and plasma complement levels (C3a and C5a), anti-rozanolixizumab antibodies levels, cytokines levels, CIDP-specific auto-antibody levels, and tetanus- and influenza A virus-specific IgG antibodies.

A total of ■ study participants participating in the parent study CIDP01 may be enrolled in this OLE study; enrollment is planned at approximately 24 sites in Europe, United States of America, and Canada, with possible extension to other regions and countries.

A Data Monitoring Committee (DMC) will be established for the study.

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2 INTRODUCTION

Chronic inflammatory demyelinating polyradiculoneuropathy is a rare disorder of the peripheral nerves characterized by chronic and progressive onset of weakness, loss of sensation, reflexes, reduction or partial block in motor nerve conduction, and often pain and imbalance. Worldwide, the prevalence of CIDP ranges from approximately 1 to 9 cases per 100,000 (Mathey et al, 2015). For many patients, CIDP results in substantial disability, limiting their activities resulting in an overall negative impact on quality of life across multiple dimensions. Progressive disease and/or relapses can result in difficulty moving arms, hands, legs, and feet, a loss in the ability to walk independently or confinement to wheelchairs and reliance on caregivers (Mahdi-Rogers et al, 2014). Healthcare costs for CIDP are substantial (Guptill et al, 2014; Mahdi-Rogers et al, 2014; Olesen et al, 2012).

Cellular and humoral immune mechanisms are thought to be involved in the pathogenesis of CIDP resulting in inflammatory lesions in the spinal roots, proximal nerve trunks and along the peripheral nerves. The essential role of the autoimmune antibodies in mediating this pathology is supported by the improvement seen after plasma exchange (PLEX) and immunoabsorption (IA). Identification of the specific antigenic target(s) of the autoimmune antibodies in CIDP is expanding with recent immunological techniques.

Although the prognosis of CIDP has markedly improved over the last decades, significant disability remains. High-dose steroids, PLEX, IA, and intravenous and subcutaneous immunoglobulin (IVIg and SCIg) have all been shown to be effective treatments for CIDP. However, comorbid diseases, including hypertension, diabetes, and psychiatric diseases, limit the use of high-dose steroids. While PLEX is effective, the procedure is burdensome for patients. Immunoglobulin treatment (IVIg and SCIg) is often used as first-line treatment but there remains a medical need for improved therapeutic options.

The neonatal major histocompatibility complex-class-I-like FcRn recycles immunoglobulin G (IgG) and albumin from most cells and transports it bi-directionally across epithelial barriers to affect systemic and mucosal immunity. It has been shown that FcRn rescues both IgG and albumin from intracellular lysosomal degradation by recycling it from the sorting endosome to the cell surface (Anderson et al, 2006). Immunoglobulin G has a half-life of approximately 3 weeks in man. This is achieved by interaction of IgG with the receptor, FcRn. Thus in effect FcRn salvages IgG, and blockade of FcRn accelerates removal of endogenous IgG.

Rozanolixizumab is a humanized anti-FcRn monoclonal antibody that has been specifically designed to inhibit IgG binding to FcRn without inhibiting albumin binding to FcRn. Rozanolixizumab is being developed as an inhibitor of FcRn activity with the aim to reduce the concentration of pathogenic IgG in patients with IgG auto-antibody mediated diseases. Rozanolixizumab was derived from a rat antibody with specificity for human FcRn. To date, rozanolixizumab has been administered to healthy study participants in a completed first-in-human (FIH) study (UP0018), a completed Phase 2 study in study participants with primary immune thrombocytopenia (ITP) (TP0001, evaluating [redacted] by sc route across 5 cohorts), and a completed Phase 2 study in study participants with myasthenia gravis (MG) (MG0002, evaluating [redacted] by sc route).

Additional information on the development of rozanolixizumab can be found in the current version of the Investigator's Brochure (IB) for rozanolixizumab.

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The extension of the development program of rozanolixizumab to the indication of CIDP is based on the underlying hypothesis that reducing the concentration of pathogenic IgG in patients with CIDP will improve the symptoms of CIDP and prevent its long-term progression. CIDP01 is the first study investigating this indication; it is a Phase 2A, multicenter, randomized, study participant-blind, investigator-blind, placebo-controlled, parallel-group study with the primary objective of evaluating the clinical efficacy of rozanolixizumab as a treatment for study participants with active CIDP who have been maintained on an immunoglobulin-dependent regimen. In addition, CIDP01 will assess the safety and tolerability of multiple dosing with rozanolixizumab including the development of antidrug antibodies (ADA) and potential to impact clinical response, and will provide information on the PK and PD of rozanolixizumab in study participants with active CIDP. The maximum duration of the study per study participant is approximately 28 weeks (up to maximum 40 weeks), consisting of a Screening Period of between 2 and 5 weeks duration, an 11-week Treatment Period, and an Observation Period of 12 weeks (up to 24 weeks). Study participants will be randomized to 1 of 2 treatment arms: rozanolixizumab [redacted] sc or placebo sc in a ratio of 1:1. Study participants will receive [redacted] of IMP.

2.1.1 Rationale for this study

CIDP04 will evaluate the long-term safety, tolerability, and efficacy of treatment with rozanolixizumab with a [redacted] dosing regimen for 24 weeks in subjects with active CIDP who have been maintained on an immunoglobulin-dependent regimen. An optional extension of the treatment period by a maximum of an additional 52 weeks, or until an Access Program or equivalent is in place, whichever comes first, will be allowed on the basis of each participant's individual benefit-risk assessment at the end of the first 24-weeks Treatment Period. Study participants may choose to self-administer the IMP during Treatment Period Part 2 under supervision of a nurse and after having received appropriate training.

The CIDP04 OLE study will provide the opportunity to assess the long-term safety of rozanolixizumab in study participants with CIDP from CIDP01.

3 STUDY OBJECTIVES

3.1 Primary objective

The primary objective of the study is to assess long-term safety and tolerability of [redacted] doses of rozanolixizumab in study participants with CIDP.

3.2 Secondary objective

The secondary objective of the study is to assess long-term clinical efficacy of [redacted] doses of rozanolixizumab.

3.3 Exploratory objectives

The exploratory objectives of the study are to assess the PD, PK, and immunological variables in the treatment course with rozanolixizumab and to assess whether long-term dosing of rozanolixizumab improves PROs. These include:

- The PD effect of rozanolixizumab as measured by the total IgG concentrations in serum

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- The effects of rozanolixizumab on the concentrations of total protein, albumin, α- and β-globulins, IgG subclasses, IgM, IgA, IgE, and serum and plasma complement levels
- The incidence and emergence of ADA with respect to immunogenicity and PK and PD
- The effect of rozanolixizumab on complement and cytokines
- The plasma concentrations of rozanolixizumab administered by sc infusion
- The PD effect of rozanolixizumab as measured by NF-L in serum
- The effect of rozanolixizumab on CIDP-specific auto-antibody levels
- The effect of rozanolixizumab on vaccine antibody levels (influenza A and tetanus)
- The effect of rozanolixizumab on exploratory biomarkers, and explore the relationship between protein and metabolite biomarkers and cause, progression, and appropriate treatment of CIDP

4 STUDY VARIABLES

For all study variables, the Baseline values for study participants who enroll directly into CIDP04 will be the Baseline values from the parent study (eg, CIDP01). For study participants with a gap period prior to enrollment in CIDP04, details of the analyses of specific Baseline will be available in the Statistical Analysis Plan (SAP).

4.1 Safety variables

4.1.1 Primary safety variables

The primary safety variable is:

- Occurrence of TEAEs

4.1.2 Other safety variables

The other safety variables are:

- TEAEs leading to permanent withdrawal of IMP
- Vital signs values and changes from Baseline (systolic and diastolic BP, PR, body temperature, and body weight) at each scheduled assessment during the Treatment and Observation Periods
- Physical examination findings
- Neurological examination findings
- 12-lead ECG values and change from Baseline at each scheduled assessment during the Treatment and Observation Periods
- Laboratory values and changes from Baseline at each scheduled assessment during the Treatment and Observation Periods (hematology, clinical chemistry, and urinalysis)
- Tuberculosis Signs and Symptoms Questionnaire at each scheduled assessment during the Treatment and Observation Periods

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- Values and change from Baseline in concentrations of total protein, albumin, α- and β-globulins at each scheduled assessment during the Treatment and Observation Periods

4.2 Other variables

4.2.1 Efficacy variables

Preliminary definitions linked to assessment of relapse:

- CIDP relapse (iRODS) is defined as a clinically important deterioration from Baseline in iRODS score, ie, a minimum clinically important differences-standard error (MCID-SE) of ≤-1.96
- CIDP relapse (adjusted INCAT) is defined as an increase from Baseline of at least 1 point in the adjusted INCAT score. The adjusted score is identical to the INCAT disability score except for the exclusion of changes in upper limb function from 0 (normal) to 1 (minor symptoms) or from 1 to 0
- CIDP relapse (maximum grip strength as assessed by site personnel) is defined as a clinically important deterioration from Baseline in grip strength as measured by site personnel, ie, a decline of >14kPa

The other efficacy variables are:

- Values and absolute change from Baseline in iRODS scores at each scheduled assessment during the Treatment and Observation Periods
- Study participant experienced CIDP relapse (iRODS) up to Week 25 and Week 77 (where applicable) from Baseline
- Time to CIDP relapse (iRODS) during the Treatment Period from Baseline
- Study participant experienced CIDP relapse (adjusted INCAT) up to Week 25 and Week 77 (where applicable) from Baseline
- Time to CIDP relapse (adjusted INCAT) during the Treatment Periods from Baseline
- Values and absolute change from Baseline in adjusted INCAT score at each scheduled assessment during the Treatment and Observation Periods
- Study participant experienced CIDP relapse (maximum grip strength as assessed by site personnel) up to Week 25 and Week 77 (where applicable) from Baseline
- Time to CIDP relapse (maximum grip strength as assessed by site personnel) during the Treatment Periods from Baseline
- Values and absolute change from Baseline in maximum grip strength score (maximum of 3 assessments) taken by site personnel at each scheduled assessment during the Treatment and Observation Periods
- Values and absolute change from Baseline in RT-MRC sum score at each scheduled assessment during the Treatment and Observation Periods
- Study participants receiving rescue medication during Treatment Periods

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- Time to rescue medication administration during Treatment Periods

4.2.2 Patient-reported outcome variables

The PRO variables are:

- Values and change from Baseline in fatigue domain scores at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in CIDP PRO instrument domain scores at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in Patient Global Impressions of Severity (PGIS) at each scheduled assessment during the Treatment and Observation Periods
- Patient Global Impressions of Change (PGIC) value at each scheduled assessment during the Treatment and Observations Periods

4.2.3 Pharmacokinetic variable

The PK variable is the plasma concentration of rozanolixizumab at each scheduled assessment during the Treatment Periods.

4.2.4 Pharmacodynamic variables

The PD variables are:

- Minimum value and maximum decrease (absolute and percentage) from Baseline in total serum IgG concentration during the study
- Values and change (absolute and percentage) from Baseline in total serum IgG concentrations at each scheduled assessment during Treatment and Observation Periods
- Values and change (absolute and percentage) from Baseline in serum IgG subclass concentrations at each scheduled assessment during Treatment and Observation Periods
- Values and change (absolute and percentage) from Baseline in NF-L levels at each scheduled assessment during Treatment and Observation Periods

4.2.5 Immunological variables

The immunological variables are:

- Values and change from Baseline in serum immunoglobulin concentrations (total IgA, IgE, and IgM) at each scheduled assessment during Treatment and Observation Periods
- Values and change from Baseline in serum complement levels (C3 and C4) and plasma complement levels (C3a and C5a) at each scheduled assessment during Treatment Period
- ADA (anti-rozanolixizumab antibodies) status (negative or confirmed positive) and the confirmed positive titer at each scheduled assessment during Treatment and Observation Periods
- Values and change from Baseline in cytokines at each scheduled assessment during Treatment and Observation Periods

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- Change in CIDP-specific auto-antibody levels in serum from Baseline during Treatment and Observation Periods
- Values and change from Baseline in tetanus- and influenza A virus-specific IgG antibodies during Treatment and Observation Periods

4.2.6 Exploratory biomarkers

The exploratory biomarker variables are:

- Protein and metabolites changes that may be measured to understand the cause, progression, and appropriate treatment of CIDP
- Exploratory biomarkers such as, but not limited to, [redacted]
- Absolute change from Baseline relating to mechanism of action, disease activity, treatment response, and clinical outcome at each scheduled assessment during the Treatment and Observation Periods

5 STUDY DESIGN

5.1 Study description

This is a Phase 2A, multicenter, single-arm, OLE study to evaluate the safety, tolerability, and efficacy of rozanolixizumab during long-term treatment of study participants with CIDP from a previous study with rozanolixizumab.

Access to CIDP04 for study participants coming from CIDP01: Study participants from CIDP01 who have completed the Treatment Period (ie, all visits up to Visit 17) without a relapse of CIDP will be offered the opportunity to be directly enrolled into this OLE study. Study participants will enter CIDP04 on the same day as the last study visit in CIDP01: Visit 17. Study participants from CIDP01 who have experienced a relapse of CIDP (during either the Treatment Period or the Observation Period), have been successfully rescued and stabilized with SOC medication and have consented to enter this OLE study, may be assessed for eligibility. The study participants who relapsed during the Treatment Period of CIDP01 will be offered entry into CIDP04 only once CIDP01 study results are available, after the blind has been broken at the end of the study, and it is confirmed they received placebo in CIDP01.

In case the study participants have a gap period between the end of the parent study and the start of this OLE study (ie, last visit in the parent study does not take place on the same day as entry of study CIDP04), a Screening Period of 2 to 5 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry in the OLE study and allow for a smooth transition between the treatment used by the study participants during the gap period and the initiation of rozanolixizumab. The CIDP04 study includes a first 24-week Treatment Period (Part 1) followed by a second Treatment Period (Part 2) of up to 52 weeks (or until an Access Program or equivalent is in place, whichever comes first). Entry to the Treatment Period (Part 2) will be contingent to a favorable individual benefit-risk after careful individual assessment has been performed for each study participant completing Treatment Period (Part 1). An 8-week Observation Period will be followed in case of premature termination or after completion of the Treatment Periods (either at end of Part 1 for study participants not continuing in Part 2 or at end

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of Part 2). The Observation Period will not be performed in the event of a study participant continuing treatment with rozanolixizumab after the end of the study (ie, in case of an Access Program), in which case only the PEOT (Visit 26) Visit will be performed.

During the Treatment Periods (Part 1 and Part 2), study participants will have weekly visits (either on site or at home) during which they will be dosed with an sc infusion of rozanolixizumab up to [redacted]. The initial dose in the study will be based on the dose the study participant has received at the completion of the parent study (eg, CIDP01). For study participants who were known to be on placebo in the parent study, a starting dose of [redacted] will be used. The maximum dose will be [redacted]. See Section 7.2 for details on treatment to be administered.

During the first 4 weeks of the Treatment Period (Part 1), all visits will be on site. During Weeks 5 to 8, home visits and on-site visits will be alternating (Weeks 5 and 7 will be on site; Weeks 6 and 8 will be at home). Starting at Week 9 and through the end of the Treatment Period (Week 24 and if applicable, Week 76), study participants will have 1 visit on site followed by 3 visits at home for every 4-week period.

After the completion of the Treatment Period(s) (starting at Week 25 for study participants only completing Part 1 or from Week 77 for study participants completing both Part 1 and Part 2 or at any early timepoint in case of PEOT), study participants will enter the 8-week Observation Period where no IMP will be administered. During the Observation Period, study participants will have on-site visits at the entry and exit of the Observation Period (Weeks 25/77, and 32/84, and home visits at Weeks 27/79 and 29/81). Study participants can return to their SOC during the Observation Period. In case the study participant enters an Access Program, no Observation Period will be performed with the exception of the PEOT (Visit 26) Visit which will be immediately completed.

At the discretion of the investigator and/or study participant, home visits can be changed to site visits (eg, for safety reasons). In case an on-site visit cannot be performed, the next visit will be performed at site instead of at home, and all safety assessments that should have been completed at the missed visits will be performed.

The assessments to be completed during each visit are presented in Table 5-1.

5.1.1 Study duration per study participant

The total duration of the study for an individual study participant will be up to 89; this includes a 2- to 5-week Screening Period, a 24-week Treatment Period (Part 1), an optional maximum 52-week Treatment Period (Part 2), or until an Access Program or equivalent is in place whichever comes first, and an 8-week Observation Period in case the participant does not enter in an Access Program (or equivalent).

The end of the study is defined as the date of the last visit of the last study participant in the study.

5.1.2 Planned number of study participants and sites

A total of [redacted] study participants participating in the parent study CIDP01 may be enrolled in this OLE study; enrollment is planned at approximately 24 sites.

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Depending on the further development of the UCB CIDP program, there may also be an opportunity for additional, future CIDP patients to enroll into CIDP04 from other parent studies at a later time point.

5.1.3 Anticipated regions and countries

Anticipated regions are Europe, United States of America, and Canada, with possible extension to other regions and countries.

5.2 Schedule of study assessments

The schedule of study assessments are provided in Table 5-1.

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [b]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [c]	S	S	S	S	S	S	H [d]	S	H [d]	S	H [d]	H [d]	H [d]	S	H [d]	S	H [d]	H [d]	S
Written informed consent [e]		X	X																	
Demographic data [e]		X	X																	
Verification of inclusion and exclusion criteria [e]		X	X																	
Withdrawal criteria			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Medical history update [e]		X	X																	
Prior and concomitant medication		X	X [f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medical procedures		X	X [f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs [g]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [b]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [c]	S	S	S	S	S	S	H [d]	S	H [d]	S	H [d]	H [d]	H [d]	S	H [d]	S	H [d]	H [d]	S
Body weight		X	X [f]												X [h]		X			X
Recording of AEs		X	X [f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Query for suicidality [i]		X	X [f]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
Fatigue scale			X [f]				X				X				X [j]		X			X
CIDP PRO Instrument			X [f]				X				X				X [j]		X			X
PGIS			X [f]				X				X				X [j]		X			X
PGIC			X [f k]				X				X				X [j]		X			X
Full physical examination		X	X [f]																	X
Brief physical examination				X	X	X	X		X		X				X		X			

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Table 5-1: Schedule of study assessments

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Assessments	**Visit type [c]**	**S**	**S**	**S**	**S**	**S**	**S**	**H [d]**	**S**	**H [d]**	**S**	**H [d]**	**H [d]**	**H [d]**	**S**	**H [d]**	**S**	**H [d]**	**H [d]**	**S**
Full neurological examination [l]		X	X [f]																	X
Brief neurological examination				X	X	X	X		X		X				X		X			
12-lead ECG		X	X [f]	X	X	X			X		X		X		X [m]		X			X
Labs (hematology, chemistry, urinalysis)		X	X [f]	X	X	X	X		X		X		X		X		X			X
Serology for HIV, hepatitis B, and hepatitis C [n]		X																		
Serum/urine pregnancy test [o]		X	X [f]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
IGRA tuberculosis test [p]		X	X [f]																	X

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Table 5-1: Schedule of study assessments

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	Visit	1 Scr [b]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
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Assessments	Visit type [c]	S	S	S	S	S	S	H [d]	S	H [d]	S	H [d]	H [d]	H [d]	S	H [d]	S	H [d]	H [d]	S
Tuberculosis Signs and Symptoms Questionnaire		X												X [q]	X [q]					X
Contact IRT		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			X
Administration of IMP			X	X	X	X	X	X	X	X	X	X	X	X	X [r]	X [r]				
Blood sampling for PK of rozanolixizumab [s]			X [f]		X				X		X [t]				X [m]		X			
ADA (Anti-rozanolixizumab antibodies)			X [f]		X				X		X [t]				X [m]		X			X
Serum complement (C3, C4) and plasma complement (C3a, C5a) [u]			X	X					X		X				X					

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [b]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
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Assessments	Visit type [c]	S	S	S	S	S	S	H [d]	S	H [d]	S	H [d]	H [d]	H [d]	S	H [d]	S	H [d]	H [d]	S
Serum cytokines [u]			X	X					X		X				X					
Vaccination-specific antibody titers (tetanus and influenza Type A)		X							X		X [v]				X [m]		X			
Immunoglobulins (total IgG and IgG subclasses)		X	X [f]	X	X	X	X	X[w]	X	X [w]	X	X [w]	X [w]	X [w]	X	X [w]	X			X
NF-L			X [f]						X						X [x]		X [y]			
IgA, IgM, IgE			X [f]	X	X	X	X		X		X				X [m]		X			X
CIDP-specific auto-antibodies			X [f]				X				X				X [x]		X [y]			X [x]

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [b]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
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Assessments	Visit type [c]	S	S	S	S	S	S	H [d]	S	H [d]	S	H [d]	H [d]	H [d]	S	H [d]	S	H [d]	H [d]	S
Blood sampling for exploratory biomarker analysis [z]			X	X					X		X									
iRODS assessment [aa]		X	X [f]	X	X	X	X		X		X				X		X			X
INCAT assessment		X	X [f]	X	X	X	X		X		X				X		X			X
Assessment of grip strength by site personnel		X	X [f]	X	X	X	X		X		X				X		X			X
RT-MRC assessment		X	X [f]	X	X	X	X		X		X				X [x]		X [y]			X [x]

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [b]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [c]	S	S	S	S	S	S	H [d]	S	H [d]	S	H [d]	H [d]	H [d]	S	H [d]	S	H [d]	H [d]	S

ADA=antidrug antibody; AE=adverse event; BL=baseline; CIDP=chronic inflammatory demyelinating polyradiculoneuropathy; C-SSRS=Columbia Suicide Severity Rating Scale; ECG=electrocardiogram; FV=Final Visit; H=Home visit; HIV=human immunodeficiency virus; ICF=Informed Consent form; IgA=immunoglobulin A; IgE=immunoglobulin E; IgG=immunoglobulin G; IgM=immunoglobulin M; IGRA=interferon gamma release assay; IMP=investigational medicinal product; INCAT=Inflammatory Neuropathy Cause and Treatment; iRODS=inflammatory Rasch-built Overall Disability Scale; IRT=interactive response technology; NF-L=neurofilament light chain; PEOT=premature end of treatment; PGIC=Patient Global Impressions of Change; PGIS=Patient Global Impressions of Severity; PK=pharmacokinetic; PRO=patient-reported outcome; RT-MRC=Rasch-built, modified-interval Medical Research Council scale, S=on-site visit; Scr=Screening visit; V=visit

Note: All assessments are to be completed in the order specified in the protocol or laboratory manual if possible. The ICF should be completed before any assessment. The PROs should be conducted in the order specified in Section 10.4 immediately after ICF (where applicable). The laboratory manual will provide further guidance on the order of sample collection.

[a] The 52-week duration can be shortened or extended in view of the availability of an access program.

[aa] Assessment to be performed before all other assessments at each visit except ICF.

[b] Only for study participants with a gap period between the parent study and entry in CIDP04.

[c] All visits have a ±2-day window. Minimum time between doses must be at least 5 days.

[d] The following visits can be performed by a healthcare professional visiting the study participant at his/her home: Visits 11 to 13, 15 to 17, 19 to 21, and 23 to 25 (Weeks 10 to 12, 14 to 16, 18 to 20, and 22 to 24). Visits in Treatment Period Part 2 will follow the same pattern: one site visit followed by 3 visits

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conducted at the participant home. Alternately, the visits can be conducted at the site as deemed necessary by site and/or study participant. Feasibility of IMP dosing in a home setting will have to be confirmed before the visit is conducted (see Section 8.2).

[e] Will not be repeated at Visit 2 if performed at Visit 1.

[f] If entry in CIDP04 (Visit 2) is done on the same day as the last visit of the parent study and in case assessment was performed at last visit of the parent study, data from the parent study will be used and corresponding assessments will not be repeated in CIDP04.

[g] During site Visits 2, 3, and 4, vital signs will be measured prior to IMP administration, at the end of the infusion, and 2 and 4h after the end of the infusion. From Visit 5 until Visit 25, vital signs will be measured predose, at the end of the infusion and 2h after the end of the infusion only. During Treatment Period Part 2, vital signs will be measured predose, at the end of the infusion. At nondosing visits, vital signs need only be taken once during the visit. For study participants requiring additional assessments due to AEs (see Table 5-2), additional vital sign measurements may be taken based on the timing of the assessments.

[h] Body weight is collected every 6 months during Treatment Period Part 2 starting at first visit in this period and will be used to select the correct volume for dose infusion from these timepoints.

[i] A full C-SSRS assessment will be performed only when the study participant has a positive response to the suicidal ideation query. If a study participant has active suicidal ideation as confirmed by the answer "Yes" to Question 4 or Question 5 of the C-SSRS assessments, the study participant will be excluded or withdrawn from the study and immediately referred to a Mental Healthcare Professional.

[j] Only performed every 24 weeks.

[k] Not required for study participants who had a Screening Visit.

[l] The full neurological examination includes a fundoscopy. In addition to the FV, a full neurological examination should be performed for any study participant who experiences severe headache (refer to Section 5.2.1 and Table 5-2).

[m] Assessment to be performed every 12 weeks (Weeks 25, 37, 49 and 61).

[n] Serology includes hepatitis C virus (HCV)-antibodies (Ab)+, hepatitis B virus antibodies (HBsAg and HBcAb), human immunodeficiency virus antibodies (HIV1 and HIV2).

[o] In case of immediate entry from the parent study, the serum pregnancy test from the parent study should not be older than 5 weeks prior to entry into this CIDP04 study and the urine pregnancy test done at Visit 2 must both be negative before dosing. In case of gap period between the parent study and entry in CIDP04, a serum test will be performed at Visit 1 (Screening). Pregnancy testing will consist of urine testing at dosing visits during the Treatment Period Part 1, monthly urine testing during Treatment Period Part 2 and at each visit during the Observation Period for women of childbearing potential. A positive urine pregnancy test must be confirmed using a serum pregnancy test. Note that the final urine pregnancy test of the study should be no longer than 90 days after the final dose of IMP.

[p] The IGRA test will be performed in a central laboratory.

[q] Tuberculosis signs and symptoms Questionnaire must be done at least every 12 weeks.

[r] Self-administration may be performed by study participant under the supervision of the home nurse after full training.

[s] Trough PK samples should be taken for all study participants receiving rozanolixizumab. At Visits 2, 4, and 8, PK samples should be taken predose and 4h postdose for all study participants. At Visits 14, 18, 22 and quarterly at site visits during Treatment Period Part 2, a predose sample only should be taken. At Visit 26, samples to be taken once during the visit.

[t] Does not apply to Visit 10.

[u] Serum complement (C3, C4), plasma complement (C3a, C5a), and serum cytokines should be taken predose at Visit 2 for all study participants. Samples should be taken predose and 4h postdose for all study participants at other scheduled visits (Visits 3, 8, 10, 14, 18, 22 and at first (Week 25) and last visit (Week 73) of Treatment Period Part 2); if an infusion reaction occurs within the first 2h, refer to Section 5.2.1 and Table 5-2.

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[v] Only at Visit 14.
[w] In case IgG levels are below 2 and the study participant does not qualify for a withdrawal, IgG levels will be monitored weekly.
[x] Assessments to be performed only at the first visit after Visit 25 (ie, 1st visit of Part 2). Visit 29/FV should not performed after Treatment Period 2.
[y] Only performed at PEOT visit when starting Observation Period directly after Treatment Period Part 1
[z] At Visits 2, 3, 8, 10, 14, 18, and 22, samples for exploratory biomarkers should be taken predose. See Table 5-2 for sampling in case of AE of interest.

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5.2.1 Additional study assessments

In addition to those detailed in Table 5-1, the assessments in Table 5-2 may be required in case of infusion reactions or AEs of interest (severe headache, moderate to severe diarrhea, moderate to severe abdominal pain, or moderate to severe vomiting). Note that additional vital sign measurements may be taken based on the timing of the assessments.

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Table 5-2: Additional study assessments

Assessment	When applicable
For study participants who experience infusion reactions (excluding local injection site reactions):	
Complements and cytokines	Samples required for all study participants are detailed in the schedule of study assessments (Table 5-1). In study participants who experience an infusion reaction within the first 2h at Visits 2, 4, 5, and 6, samples should also be taken 2 and 4 hours postdose (see Section 9.1.9 and Section 18.1). In study participants who experience an infusion reaction within 2 hours at Visits 3, 8, 10, 14, 18, 22 and "S" visits during Treatment Period Part 2, samples should be taken 2 hours postdose (see Section 9.1.9 and Section 18.1).
For study participants who experience an AE of interest, including severe headache, moderate to severe diarrhea, moderate to severe abdominal pain, or moderate to severe vomiting: If the AE is initially reported at a home visit, the study participant should be reviewed at the study site as soon as is practically possible for further investigation.	
Exploratory biomarkers	Samples required for all study participants are detailed in the schedule of study assessments (Table 5-1). In study participants who experience an AE of interest (as defined in Section 9.1.1.4) at Visits 2, 3, 8, 10, 14, 18, 22 and "S" visits during Treatment Period Part 2, samples should also be taken 4 hours postdose.
For study participants who experience severe and/or serious headache:	
Headache Questionnaire	In study participants who report severe and/or serious headache, this assessment will be performed daily until resolution (ie, if headache becomes moderate or mild, normal collection of AEs should apply) (see Section 9.1.10).
Full neurological examination	Assessments required for all study participants are detailed in the schedule of study assessments (Table 5-1). In study participants who report severe and/or serious headache at the clinic visit, a full neurological examination (including fundoscopy) should be performed (see Section 9.1.10). In study participants who report a severe headache whilst at home, a visit to the site for the full neurological examination should be arranged for as soon as is practically possible.
Other	In study participants who report severe headache, other diagnostic procedures including but not limited to CT scan, MRI and/or LP for CSF collection are to be performed if indicated at the discretion of the investigator (see Section 9.1.10).
For study participants who experience moderate or severe diarrhea:	
Stool sample assessment	In study participants who report moderate or severe diarrhea, stool collection and analysis will be performed. The frequency of stool sampling will be as clinically indicated in the opinion of the investigator. Analysis of stool samples will be performed locally (see Section 9.1.11). If the moderate or severe diarrhea is initially reported at a home visit or during a telephone call, the study participant should be reviewed at the study site as soon as practically possible.

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Table 5-2: Additional study assessments

Assessment	When applicable

AE=adverse event; CSF=cerebral spinal fluid; CT=computed tomography; LP=lumbar puncture; MRI=magnetic resonance imaging

5.3 Rationale for study design and selection of dose

This OLE study will provide study participants with CIDP who participated in the parent study (eg, CIDP01) the opportunity to have continued access to rozanolixizumab. CIDP04 will assess the safety, tolerability, and efficacy of a longer-term treatment with rozanolixizumab in these study participants.

The initial dose of rozanolixizumab will be based on the dose the study participant has received at the completion of the parent study (eg, CIDP01). For study participants who were known to be on placebo in parent study, a starting dose of [redacted] will be used. The dose may be reduced to [redacted] is not tolerable (eg, severe headache, Section 9.1.10), or in case of IgG levels are <1g/L (see Section 6.4.1.3). The dose and regimen of IMP to be used in the current study (rozanolixizumab [redacted] sc) is based on results from the FIH study UP0018, alongside the safety data from the MG and ITP studies (MG0002 and TP0001). CIDP04, similar to the parent study, CIDP01, will utilize a liquid formulation at [redacted]

6 SELECTION AND WITHDRAWAL OF STUDY PARTICIPANTS

6.1 Inclusion criteria

To be eligible to participate in this study, all of the following criteria must be met:

1. An Institutional Review Board (IRB)/Independent Ethics Committee (IEC)-approved written Informed Consent form (ICF) is signed and dated by the study participant.
2. Study participant who has completed one of the previous rozanolixizumab study(ies) that allow access to the present study.

   For example, for study participants coming from CIDP01 the following criteria will have to be met:

   - Study participant has completed the Treatment Period of the parent study with no relapse of CIDP disease and has chosen to enter this OLE study directly upon completion of the Treatment Period of the parent study, or
   - Study participant has experienced a relapse of CIDP during the parent study (either during the Treatment Period or the treatment free Observation Period), has been successfully rescued and stabilized with eg, IVIg based on assessment of the investigator (maximum of 3 months of stabilization treatment), and has chosen to enter this OLE study. Study participants who already relapsed during the Treatment Period of CIDP01 must have been assigned to placebo treatment during that period in order to be able to qualify for enrollment into CIDP04.

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3. The study participant is considered reliable and capable of adhering to the protocol visit schedule, or medication intake according to the judgment of the investigator, and has been compliant with the parent study assessments.

4. Female study participants of child-bearing potential must have the results of a negative serum pregnancy test from either the parent study (not older than 5 weeks) or the Screening Visit available at the CIDP04 Baseline (Visit 2), and a urine pregnancy test must be negative when study participant enters CIDP04 and prior to further dosing at each study visit thereafter.

   Female study participants of childbearing potential must agree to use a highly effective method of birth control, during the study and for a period of 3 months after their final dose of IMP. Highly effective forms of birth control are methods that achieve a failure rate of less than 1% per year when used consistently and correctly. According to the International Council for Harmonisation (ICH) M3 R2, highly effective methods of birth control include:

   – Combined (estrogen- and progesterone-containing) hormonal contraception (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for study participants entering CIDP04 without a Screening Visit, and should remain stable during the study).
   – Progesterone-only hormonal contraceptives (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for study participants entering CIDP04 without a Screening Visit, and should remain stable during the study).
   – Progesterone-releasing intrauterine systems or the TCu 380A intrauterine device.
   – Vasectomized partner (provided sole partner and partner has medical proof of surgical success).
   – True heterosexual sexual abstinence is an acceptable form of contraception when this is in line with the preferred and usual lifestyle of the person. Periodic abstinence (eg, calendar, ovulation, symptothermal, postovulation methods), declaration of abstinence for the duration of the study, and withdrawal are not acceptable methods of contraception.
   – Women not agreeing to use birth control must be of nonchildbearing potential, defined as being:
   – Postmenopausal (for at least 2 years before the Screening Visit of CIDP04 or the parent study if no Screening Visit is scheduled in CIDP04), verified by serum follicle-stimulating hormone level >40mIU/mL at the Screening Visit, or
   – Permanently sterilized (eg, bilateral tubal occlusion, hysterectomy, bilateral salpingectomy), or
   – Congenitally sterile

5. Male study participants with a partner of childbearing potential must be willing to use a condom when sexually active during the study and for 3 months after the final administration of IMP. In addition, the female partner of childbearing potential of a male study participant

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must be willing to use a highly effective method of contraception (as above), during the study period and for 3 months after the final administration of IMP. Sperm donation is not permitted during the study and for 3 months after final administration of IMP.

6. For study participants entering CIDP04 after a gap period since the parent study: Study participant is on a stable dosage (not more than ±20% deviation) for SCIg or IVIg and a fixed interval (eg, once weekly ±2 days for SCIg or every 2 to 6 weeks ±5 days IVIg, respectively) for stability in functioning between dosing.

6.2 Exclusion criteria

Study participants are not permitted to enroll in the study if any of the following criteria is met:

1. Study participant is currently participating in another study of an IMP (or a medical device).
2. Female study participant who is pregnant or lactating, or planning to become pregnant during the study and until 2 months following completion of the study.
3. Study participant has any medical (acute or chronic illness) or psychiatric condition that, in the opinion of the investigator, could harm the study participant or would compromise the study participant's ability to participate in this study.
4. Study participant has 12-lead ECG with abnormalities considered to be clinically significant upon medical review.
5. Study participant has renal impairment, defined as serum creatinine level of ≥1.4mg/dL for females and ≥1.5mg/dL for males.
6. Study participant has an absolute neutrophil count <1500/mm^3 (1.5x10^9/L).
7. Study participant has >2x upper limit of normal (ULN) of any of the following: alanine aminotransferase (ALT), aspartate aminotransferase (AST), or alkaline phosphatase (ALP), or >ULN total bilirubin (≥1.5xULN total bilirubin if known Gilbert's syndrome). If study participant has elevations only in total bilirubin that are >ULN and <1.5xULN, fractionate bilirubin to identify possible undiagnosed Gilbert's syndrome (ie, direct bilirubin <35%).

   For study participants with a Baseline result >ULN for ALT, AST, ALP, or total bilirubin, a Baseline diagnosis and/or the cause of any clinically meaningful elevation must be understood and recorded in the electronic Case Report form (eCRF).

   If study participant has >ULN ALT, AST, or ALP that does not meet the exclusion limit at the time of entry in CIDP04 (either Screening [Visit1] or Baseline [Visit 2]), repeat the tests, if possible, prior to dosing to ensure there is no further ongoing clinically relevant increase. In case of a clinically relevant increase, inclusion of the study participant must be discussed with the Medical Monitor.

   Tests that result in ALT, AST, or ALP up to 25% above the exclusion limit may be repeated once for confirmation. This applies to study participants who had a Screening Visit and includes rescreening.
8. Study participant has a clinically relevant active infection (eg, sepsis, pneumonia, abscess).

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9. Study participant has active suicidal ideation as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the "Since Last Visit" version of the Columbia Suicide Severity Rating Scale (C-SSRS) at Baseline Visit (Visit 2),

   or

   Study participant has a lifetime history of suicide attempt (including an active attempt, interrupted attempt, or aborted attempt), or has suicidal ideation in the past 6 months as indicated by a positive response ("Yes") to either Question 4 or Question 5 on the Screening C-SSRS.

   The study participant should be referred immediately to a Mental Healthcare Professional and must be withdrawn from the study.

10. Study participant has a known hypersensitivity to any components of rozanolixizumab.
11. Study participant intends to have a live vaccination during the course of the study or within 7 weeks following the final dose of rozanolixizumab.
12. Study participant has an ongoing serious adverse event (SAE) or a medical condition in the parent study that the investigator considers to put the study participant at a significantly increased risk of participating in CIDP04.
13. Study participant has any planned elective surgery due to occur during the study dosing period which in the opinion of the investigator could interfere with study procedures.

6.2.1 Additional exclusion criteria for study participants with a gap period between the parent study and entry in CIDP04

14. Study participant has a current diagnosis or has a history of Type 1 or Type 2 diabetes mellitus and/or hemoglobin A1c level >6.0%.
15. Study participant with IgM paraproteinemia.
16. Study participant has known IgM-mediated neuropathy (eg, multifocal motor neuropathy).
17. Study participant has clinical or known evidence of associated systemic diseases that might cause neuropathy, including but not limited to connective tissue disease, Lyme disease, Castleman's disease and systemic lupus erythematosus, malignant plasma cell dysplasia, or treatment with agents that might lead to neuropathy (eg, amiodarone therapy).
18. Study participant on an average dose less than 0.4g IgG/kg/month over the past 4 months.
19. Study participant has a history of clinically relevant ongoing chronic infections including but not limited to human immunodeficiency virus (HIV), hepatitis B, hepatitis C, or is tested positive for human immunodeficiency virus antibody 1 (HIV1), human immunodeficiency virus antibody 2 (HIV2), hepatitis B surface antigen, hepatitis B core antibody without hepatitis B surface antibody test positive, or hepatitis C antibody at the Screening Visit.
20. Study participant with known tuberculosis (TB) infection, at high risk of acquiring TB infection, or latent tuberculosis infection (LTBI), or current/history of nontuberculosis mycobacteria (NTMB) are excluded.

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21. Study participant has a history of alcohol use disorder or other substance use disorder (as per Diagnostic and Statistical Manual of Mental Disorders-5 [American Psychiatric Association, 2013]) within 12 months of Screening Visit.
22. Study participant has a clinically relevant active infection (eg, sepsis, pneumonia, abscess) or has had a serious infection (resulting in hospitalization or requiring parenteral antibiotic treatment) within 4 weeks prior to the first dose of IMP.
23. Study participant has active neoplastic disease or history of neoplastic disease within 5 years of Screening Visit (except for basal or squamous cell carcinoma of the skin or carcinoma in situ of the uterine cervix that has been definitively treated with SOC approaches).
24. Study participant has received a live vaccination within 8 weeks prior to the Baseline Visit.
25. Study participant has received any experimental biological agent (except rozanolixizumab) within or outside of a clinical study in the past 3 months or within 5 half-lives prior to Baseline (whichever is longer) (refer to Table 6-1).
26. Study participant has had prior treatment with rituximab, ofatumumab, or ocrelizumab in the 6 months prior to the Baseline Visit or study participant has had prior treatment with rituximab, ofatumumab, or ocrelizumab in the 12 months prior to Baseline and B cells are not within the normal range.
27. Study participant has been treated with immunosuppressants, biologics (except for rozanolixizumab), and other therapies in the recent timeframe as detailed in Table 6-1 OR has been on permitted medications detailed in Table 7-3, but has not been on stable dosing regimens of those medications as detailed in Table 7-3.

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Table 6-1: Time restrictions required prior to Baseline Visit (Visit 2) for immunosuppressants, biologics, and other therapies

Generic name	Time restrictions required prior to Baseline Visit (regardless of route)
Immunosuppressants	
Cyclophosphamide	[redacted]
Pimecrolimus	
Vinca alkaloids (vincristine, vinblastine)	
Biologics (mAbs and fusion proteins)	
Abatacept (CTLA 4-Ig)	
Belimumab	
Golimumab	
Natalizumab	
Ofatumumab	
Rituximab	
Ocrelizumab	
Atacicept (TACI-Ig)	
Veltuzumab	
Other biologics	
Others	
Rigerimod	
PLEX	

CTLA 4-Ig=cytotoxic T lymphocyte-associated molecule-4 immunoglobulin; mAb=monoclonal antibody; PLEX=plasma exchange; TACI-Ig=transmembrane activator and calcium modulator and cyclophilin ligand interactor-immunoglobulin

NOTE: For other immunotherapies not included in the table, consult with Medical Monitor prior to enrollment.

6.3 Rescreening of study participants (only for study participants who had a Screening Visit)

For study participants otherwise fully eligible but not able to enter the study as planned for nonclinical reasons, rescreening may be allowed at the discretion of the investigator, following discussion with the sponsor's Medical Monitor and/or Study Physician.

If a study participant has 1 isolated test result in the exclusionary range that is deemed not being clinically significant by the investigator, retesting may be allowed at the discretion of the investigator, following discussion with the sponsor's Medical Monitor and/or Study Physician. If the normalization of the test result occurs within the Screening Period, then no other screening procedures need to be repeated.

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6.4 Withdrawal criteria

Study participants are free to withdraw from the study at any time, without prejudice to their continued care.

Study participants ***MUST be withdrawn from the study*** if any of the following events occur:

1. Study participant withdraws his/her consent.
2. Study participant becomes pregnant during the study, as confirmed by a positive pregnancy test.

Study participants ***must permanently discontinue IMP*** if any of the following events occur:

1. Study participant develops an illness that would interfere with his/her continued participation.

- Study participant has an AE of severe infusion reaction requiring corticosteroid and/or epinephrine therapy (see Section 9.1.9).
- Study participant has an AE of severe anaphylactic reaction requiring corticosteroid and/or epinephrine therapy.
- Study participant has a TB test that is confirmed positive or any further evidence suggestive of potential TB infection (eg, exposure) and further examinations result in a diagnosis of active TB or LTBI (refer to Section 9.3.6 for further details and instructions).
- If an NTMBI is identified during a study, the same withdrawal procedures as those used for an active TB infection identified during the study should be followed.

2. Study participant has active suicidal ideation as indicated by a positive response (Yes) to either Question 4 or Question 5 of the "Since Last Visit" version of the C-SSRS. The study participant should be referred immediately to a Mental Healthcare Professional.
3. The sponsor or a regulatory agency requests withdrawal of the study participant.
4. Study participant needs or takes PLEX, dexamethasone, or rituximab.
5. Study participant is treated with rescue medication and/or relapses during the Treatment Period (refer to Section 7.8.3).

Study participants ***may be discontinued from IMP*** at the discretion of the investigator, Medical Monitor, and Study Physician if any of the following events occur:

1. Study participant takes prohibited concomitant medications during the Treatment Period as defined in this protocol (refer to Section 7.8.2).
2. Study participant experiences a severe AE of headache that is considered related to the IMP in the opinion of the investigator (Section 9.1.10). Following an event of a severe headache, a study participant may continue participation in the study if the study participant is willing to do so and the investigator, Medical Monitor, and Study Physician agree that the study participant's continuation in the study poses no significant risk for the study participant. The use of symptomatic headache treatment is allowed at the discretion of the investigator. The IMP dose can be reduced if the headache persists despite symptomatic treatment. The IMP

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dose may be reduced to [redacted] (refer to Section 9.1.10 for details on the management of headaches and Section 7.2 for treatment to be administered).

3. Study participant experiences severe AE of gastrointestinal disturbance that is considered related to the IMP in the opinion of the investigator. Following an event of a severe gastrointestinal disturbance, a study participant may continue in the study if they are willing to do so and the investigator and Medical Monitor agree that the study participant's continuation in the study poses no significant risk.

Study participants ***may be withdrawn from the study*** at the discretion of the investigator, Medical Monitor, and Study Physician if any of the following events occur:

1. Study participant is noncompliant with the study procedures or medications in the opinion of the investigator.
2. In case of intake of prohibited concomitant medication other than IVIg, SCIg, PLEX, dexamethasone or rituximab, the investigator will (where possible) discuss with the Medical Monitor and/or sponsor Study Physician and a *decision will be made whether the study participant should discontinue IMP*.

Study participants who withdraw from the study or discontinue IMP during any of the Treatment Periods (Part 1 or Part 2) should complete the assessments outlined for Visit 26/premature end of treatment (PEOT) (see Table 5-1 and Section 8.4.1). Study participants who withdraw from the study will be encouraged to return to the clinic for all visits during the Observation Period (which should occur every 2 weeks) following their final dose of IMP) and the Final Visit (FV) (scheduled 8 weeks after final dose of IMP). The study participants can return to their SOC during the Observation Period.

Investigators should attempt to obtain information on study participants in the case of withdrawal.

For study participants considered as lost to follow up, the investigator should try (at least 1 phone call and 1 written message to the study participant), and document his/her effort (date and summary of the phone call and copy of the written message in the source documents), to complete the final evaluation. All results of these evaluations and observations, together with a narrative description of the reason(s) for removing the study participant, must be recorded in the source documents. The eCRF must document the primary reason for withdrawal or discontinuation, with the reason and date for withdrawal or discontinuation.

Investigators should contact the Medical Monitor, whenever possible, to discuss the withdrawal of a study participant in advance.

Study participants who withdraw from the study will not be replaced.

6.4.1 Temporary discontinuation of IMP

6.4.1.1 Serious infection

Treatment must be discontinued if study participant has a serious infective episode requiring eg, hospitalization, or iv antibiotic therapy (including but not limited to bacteremia or sepsis, bacterial meningitis, osteomyelitis or septic arthritis, bacterial pneumonia, or visceral abscess).

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6.4.1.2 Hypogammaglobulinemia and non-serious persisting or recurrent infection

In the event of a non-serious infection, the Benefit-Risk of continuing treatment with IMP must be carefully evaluated by the Investigator in collaboration with the Medical Monitor and the Study Physician. Treatment may be temporarily discontinued for the study participant who develops a non-serious persisting or recurrent infection with a serum total IgG levels between ≥1g/L and <2g/L (see Section 7.9). Upon resolution of infection and the IgG levels returning to ≥2g/L, the study participant may be allowed to restart treatment with IMP (at the same dose for study participants in Treatment Period Part 1, or at the same dose or at the reduced dose of [redacted] for study participants in Treatment Period Part 2) at the discretion of the investigator and in agreement with Medical Monitor and Study Physician, if the study participant is willing and if the benefit-risk remains favorable for the study participant.

6.4.1.3 Hypogammaglobulinemia irrespective of infection

Treatment will be temporarily discontinued for the study participant who develops an event of hypogammaglobulinemia with a serum total IgG <1g/L (see Section 7.9) irrespective of infection. When the IgG level reaches ≥2g/L, the study participant may be allowed to restart treatment with IMP (at the same dose for study participants in Treatment Period Part 1, or at the same dose or at the reduced dose of [redacted] for study participants in Treatment Period Part 2) at the discretion of the investigator and in agreement with Medical Monitor and Study Physician, if the study participant is willing and if the benefit-risk remains favorable for the study participant.

6.4.2 Potential drug-induced liver injury IMP discontinuation criteria

Study participants with potential drug-induced liver injury (PDILI) must be assessed to determine if IMP must be discontinued. In addition, all concomitant medications and herbal supplements that are not medically necessary should also be discontinued.

The PDILI criteria below require ***immediate and permanent*** discontinuation of IMP:

- Study participants with either of the following:
  - ALT or AST ≥5xULN
  - ALT or AST ≥3xULN and coexisting total bilirubin ≥2xULN

The PDILI criterion below requires immediate discontinuation of IMP:

- Study participants with ALT or AST ≥3xULN who exhibit temporally associated symptoms of hepatitis or hypersensitivity. Hepatitis symptoms include fatigue, nausea, vomiting, right upper quadrant pain or tenderness. Hypersensitivity symptoms include fever (without clear alternative cause), rash, or eosinophilia (ie, >5%).

If a nondrug-related cause for the symptoms can be confirmed, these study participants may resume IMP administration after discussion with the responsible UCB physician, but only when the requirements for rechallenge with IMP as provided in Section 9.2.1.2.1 are followed.

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The PDILI criterion below allows for study participants to continue on IMP at the discretion of the investigator.

- Study participants with ALT or AST ≥3xULN (and ≥2x Baseline) and <5xULN, total bilirubin <2xULN, and no eosinophilia (ie, ≤5%), with no fever, rash, or symptoms of hepatitis (eg, fatigue, nausea, vomiting, right upper quadrant pain or tenderness).

Evaluation of PDILI must be initiated as described in Section 9.2.1. If study participants are unable to comply with the applicable monitoring schedule, IMP must be discontinued immediately.

Investigators should attempt to obtain information on study participants in the case of IMP discontinuation to complete the final evaluation. Study participants with PDILI should not be withdrawn from the study until investigation and monitoring are complete. All results of these evaluations and observations, as well as the reason(s) for IMP discontinuation and study participant withdrawal (if applicable), must be recorded in the source documents. The eCRF must document the primary reason for IMP discontinuation.

7 STUDY TREATMENT

7.1 Description of investigational medicinal product

[redacted]

Details of the IMP and its specifications are provided in the IMP Handling Manual.

7.2 Treatment to be administered

The initial dose administered will be based on the dose at the time of completion of the Treatment Period from the parent study (eg, CIDP01). For subjects who had a gap period between the parent study (eg, CIDP01) and CIDP04, a starting dose of [redacted] will be used (see Table 7-1). The dose used in the study may be reduced based on individual tolerability to [redacted] (see Table 7-2) (eg, severe headache) but the maximum dose used will be [redacted] The dose used during Treatment Period Part 2 may be reduced to [redacted] in case of recurrent low observed IgG levels for a participant. Treatment temporary halt may also be implemented in some situation (see Section 6.4.1).

Eligible study participants will receive rozanolixizumab [redacted] by sc infusion for 24 weeks during Treatment Period Part 1 (from Visit 2 to Visit 25) and during an optional additional 52 weeks during Treatment Period Part 2. Treatment Period 2 may be shortened depending on availability of an Access Program or equivalent.

Study participants may choose to self-administer the IMP during Treatment Period Part 2 under supervision of a nurse and after having received appropriate training.

[redacted]

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Table 7-1: IMP doses to be administered (equivalent to approximately [redacted]) by body weight

Body weight ranges	IMP doses to be administered (equivalent to approximately [redacted][a])	IMP volume to be administered
≥40 to <49kg	[redacted]	[redacted]
≥49 to <63kg	[redacted]	[redacted]
≥63 to <77kg	[redacted]	[redacted]
≥77 to <91kg	[redacted]	[redacted]
≥91 to <105kg	[redacted]	[redacted]
≥105 to <119kg	[redacted]	[redacted]
≥119 to <133kg	[redacted]	[redacted]
≥133 to <147kg	[redacted]	[redacted]
≥147 to <161kg	[redacted]	[redacted]
≥161 to 170kg	[redacted]	[redacted]

IMP= investigational medicinal product

[a] Doses administered will be ±10% of the intended dose, except for study participants with a body weight of 47 to 50kg and 63kg.

Table 7-2: IMP doses to be administered (equivalent to approximately [redacted]) by body weight

Body weight ranges	IMP doses to be administered (equivalent to approximately [redacted])	IMP volume to be administered
≥40 to <49kg	[redacted]	[redacted]
≥49 to <69kg	[redacted]	[redacted]
≥69 to <89kg	[redacted]	[redacted]
≥89 to <109kg	[redacted]	[redacted]
≥109 to <129kg	[redacted]	[redacted]
≥129 to <149kg	[redacted]	[redacted]
≥149 to <169kg	[redacted]	[redacted]
≥169 to 170kg	[redacted]	[redacted]

IMP= investigational medicinal product

The IMP will be administered at the clinic or in a home setting (refer to Table 5-1for details). Home administration is study participant to a set of conditions (see Section 8.2) to ensure study participant safety.

The IMP will be administered as a sc infusion using a syringe pump. [redacted]

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[redacted] The chronology of these events should be recorded accurately in the source data and eCRF.

The study participant's body weight at entry into CIDP04 (either at Screening [Visit 1] or Baseline [Visit 2]) will be used to select the volume for dose infusion throughout Treatment Period Part 1. Body weight will be reevaluated at start of the Treatment Period Part 2, and every 6 months, and will be used to select the correct volume for dose infusion from these timepoints.

The exact procedure for dose preparation according to body weight will be provided in the IMP Handling Manual.

7.3 Packaging

[redacted]

Details of the IMP and its specifications are provided in the IMP Handling Manual.

7.4 Labeling

Clinical drug supplies will be labeled in accordance with the current ICH guidelines on Good Clinical Practice (GCP) and Good Manufacturing Practice and will include any locally required statements. If necessary, labels will be translated into the local language.

7.5 Handling and storage requirements

The investigator (or designee) is responsible for the safe and proper storage of IMP at the site. Investigational medicinal product stored by the investigator is to be kept in a secured area with limited access according to the storage conditions mentioned on the label.

Appropriate storage conditions must be ensured either by controlling the temperature (eg, room, refrigeration unit) or by completion of a temperature log in accordance with local requirements on a regular basis (eg, every work day), showing actual and minimum/maximum temperatures reached over the time interval.

In case an out-of-range temperature is noted, it must be immediately reported as per instructions contained in the IMP Handling Manual.

The investigator (or designee) will instruct the study participant to store the IMP following the instructions on the label.

7.6 Drug accountability

A Drug Accountability form will be used to record IMP dispensing and return information on a by-study participant basis and will serve as source documentation during the course of the study. Details of any IMP lost, damaged (due to breakage or wastage), not used, partially used,

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disposed of at the study site, or returned to the sponsor or designee must also be recorded on the appropriate forms. All supplies and pharmacy documentation must be made available throughout the study for UCB (or designee) to review.

The investigator (or designee) is responsible for retaining all used, unused, and partially used containers of IMP until returned or destroyed (all details are provided in the IMP Handling Manual).

The investigator may assign some of the investigator's duties for drug accountability at the study site to an appropriate pharmacist/designee.

The investigator must ensure that the IMP is used only in accordance with the protocol.

Periodically, and/or after completion of the clinical phase of the study, all used (including empty containers)/partially used, unused, damaged, and/or expired IMP must be reconciled and either destroyed at the site according to local laws, regulations, and UCB Standard Operating Procedures (SOPs) or returned to UCB (or designee). Investigational medicinal product intended for the study cannot be used for any other purpose than that described in this protocol.

7.7 Procedures for monitoring study participant compliance

Study participant compliance will be ensured by the administration of IMP by sc infusion by designated site personnel. Drug accountability must be recorded on the Drug Accountability form.

7.8 Concomitant medications/treatments

7.8.1 Permitted concomitant treatments (medications and therapies)

Concomitant treatments/medications permitted at a stable dose during the course of the study are detailed in Table 7-3.

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Table 7-3: Permitted concomitant medications

Permitted medication	Allowed dosages	Comment
Oral corticosteroids (prednisolone)	≤30mg/day	Stable [redacted] prior to entry
Methotrexate	≤30mg/week	[redacted] stable dose [redacted] prior to entry
Mycophenolate mofetil	≤3g/day	[redacted] stable dose [redacted] prior to entry
Cyclosporine [a]	≤5mg/kg/day for unmodified ≤4mg/kg/day for modified (microemulsion)	[redacted] stable dose [redacted] prior to entry
Azathioprine	≤3mg/kg/day	[redacted] stable dose [redacted] prior to entry
Tacrolimus [b]	≤5mg/day	[redacted] stable dose [redacted] prior to entry

[a] Doses higher than listed are permissible if plasma trough level is ≤300ng/L.
[b] If the total daily weight-based dose is >5mg, then a plasma trough level should be checked to ensure study participant is not above the recommended therapeutic range.

The use of cannabidiols and medicinal marijuana (prescribed by a physician) is also permitted. When applicable, the study participant must be on a stable dose of cannabidiols and/or medicinal marijuana for [redacted] prior to Screening Visit and remain stable for the duration of the study.

7.8.2 Prohibited concomitant treatments (medications and therapies)

The following concomitant medications are prohibited during the Treatment Period:

- IVIg and SCIg (refer to Section 7.8.3)
- All biologics including rituximab
- Cyclophosphamide
- Pimecrolimus
- IPP-201101 (Lupuzor™)
- Systemic dexamethasone
- PLEX
- IA

If a study participant requires or takes IVIg, SCIg, PLEX, dexamethasone, or rituximab, they must be discontinued from IMP. In all other cases of intake of prohibited concomitant medication, the investigator will (where possible) discuss with the Medical Monitor and/or Sponsor Study Physician and a decision will be made whether the study participant should discontinue IMP (see Section 6.4).

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If a study participant is discontinued from IMP they should be encouraged to complete Visit 26/PEOT and complete the Observation Period (see Table 5-1 and Section 6.4).

7.8.3 Rescue medication

If, at any time during this OLE study, a study participant relapses according to the predefined criteria for relapse as specified in Section 4.2.1 using the study participant's score on iRODS, INCAT, or maximum grip strength as assessed by the site personnel and supported by the medical judgement of the investigator, then rescue therapy must be considered and the study participant withdrawn from IMP (see Section 6.4). The study participant will return to the SOC Ig treatment (eg, IVIg of 2g/kg) at the investigator's discretion.

7.9 Blinding

Not applicable; this is an open-label study. However, in order to maintain the blind of the parent study (eg, CIDP01) study participant's IgG levels will be blinded to the investigator for the initial 4 weeks treatment of every study participant in CIDP04. The duration of 4 weeks may be adjusted during the course of the study based on results from CIDP01 and CIDP04.

7.10 Randomization and numbering of study participants

Randomization is not applicable in the current study. Study participants will be identified with the study participant number they received in the parent study.

An interactive response technology (IRT) will generate individual assignments for study participants, as appropriate, according to the visit schedule and the dose the study participant should receive.

The study participant number will be required in all communication between the investigator or designee and the IRT regarding a particular study participant.

8 STUDY PROCEDURES BY VISIT

Study visits should preferably be conducted at the same time of the day throughout the study. Details of the study assessments to be performed at specific time points prior to and after IMP administration are provided in Table 5-1. An outline of all assessments performed is provided in the following sections. The ICF should be completed before any assessment. The PROs should be conducted in the order specified in Section 10.4 immediately after ICF is completed (where applicable). The laboratory manual will provide further guidance on the order of sample collection. Additional assessments that may be required in case of infusion reactions or AEs of interest (severe headache, moderate to severe diarrhea, moderate to severe abdominal pain, or moderate to severe vomiting) are provided in Table 5-2; these assessments are not included in the by-visit study procedures within this section.

In case an on-site visit cannot be performed, the subsequent visit will be performed at the site instead of at home, and all safety assessments that should have been completed at the missed visit will be performed.

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8.1 Screening, Visit 1 (Weeks -5 to -2)

The Screening Visit is only for study participants with a gap period between the parent study and entry in CIDP04.

The following procedures will be performed at the Screening Visit (or as close as possible to the Screening date):

- Informed consent process including obtaining written informed consent from the study participant
- iRODS assessment
- Query for suicidality (C-SSRS)
- Tuberculosis Signs and Symptoms Questionnaire
- Record study participant demographics
- Verify (to the extent possible with available information at Screening, Visit 1) that study participant fulfills all the inclusion criteria and none of the exclusion criteria
- Medical history update
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (taken once during the visit)
- Body weight (Screening weight will be used for calculation of the infusion dose)
- Recording of AEs
- 12-lead ECG
- Full physical examination
- Full neurological examination
- Contact IRT
- Blood sample (the Laboratory Manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology, clinical chemistry, serology [including hepatitis C and hepatitis B virus-antibodies, HIV1, and HIV2], and interferon gamma release assay [IGRA] for active and latent TB)
  - Serum pregnancy test for women of childbearing potential
  - Immunoglobulins (total IgG and IgG subclasses)
  - Vaccination-specific antibody titers (tetanus and influenza Type A)
- Urine sample for urinalysis
- INCAT assessment

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- Assessment of grip strength by site personnel
- RT-MRC assessment
- Provide an appointment to the next visit according to the following guidance:
  - For study participants on an IVIg 3- to 6-week regimen, Baseline Visit should occur 1 week before the next planned IVIg dose (according to the Baseline IVIg regimen). However, if that specific date is not possible, the Baseline Visit (Visit 2) could be up to 1 week after that date.
  - Study participants on a 2-week IVIg treatment regimen will continue on their regular schedule for 1 further IVIg treatment until Visit 2. Visit 2 will occur 1 week before the planned IVIg dose. However, if that specific date is not possible, Visit 2 could be up to 1 week after that date.
  - Study participants on a weekly SCIg treatment regimen will continue on their regular schedule for at least 1 further SCIg treatment until Visit 2. Visit 2 should occur on the day of a planned dose (according to the Baseline SCIg regimen). However, if that specific date is not possible, Visit 2 should be within a window ±2 days of that date.

  This will ensure continuation of treatment so that study participants do not relapse prior to start of study treatment.

8.2 Treatment Period Part 1, Visits 2 to 25 (Weeks 1 to 24)

During the 24-week Treatment Period, the at-home visits will be conducted by fully trained healthcare professional visiting the study participant at his/her home. Alternatively, these visits can be conducted at the site as deemed necessary by site personnel and/or study participant. Where dosing is done at home, the same safety monitoring schedule will be followed as if in clinic. The home nurse will be present during the full duration of the visit. Home visits can be conducted in case the following conditions are met:

- The study participant is willing to be dosed and monitored at home over a 2-hour period by a home nurse.
- The study participant has shown good acute tolerability to previous administrations of IMP (namely, he/she must have had no moderate or severe infusion reactions or other AEs that the investigator considers could increase the risk of home administration).
- The study participant does not require specific medical supervision based on his/her medical history/condition.
- The team delivering the home dose must be trained in the identification and management of infusion reactions and hypersensitivity and must have access to immediate treatments (eg, an EpiPen).
- The study participant's home allows rapid access to emergency treatment if required (ie, the study participant must not live so remotely that a reasonable arrival time of an ambulance could not be predicted).
- The investigator is contactable to support the healthcare provider if needed.

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- UCB has not requested to limit the possibility to perform home visits (eg, based on DMC recommendation).

The investigator will be asked to complete a checklist confirming all criteria have been fully evaluated and met before the first home dosing visit can take place, and will be reconfirmed in case of changes to the study participant's condition. This checklist will be shared with the UCB Study Physician and reviewed before IMP administration in a home setting can take place.

8.2.1 Visit 2, Baseline (Week 1)

The following procedures will be performed at Visit 2 (Week 1). If study participant enters CIDP04 at Visit 2 and the assessment was performed at the last visit in the parent study (eg, CIDP01) (or at Visit 16 for NF-L), the assessment will not be repeated and will be marked as "not to repeat" in the list below:

- Informed consent process including obtaining written informed consent from the study participant (for study participants who did not perform Screening Visit [Visit 1])
- PROs should be conducted in the order specified in Section 10.4:
  - iRODS assessment - to be performed before any other assessment (not to repeat)
  - CIDP PRO instrument (not to repeat)
  - Fatigue scale (not to repeat)
  - PGIS (not to repeat)
  - PGIC (not to repeat) - not required for study participants who had a Screening Visit
- Query for suicidality (not to repeat)
- Record study participant demographics (for study participants who did not perform Screening Visit [Visit 1])
- Verify that study participant fulfills all the inclusion criteria and none of the exclusion criteria (for study participants who did not perform Screening Visit [Visit 1])
- Withdrawal criteria assessment
- Medical history update (for study participants who did not perform Screening Visit [Visit 1])
- Prior and concomitant medications (not to repeat)
- Concomitant medical procedures (not to repeat)
- Vital signs (prior to IMP administration, at the end of the infusion, at 2 and 4h after the end of the infusion)
- Body weight assessment (Visit 2 weight will be used for calculation of the infusion dose for study participants without screening visit) (not to repeat)
- Recording of AEs (not to repeat)
- Full physical examination (not to repeat)
- Full neurological examination (not to repeat)

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- 12-lead ECG (not to repeat)
- Blood sample (all samples should be taken predose unless otherwise specified; the Laboratory Manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology, clinical chemistry, and IGRA for active and latent TB) (not to repeat)
  - PK of rozanolixizumab (predose and 4h postdose) (not to repeat predose sample if performed at last visit in the parent study)
  - ADA (anti-rozanolixizumab antibodies) (not to repeat)
  - Serum complement (C3, C4) and plasma complement (C3a, C5a)
  - Serum cytokines (predose)
  - Immunoglobulins (total IgG and IgG subclasses) (not to repeat)
  - IgA, IgM, IgE (not to repeat)
  - CIDP-specific auto-antibodies (not to repeat except if last visit in the parent study was FV)
  - NF-L (not to repeat)
  - Exploratory biomarker analysis
  - Serum pregnancy test for women of childbearing potential (not to repeat if performed within 5 weeks of entry in CIDP04)
- Urine sample for urinalysis (not to repeat)
- Urine pregnancy test for women of childbearing potential (which must be confirmed negative prior to study participant dosing) (not to repeat)
- Contact IRT
- Administer IMP
- INCAT assessment (predose) (not to repeat)
- Assessment of grip strength by site personnel (predose) (not to repeat)
- RT-MRC assessment (not to repeat) (predose)

8.2.2 Visit 3 (Week 2)

The following procedures will be performed at Visit 3 (Week 2):

- iRODS assessment - to be performed before any other assessment
- Query for suicidality (predose)
- Withdrawal criteria assessment
- Prior and concomitant medications

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- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion, at 2 and 4h after the end of the infusion)
- Recording of AEs
- Brief physical examination
- Brief neurological examination
- 12-lead ECG
- Contact IRT
- Administration of IMP
- Urine sample for urinalysis (predose)
- Urine pregnancy test for women of childbearing potential (which must be confirmed negative prior to study participant dosing)
- Blood sample (all samples should be taken predose unless otherwise specified; the Laboratory Manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - Serum complement (C3, C4) and plasma complement (C3a, C5a) (predose and 4h postdose)
  - Serum cytokines (predose and 4h postdose)
  - Immunoglobulins (total IgG and IgG subclasses)
  - IgA, IgM, IgE
  - Exploratory biomarker analysis
- INCAT assessment
- RT-MRC assessment
- Assessment of grip strength by site personnel

8.2.3 Visit 4 (Week 3)

The following procedures will be performed at Visit 4 (Week 3):

- iRODS assessment - to be performed before any other assessment
- Query for suicidality (predose)
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures

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- Vital signs (prior to IMP administration, at the end of the infusion, at 2 and 4h after the end of the infusion)
- 12-lead ECG
- Recording of AEs
- Brief physical examination
- Brief neurological examination
- Contact IRT
- Administration of IMP
- Urine sample for urinalysis (predose)
- Urine pregnancy test for women of childbearing potential (which must be confirmed negative prior to study participant dosing)
- Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - PK of rozanolixizumab (predose and 4h postdose)
  - ADA (anti-rozanolixizumab antibodies)
  - Immunoglobulins (total IgG and IgG subclasses)
  - IgA, IgM, IgE
- INCAT assessment (predose)
- RT-MRC assessment (predose)
- Assessment of grip strength by site personnel

8.2.4 Visit 5 (Week 4)

The following procedures will be performed at Visit 5 (Week 4):

- iRODS assessment– to be performed before any other assessment
- Query for suicidality (predose)
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)
- 12-lead ECG
- Recording of AEs

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- Brief physical examination
- Brief neurological examination
- Urine sample for urinalysis and urine pregnancy test
- Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - Immunoglobulins (total IgG, IgG subclasses)
  - IgA, IgM, IgE
- Contact IRT
- Administer IMP
- INCAT assessment
- RT-MRC assessment
- Assessment of grip strength by site personnel

8.2.5 Visit 6 (Week 5)

The following procedures will be performed at Visit 6 (Week 5):

- PROs should be conducted in the order specified in Section 10.4:
  - iRODS assessment – to be performed before any other assessment
  - CIDP PRO instrument
  - Fatigue scale
  - PGIS
  - PGIC
- Query for suicidality
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)
- Recording of AEs
- Brief physical examination
- Brief neurological examination
- Urine sample for urinalysis and urine pregnancy test

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- Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - Immunoglobulins (total IgG and IgG subclasses)
  - IgA, IgM, IgE
  - CIDP-specific auto-antibodies
- Contact IRT
- Administer IMP
- INCAT assessment
- RT-MRC assessment
- Assessment of grip strength by site personnel

8.2.6 Visit 7 (Week 6), Home Visit

The following procedures will be performed at Visit 7 (Week 6) by a healthcare professional visiting the study participant at his/her home:

- Query for suicidality
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)
- Recording of AEs
- Urine pregnancy test
- Contact IRT
- Administer IMP

8.2.7 Visit 8 (Week 7)

The following procedures will be performed at Visit 8 (Week 7):

- iRODS assessment - to be performed before any other assessment
- Query for suicidality
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures

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- Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)
- 12-lead ECG
- Recording of AEs
- Brief physical examination
- Brief neurological examination
- Urine sample for urinalysis and urine pregnancy test
- Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - PK of rozanolixizumab (predose and 4h postdose)
  - ADA (anti-rozanolixizumab antibodies)
  - Serum complement (C3, C4) and plasma complement (C3a, C5a) (predose and 4h postdose)
  - Serum cytokines (predose and 4h post dose)
  - Vaccination-specific antibody titers (tetanus and influenza Type A)
  - Immunoglobulins (total IgG and IgG subclasses)
  - NF-L
  - IgA, IgM, IgE
  - Exploratory biomarker analysis
- Contact IRT
- Administer IMP
- INCAT assessment
- RT-MRC assessment
- Assessment of grip strength by site personnel

8.2.8 Visits 9 (Week 8), Home Visit

The procedures performed at this visit are the same as performed for Visit 7 (Week 6); refer to Section 8.2.6 for details.

8.2.9 Visits 10, 14, 18, and 22 (Weeks 9,13, 17, and 21)

The following procedures will be performed at Visits 10, 14, 18, and 22 (Weeks 9, 13, 17, and 21):

- PROs should be conducted in the order specified in Section 10.4:
  - iRODS assessment – to be performed before any other assessment

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  - CIDP PRO instrument
  - Fatigue scale
  - PGIS
  - PGIC
- Query for suicidality
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)
- 12-lead ECG
- Recording of AEs
- Brief physical examination
- Brief neurological examination
- Urine sample for urinalysis and urine pregnancy test
- Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - PK of rozanolixizumab (does not apply to Visit 10)
  - ADA (anti-rozanolixizumab antibodies) (does not apply to Visit 10)
  - Serum complement (C3, C4) and plasma complement (C3a, C5a) (predose and 4h postdose)
  - Serum cytokines (predose and 4h postdose)
  - Vaccination-specific antibody titers (tetanus and influenza Type A) (only at Visit 14)
  - Immunoglobulins (total IgG and IgG subclasses)
  - IgA, IgM, IgE
  - CIDP-specific auto-antibodies
  - Exploratory biomarker analysis
- Contact IRT
- Administer IMP
- INCAT assessment
- RT-MRC assessment

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- Assessment of grip strength by site personnel

8.2.10 Home Visits 11 to 13, 15 to 17, 19 to 21, and 23 to 25 (Weeks 10 to 12, 14 to 16, 18 to 20, and 22 to 24)

The following procedures will be performed at Visits 11 to 13, 15 to 17, 19 to 21, and 23 to 25 (Weeks 10 to 12, 14 to 16, 18 to 20, and 22 to 24) by a healthcare professional visiting the study participant at his/her home:

- Query for suicidality
- Tuberculosis Signs and Symptoms Questionnaire (only at Visit 13, 17, 21, and 25)
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)
- Recording of AEs
- 12-lead ECG (only at Visits 12, 16, 20, and 24)
- Blood sample for clinical laboratory tests (ie, hematology and clinical chemistry) (only at Visits 12, 16, 20, and 24)
- Urine sample for urinalysis (only at Visits 12, 16, 20, and 24)
- Urine pregnancy test
- Contact IRT
- Administer IMP

8.3 Treatment Period Part 2 (Weeks 25 to 76)

Entry into the Treatment Period (Part 2) will be subject to a careful individual assessment of the benefit-risk for each study participant completing Treatment Period (Part 1) following a discussion with the Sponsor's Medical Monitor and/or Study Physician. The first visit of Treatment Period Part 2 will be performed at site at Week 25 followed by 3 weekly visits at the study participant's home. This sequence will be repeated until the end of the Treatment Period Part 2. The visits during this period will be numbered sequentially.

Study participants may choose to self-administer the IMP during Treatment Period 2 under supervision of a nurse and after having received appropriate training.

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8.3.1 Additional site visits during maximum 52-week Treatment Period Part 2 (monthly starting at Week 25) or until availability of an Access Program (whichever comes first)

The first visit of Treatment Period Part 2 will be performed on site at Week 25. Site visits will be performed monthly. The following procedures will be performed at monthly frequency unless otherwise defined:

- PROs should be conducted in the order specified in Section 10.4:
  - iRODS assessment – to be performed before any other assessment
  - Fatigue scale (every 24 weeks)
  - CIDP PRO instrument (every 24 weeks)
  - PGIS (every 24 weeks)
  - PGIC (every 24 weeks)
- Query for suicidality
- Tuberculosis Signs and Symptoms Questionnaire (every 12 weeks)
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion)
- Body weight (Week 25 and Week 49)
- Recording of AEs
- Brief physical examination
- Brief neurological examination
- 12-lead ECG (on-site visits only [Weeks 25, 37, 49, 61])
- Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - PK of rozanolixizumab (on-site visits only [Weeks 25, 37, 49, 61])
  - ADA (anti-rozanolixizumab antibodies) (on-site visits only [Week 25, 37, 49, 61])
  - Serum complement (C3, C4) and plasma complement (C3a, C5a) (predose and 4h postdose) (at Weeks 25 and 73)
  - Serum cytokines (predose and 4h postdose) (at Weeks 25 and 73)
  - Vaccination-specific antibody titers (tetanus and influenza Type A) (on-site visits only [Weeks 25, 37, 49, 61])
  - Immunoglobulins (total IgG and IgG subclasses)

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  - IgA, IgM, IgE (on-site visits only [Weeks 25, 37, 49, 61])
  - NF-L (only at Week 25)
  - CIDP specific auto-antibodies (only at Week 25)
- Urine pregnancy test
- Contact IRT
- Administer IMP – self-administration by the study participant under the supervision of the nurse (to confirm that study participant is proceeding correctly) may be considered provided the participant is willing to do so, the participant has been adequately trained by the site personnel according to Self-administration training guidance document
- INCAT assessment
- Assessment of grip strength by site personnel

8.3.2 Additional home visits during Treatment Period Part 2 (weekly in between site visits starting at Week 26 or until availability of an Access Program (whichever comes first)

The following procedures will be performed during the Treatment Period Part 2 by a healthcare professional visiting the study participant at his or her home. Visits will be performed weekly in between monthly site visits (Section 8.3.1):

- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (prior to IMP administration, at the end of the infusion)
- Recording of AEs
- Contact IRT
- Administer IMP (unless IMP is temporarily discontinued (see Section 6.4.1.3) – self-administration by the study participant under the supervision of the home nurse may be considered provided the participant is willing to do it and has been adequately trained by the site personnel according to Self-administration training guidance document.

8.4 Observation Period, Visits 26 to 29 (Weeks 25 to 32 study participants completing Treatment Period Part 1 only and Weeks 77 to 84 for study participants completing Treatment Period Part 1 and Part 2)

Following the final dose of rozanolixizumab at Week 24 (Visit 25) or Week 76, 4 subsequent visits will be scheduled over 8 weeks (Visits 26 to 29) to collect safety and efficacy data for study-related outcome measures and procedures unless the study participant continues rozanolixizumab treatment under an Access Program or equivalent. In the latter case, only the PEOT Visit (Visit 26) will be performed. Visit 27 and Visit 28 are home nursing visits to be

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conducted by a healthcare professional visiting the study participant at his/her home; these visits can be conducted at the site as deemed necessary by site personnel and/or study participant.

All study participants who do not continue on rozanolixizumab in an Access Program should perform all visits of the Observation Period, including the FV (scheduled 8 weeks after the final dose of IMP). If at any time during the Observation Period the study participant relapses (according to the medical judgement of the investigator supported by, eg, study participant's score on iRODS, INCAT, or maximum grip strength [assessed by site personnel]), then rescue medication must be considered. The study participant will return to the SOC (ie, Ig treatment) as rescue medication at the time of relapse.

8.4.1 Visit 26 (Week 25 or Week 77 or PEOT)

The following procedures will be performed at Visit 26 (Week 25 or Week 77 or PEOT):

- PROs should be conducted in the order specified in Section 10.4:
  - iRODS assessment – to be performed before any other assessment
  - Fatigue scale
  - CIDP PRO instrument
  - PGIS
  - PGIC
- Query for suicidality
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (taken once during the visit)
- Body weight
- 12-lead ECG
- Recording of AEs
- Brief physical examination
- Brief neurological examination
- Urine sample for urinalysis
- Urine pregnancy test for women of childbearing potential
- Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:
  - Clinical laboratory tests (ie, hematology and clinical chemistry)
  - PK of rozanolixizumab
  - ADA (anti-rozanolixizumab antibodies)

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  - Immunoglobulins (total IgG, IgG subclasses)
  - NF-L (Visit 26 [Week 25] only or PEOT only if Treatment Period 1 is performed)
  - IgA, IgM, IgE
  - CIDP specific auto-antibodies (Visit 26 [Week 25] only or PEOT only if Treatment Period 1 is performed)
  - Vaccination-specific antibody titers (tetanus and influenza Type A)
- Contact IRT
- INCAT assessment
- RT-MRC assessment (Visit 26 [Week 25] only)
- Assessment of grip strength by site personnel

8.4.2 Visits 27 and 28 (Weeks 27 and 29, and at 79 and 81), Home Visits

The following procedures will be performed at Visits 27 and 28 (Weeks 27 and 29, and at 79 and 81) by a healthcare professional visiting the study participant at his/her home:

- Query for suicidality
- Withdrawal criteria assessment
- Prior and concomitant medications
- Concomitant medical procedures
- Vital signs (taken once during the visit)
- Recording of AEs
- Urine pregnancy test

8.4.3 Visit 29/FV (Week 32/84)

The following procedures will be performed at Visit 29/FV (Week 32/84):

- PROs should be conducted in the order specified in Section 10.4:
  - iRODS assessment – to be performed before any other assessment
  - Fatigue scale
  - CIDP (PRO instrument)
  - PGIS
  - PGIC
- Query for suicidality
- Prior and concomitant medications
- Concomitant medical procedures

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- Vital signs (taken once during the visit)
- Body weight
- 12-lead ECG
- Recording of AEs
- Full physical examination
- Full neurological examination
- Urine sample for urinalysis
- Urine pregnancy test for women of childbearing potential
- Blood sample for (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection):
  - Clinical laboratory tests (ie, hematology, clinical chemistry, and IGRA for active and latent TB)
  - ADA (anti-rozanolixizumab antibodies)
  - Immunoglobulins (total IgG and IgG subclasses)
  - IgA, IgM, IgE
  - CIDP-specific auto-antibodies
- Tuberculosis Signs and Symptoms Questionnaire
- Contact IRT
- INCAT assessment
- RT-MRC assessment
- Assessment of grip strength by site personnel

8.5 Premature end of treatment and Final Visit

All study participants who withdraw early from the Treatment Period should attend a PEOT Visit, which will be scheduled as close as possible to the date of the decision for the study or treatment withdrawal.

Study participants are encouraged to complete all visits of the Observation Period following the PEOT Visit by either coming to the clinic or as home nursing visits, if appropriate.

In case a study participant is not willing to attend the visits in the Observation Period, the study participant should still be strongly encouraged to attend at least the PEOT Visit and the FV.

The FV should be scheduled 8 weeks after their final dose of IMP.

The assessments to be done at the PEOT Visit and the FV are the same as those at Visit 26 and Visit 29, respectively.

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A study participant entering the Access Program after completion of part or full Treatment Period 2 without any relapse will not complete the Observation Period but will only perform the PEOT/V26 one week after the last IMP dispensing for the study.

8.6 Unscheduled Visit/Telephone call

At any time, a study participant may have an unscheduled study visit/telephone call if the investigator and/or the study participant deem it necessary. An unscheduled visit may be conducted due to safety or efficacy reasons and appropriate assessments will be conducted in relation to the reason for the visit. All information, including reason for visit, any information on AEs, etc, should be collected in the source documents and recorded in the appropriate section of the eCRF.

9 ASSESSMENT OF SAFETY

9.1 Adverse events

9.1.1 Definitions

9.1.1.1 Adverse event

An AE is any untoward medical occurrence in a patient or clinical investigation study participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

In order to ensure complete safety data collection, all AEs occurring during the study (ie, after the signing of the ICF), including any pretreatment and posttreatment periods required by the protocol, must be reported in the eCRF even if no IMP was taken but specific study procedures were conducted. This includes all AEs not present prior to the initial visit and all AEs that recurred or worsened after the initial visit.

Signs or symptoms of the condition/disease for which the IMP is being studied should be recorded as AEs only if their nature changes considerably or their frequency or intensity increases in a clinically significant manner as compared to the clinical profile known to the investigator from the study participant's history or the Baseline Period.

9.1.1.2 Serious adverse event

Once it is determined that a study participant experienced an AE, the seriousness of the AE must be determined. An SAE must meet 1 or more of the following criteria:

- Death
- Life-threatening

  (Life-threatening does not include a reaction that might have caused death had it occurred in a more severe form.)
- Significant or persistent disability/incapacity
- Congenital anomaly/birth defect (including that occurring in a fetus)

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- Important medical event that, based upon appropriate medical judgment, may jeopardize the patient or study participant and may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious

  (Important medical events may include, but are not limited to, potential Hy's Law [see Section 9.2], allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.)

- Initial inpatient hospitalization or prolongation of hospitalization

  (A patient admitted to a hospital, even if he/she is released on the same day, meets the criteria for the initial inpatient hospitalization. An emergency room visit that results in admission to the hospital would also qualify for the initial inpatient hospitalization criteria. However, emergency room visits that do not result in admission to the hospital would not qualify for this criteria and, instead, should be evaluated for 1 of the other criteria in the definition of serious [eg, life-threatening adverse experience, important medical event].

  Hospitalizations for reasons not associated with the occurrence of an AE [eg, preplanned surgery or elective surgery for a pre-existing condition that has not worsened or manifested in an unusual or uncharacteristic manner] do not qualify for reporting. For example, if a study participant has a condition recorded on his/her medical history and later has a preplanned surgery for this condition, it is not appropriate to record the surgery or hospitalization as an SAE, since there is no AE upon which to assess the serious criteria. Please note that, if the pre-existing condition has worsened or manifested in an unusual or uncharacteristic manner, this would then qualify as an AE and, if necessary, the seriousness of the event would need to be determined.)

9.1.1.2.1 Anticipated serious adverse events

The following Anticipated SAEs, fatigue, infection and headache are anticipated to occur in the population studied in this protocol at some frequency that is independent of drug exposure.

This information does not change the investigator's obligation to report all SAEs (including Anticipated SAEs) as detailed in Section 9.1.2.3.

9.1.1.3 Adverse events of special interest

An AE of special interest is any AE that a regulatory authority has mandated be reported on an expedited basis, regardless of the seriousness, expectedness, or relatedness of the AE to the administration of a UCB product/compound.

Potential Hy's Law, defined as ≥3xULN ALT or AST with coexisting ≥2xULN total bilirubin in the absence of ≥2xULN ALP, with no alternative explanation for the biochemical abnormality, must ALWAYS be reported to UCB as an AE of special interest (ie, without waiting for any additional etiologic investigations to have been concluded). Follow-up information should then be reported if an alternative etiology is identified during investigation and monitoring of the study participant.

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9.1.1.4 Adverse events of interest

For rozanolixizumab, AEs of interest that require immediate reporting to UCB are:

- Severe headache
- Moderate to severe diarrhea
- Moderate to severe abdominal pain
- Moderate to severe vomiting

These events should be reported to UCB within 24h, regardless of seriousness, by completing the eCRF. If the electronic system is unavailable for more than 24 hours, then the site will use the paper SAE data collection tool (see Section 9.1.2.3 for the reporting process).

Additional assessments that may be required in case of AEs of interest are presented in Table 5-2.

9.1.2 Procedures for reporting and recording adverse events

The study participant will be given the opportunity to report AEs spontaneously. A general prompt will also be given at each study visit to detect AEs. For example:

"Did you notice anything unusual about your health (since your last visit)?"

In addition, the investigator should review any self-assessment procedures (eg, e-diary cards) employed in the study.

9.1.2.1 Description of adverse events

When recording an AE, the investigator should use the overall diagnosis or syndrome using standard medical terminology, rather than recording individual symptoms or signs. The eCRF and source documents should be consistent. Any discrepancies between the study participant's own words on his/her own records (eg, e-diary card) and the corresponding medical terminology should be clarified in the source documentation.

Details for completion of the Adverse Event eCRF (including judgment of relationship to IMP) are described in the eCRF Completion Guidelines.

- Mild: An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities
- Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities
- Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.
- An event is defined as 'serious' when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe (eg, a severe AE may be either serious or not serious, depending on whether these criteria are also met).

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9.1.2.2 Rule for repetition of an adverse event

An increase in the intensity of an AE should lead to the repetition of the AE being reported with:

- The outcome date of the first AE that is not related to the natural course of the disease being the same as the start date of the repeated AE, and the outcome of "worsening"
- The AE verbatim term being the same for the first and repeated AE, so that the repeated AE can be easily identified as the worsening of the first one

9.1.2.3 Additional procedures for reporting serious adverse events

If an SAE is reported, UCB must be informed within 24h of receipt of this information by the site. The primary mechanism for reporting an SAE to UCB will be the eCRF (using the eCRF SAE page). If the electronic system is unavailable for more than 24 hours, the investigator must forward to UCB (or its representative) a duly completed paper SAE data collection tool provided by UCB, even if the data are incomplete, or if it is obvious that more data will be needed in order to draw any conclusions (see contact information for SAE reporting listed in the Serious Adverse Event Reporting section at the front of the protocol). The site will enter the SAE data into the electronic system as soon as it becomes available.

The investigator SAE Report form must be completed in English.

It is important for the investigator, when completing the SAE data collection tool, to include the assessment as to a causal relationship between the SAE and the IMP administration. This insight from the investigator is very important for UCB to consider in assessing the safety of the IMP and in determining whether the SAE requires reporting to the regulatory authorities in an expedited manner.

Additional information (eg, autopsy or laboratory reports) received by the investigator must be provided within 24h. All documents in the local language must be accompanied by a translation in English, or the relevant information included in the same document must be summarized in the investigator SAE data collection tool.

The investigator is specifically requested to collect and report to UCB (or its representative) any SAEs (even if the investigator is certain that they are in no way associated with the IMP), up to 30 days from the end of the study for each study participant, and to also inform participating study participants of the need to inform the investigator of any SAE within this period. Serious AEs that the investigator thinks may be associated with the IMP must be reported to UCB regardless of the time between the event and the end of the study.

Upon receipt of the SAE data collection tool, UCB will perform an assessment of expectedness of the reported SAE. The assessment of the expectedness of the SAE is based on the IB.

After the study is completed at a given site, the electronic data collection tool will be taken off-line to prevent the entry of new data or changes to existing data.

If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic data collection tool has been taken off-line, then the site can report this information on a paper SAE form.

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9.1.2.4 Immediate reporting of adverse events

The following AEs must be reported immediately using the SAE data collection tool according to the procedure in Section 9.1.2.3:

- SAE: AE that the investigator classifies as serious by the above definitions regardless of causality
- Suspected transmission of an infectious agent via a medicinal product
- AE of special interest (see Section 9.1.1.3)
- AE of interest (see Section 9.1.1.4)
- Confirmed LTBI, active TB, and NTMBI (see Section 9.3.6)

9.1.3 Follow up of adverse events

An AE should be followed until it has resolved, has a stable sequelae, the investigator determines that it is no longer clinically significant, or the study participant is lost to follow up. This follow-up requirement applies to AEs, SAEs, and AEs of special interest; further details regarding follow up of PDILI events is provided in Section 9.2.1.4.

If an AE is ongoing at the end of the study for a study participant, follow up should be provided until resolution/stable level of sequelae is achieved, or until the investigator no longer deems that it is clinically significant, or until the study participant is lost to follow up. If no follow up is provided, the investigator must provide a justification. The follow up will usually be continued for 8 weeks after the study participant has discontinued his/her IMP.

Information on SAEs obtained after clinical database lock will be captured through the Patient Safety (PS) database without limitation of time.

9.1.4 Pregnancy

If an investigator is notified that a study participant has become pregnant after the first intake of any IMP, the investigator must immediately notify UCB's PS department by providing the completed Pregnancy Report and Outcome form (for contact details see SAE reporting information at the beginning of this protocol). The study participant should be withdrawn from the study as soon as pregnancy is known (by positive pregnancy test), and the following should be completed:

- The study participant should return for a PEOT Visit.
- The study participant should immediately stop the intake of the IMP as instructed at the PEOT Visit.
- An FV should be scheduled 8 weeks after the study participant has discontinued her IMP.

The investigator must inform the study participant of information currently known about potential risks and about available treatment alternatives.

The pregnancy will be documented on the Pregnancy Report and Outcome form provided to the investigator. The progression of the pregnancy and the eventual birth (if applicable) must be followed up using the Pregnancy Report and Outcome form in which the investigator has to

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report on the health of the mother and of the child. Every reasonable attempt should be made to follow the health of the child for 30 days after birth for any significant medical issues. In certain circumstances, UCB may request that follow up is continued for a period longer than 30 days. If the study participant is lost to follow up and/or refuses to give information, written documentation of attempts to contact the study participant needs to be provided by the investigator and filed at the site. UCB's PS department is the primary contact for any questions related to the data collection for the pregnancy, eventual birth, and follow up.

In cases where the partner of a male study participant enrolled in a clinical study becomes pregnant, the investigator or designee is asked to contact the study participant to request consent of the partner via the Partner Pregnancy Consent form that has been approved by the responsible IRB/IEC and should be available in the investigator site file. In case of questions about the consent process, the investigator may contact the UCB/contract research organization (CRO) contract monitor for the study. The investigator will complete the Pregnancy Report and Outcome form and send it to UCB's PS department (for contact details see SAE reporting information at the beginning of this protocol) only after the partner has agreed that additional information can be captured and has provided the signed Partner Pregnancy Consent form. UCB's PS department is also the primary contact for any questions related to the data collection for the partner pregnancy, eventual birth, and follow up.

A pregnancy becomes a SAE in the following circumstances: miscarriage, abortion (elective or spontaneous), unintended pregnancy after hormonal contraceptive failure (if the hormonal contraceptive was correctly used), ectopic pregnancy, fetal demise, or any congenital anomaly/birth defect of the baby. Those SAEs must be additionally reported using the investigator SAE data collection tool.

9.1.5 Suspected transmission of an infectious agent via a medicinal product

For the purposes of reporting, any suspected transmission of an infectious agent via a medicinal product should be considered as an SAE; such cases must be reported immediately, recorded in the AE module of the eCRF, and followed as any other SAE. Any organism, virus, or infectious particle (eg, prion protein transmitting transmissible spongiform encephalopathy), pathogenic or nonpathogenic, is considered an infectious agent.

9.1.6 Overdose of investigational medicinal product

Excessive dosing (beyond that prescribed in the protocol and including overdose ie, >10% above [redacted]) should be recorded in the eCRF. Any SAE or nonserious AE associated with excessive dosing must be followed as any other SAE or nonserious AE. These events are only considered AEs or SAEs if there are associated clinical signs and symptoms or if the act of taking the excess medicine itself is an AE or SAE (eg, suicide attempt).

9.1.7 Safety signal detection

Selected data from this study will be reviewed periodically to detect as early as possible any safety concern(s) related to the IMP so that investigators, clinical study participants, regulatory authorities, and IRBs/IECs will be informed appropriately and as early as possible. A DMC will be responsible for monitoring safety data during the study. Further details are provided in Section 14.7.

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The Study Physician or medically qualified designee/equivalent will conduct an ongoing review of SAEs and perform ongoing SAE reconciliations in collaboration with the PS representative.

As appropriate for the stage of development and accumulated experience with the IMP, medically qualified personnel at UCB may identify additional safety measures (eg, AEs, vital signs, laboratory or ECG results) for which data will be periodically reviewed during the course of the study.

9.1.8 Suicidality

At Screening, the investigator will query each study participant if he/she has a lifetime history of suicide attempt (including an active attempt, interrupted attempt, or aborted attempt) or suicidal ideation in the past 6 months. A full C-SSRS "Lifetime recent" assessment will be performed only when the study participant has a positive response to this query. This scale will be assessed by trained study personnel. When suicide attempt or suicidal ideation is confirmed by a positive response (Yes) to either Question 4 or Question 5 of the C-SSRS, the study participant must be excluded and immediately referred to a Mental Healthcare Professional.

At each clinical visit, the investigator must query the suicidal ideation since the last visit. A full C-SSRS "Since last visit" assessment will be performed only when the study participant has a positive response to this query. When suicide attempt or suicidal ideation is confirmed by a positive response (Yes) to either Question 4 or Question 5 of the C-SSRS, the study participant must be withdrawn and immediately referred to a Mental Healthcare Professional. Details of the case must be documented by the investigator (principal investigator or investigator physician, not site staff conducting the C-SSRS) and provided to UCB via the SAE reporting process.

9.1.9 Hypersensitivity and adverse reactions

The grading for infusion-related reactions according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 (Jun 2017) is provided in Table 9-4. In the event of a severe or life-threatening (ie, Grade 3 or 4) infusion reaction, the study participant must permanently discontinue IMP and be managed as described in Section 18.1.

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Table 9-4: Infusion-related reaction grading according to the NCI Common Terminology Criteria for adverse events version 5.0 (Jun 2017)

Grading	Infusion-related reaction
1	Mild transient reaction: infusion interruption not indicated; intervention not indicated
2	Moderate: Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (for example, antihistamines, NSAIDs, narcotics, iv fluids); prophylactic medications indicated for ≤24h
3	Severe: Prolonged (eg, not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae
4	Life-threatening consequences; urgent intervention indicated
5	Death

iv=intravenous; NCI=National Cancer Institute; NSAID=nonsteroidal anti-inflammatory drugs

In case of occurrence of a hypersensitivity reaction (except for local injection site reaction) and depending upon its severity, appropriate countermeasures will immediately be taken by the investigator. In the event the infusion reaction occurs during a home visit, the home nurse will be trained to follow all steps as detailed in the study manual and will liaise with the investigator for the proper handling of the case. Serum complement (C3, C4), plasma complement (C3a, C5a), and serum cytokine samples must be collected from study participants experiencing infusion reactions (Table 5-2).

If the investigator does not initially choose to discontinue the infusion of IMP and symptoms persist or escalate during continued infusion, the infusion should be stopped. In case of any severe infusion reaction(s), the infusion of IMP must be stopped immediately and appropriate treatment initiated, as necessary, at the discretion of the investigator and in accordance with the SOC. When infusion reactions occurred while the IMP has not been stopped, the investigator should closely assess the adequacy of home administrations (refer to Section 8.2) and consult with UCB Study Physician before considering home administration after the infusion reactions.

Suspected anaphylactic reactions should be diagnosed using Sampson's Criteria (Sampson et al, 2006) as described in Section 18.2. In the event of an anaphylactic reaction meeting Sampson criterion 1 or 2, the infusion must be discontinued immediately and emergency resuscitation measures implemented.

9.1.10 Management of headache

Based on current available clinical data, headache is the most commonly reported adverse drug reaction in study participants treated with rozanolixizumab. Study participants should be well informed of this potential adverse drug reaction and should be instructed on how to manage it.

Treatment of headaches should be as per national guidelines and take medical history of previous headaches, concomitant medication, and co-morbidities (eg, asthma) in consideration. In case of continued tolerance issues, and if symptomatic headache medication (eg, acetylsalicylic acid

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1000mg) is not sufficient, a further step can be to reduce dose of IMP to [redacted] (see Section 7.2).

Determination of the severity of headache will be consistent with National Cancer Institute CTCAE version 5.0. Severe headache is defined as severe pain limiting self-care activities of daily living (ADL). Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications. Treatment of headache will be provided as clinically indicated according to the national guidelines.

Study participants experiencing severe and/or serious headache will complete the Headache Questionnaire daily until resolution (ie, if headache becomes nonserious, moderate or mild, or completely resolved, whichever comes first). At the clinic visit when the severe headache is reported, the Headache Questionnaire will be followed by a neurological assessment (including fundoscopy). If the severe or serious headache is initially reported at a home visit or during a telephone call, the study participant should be reviewed at the study site as soon as is practically possible for further investigations. Study participants should be monitored for signs and symptoms suggestive of central nervous system involvement and evaluated immediately if other causes (eg, meningitis, intracranial bleeding) are suspected. Further neurological workup may be performed (if indicated) at the discretion of the investigator and may include a computed tomography scan, magnetic resonance imaging and/or a lumbar puncture for cerebral spinal fluid collection. In addition, samples for exploratory safety biomarkers should be collected for study participants experiencing severe or serious headache when possible (Table 5-2). These investigations will be performed to further understand the mechanism of headache in these study participants.

Details of neurological examination to be performed are provided in Section 9.3.4. The Headache Questionnaire will be provided in the study procedures manual.

9.1.11 Management of moderate or severe diarrhea

Moderate or severe diarrhea is defined as an increase of ≥4 stools per day over Baseline or incontinence due to urgency of diarrhea or new/prolonged hospitalization for management of diarrhea or limiting self-care ADL or life-threatening consequences requiring urgent medical intervention. Determination of the severity of diarrhea will be consistent with CTCAE version 5.0.

Stool collection and analysis will be performed for study participants reporting moderate or severe diarrhea. The frequency of stool sampling will be as clinically indicated in the opinion of the investigator and assessed per local guidance. Analysis of stool samples will be performed locally. In addition, collection of blood samples for the assessment of exploratory safety biomarkers is required for study participants with severe GI disturbances including diarrhea.

Treatment of diarrhea will be provided as clinically indicated according to the local guidelines.

9.2 Laboratory measurements

Blood and urine specimens for routine assay of hematology, clinical chemistry, and urinalysis testing, as well as pregnancy testing and serology testing will be performed according to the schedule of assessments (Table 5-1) to monitor the safety of study participants. All parameters will be assessed by the designated central laboratory with the exception of the urine pregnancy

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test prior to each dose. Specific details regarding the handling and processing of serum chemistry, hematology, and urinalysis samples are provided in the study laboratory manual.

The following laboratory parameters will be measured as detailed in Table 9-5.

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Table 9-5: Laboratory measurements

Hematology	Chemistry	Urinalysis [a]
Hemoglobin	ALP	pH
Hematocrit	ALT	Protein
RBC	AST	Glucose
WBC (including differential)	GGT	Ketone
Platelet count	Total bilirubin [b]	Urobilinogen
	LDH	Bilirubin
	Creatine kinase	Blood
Serology [c]	Total protein	Nitrite
HBsAg, HBcAb	Albumin	Leukocytes
HCV Ab	Alpha- and beta–globulins	
HIV (anti-HIV1 or anti-HIV2 antibodies)	Urea-nitrogen	
Tuberculosis	Creatinine	Albumin
	Triglycerides	Creatinine
	Total-cholesterol	
	LDL cholesterol	**Pregnancy test**
	HDL cholesterol	Serum HCG [d]
	Electrolytes (calcium, phosphate, sodium, potassium, chloride, and magnesium)	Urine HCG [e]
	Amylase	
	hsCRP	
	Procalcitonin	
	HBA1c [f]	

Ab=antibody; ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; GGT=gamma-glutamyltransferase; HBcAb=hepatitis B core antibody; HBsAg=hepatitis B surface antigen; HCG=human chorionic gonadotropin; HCV=hepatitis C virus; HDL=high density lipoprotein; HIV=human immunodeficiency virus; hsCRP=high sensitivity C-reactive protein; IGRA=interferon gamma release assay; IMP=investigational medicinal product; LDH=lactate dehydrogenase; LDL=low density lipoprotein; RBC=red blood cell; WBC=white blood cell

[a] Urine microscopy will be performed if urine is positive for protein, blood, nitrite, or leukocytes.

[b] Direct bilirubin will also be measured when total bilirubin is elevated.

[c] Serology performed at Screening only. An IGRA should be performed for active or latent tuberculosis testing.

[d] Serum pregnancy test performed) only for women of childbearing potential when study participant enters CIDP04 (either at Screening [Visit 1] or Baseline [Visit 2]).

[e] Urine pregnancy test (dipstick) for women of childbearing potential performed prior to dosing (and confirmed negative) at dosing visits and each visit of the Observation Period. Note that the final urinary pregnancy test of the study should be no longer than 90 days after the final dose of IMP.

[f] Performed at Screening only.

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9.2.1 Evaluation of PDILI

The PDILI IMP discontinuation criteria for this study are provided in Section 6.4.2, with the accompanying required follow-up investigation and monitoring detailed below. All PDILI events must be reported as AEs and reported to the study site and sponsor within 24h of learning of their occurrence. Any PDILI event that meets the criterion for potential Hy's Law must be reported as an AE of special interest, and, if applicable, also reported as an SAE (see Section 9.1.1.2).

Evaluation of PDILI consists of the diagnostic testing and continued monitoring included in Table 9-6 (specific tests dependent on laboratory results and corresponding symptoms) and consultation with a local hepatologist (if applicable; discussed in Section 9.2.1.1). The local hepatologist is the expert usually consulted by the treating physician for assessment and management of potential hepatic disease. This would usually be a hepatologist, but may be a gastroenterologist. Additional investigation and monitoring may be required and adapted based on the diagnosis after the cause of the liver injury/abnormality is confirmed (details in Section 9.2.1.4).

The results of all monitoring, including laboratory testing and other testing, should be made available to the study site and sponsor.

All initial tests resulting in abnormal hepatic laboratory values need to be repeated, but appropriate medical action must not be delayed waiting for the repeat result.

If tests are done locally for more rapid results, a concurrent sample should also be sent to the central laboratory whenever possible. Medical care decisions are to be made initially using the most rapidly available results and a conservative approach must be taken if the results from the 2 laboratory tests are significantly different. Data from the local and central laboratory are to be recorded on the applicable eCRF pages.

When IMP is discontinued, all concomitant medications and herbal supplements that are not medically necessary should also be discontinued. In these cases, the investigator should also consider dose reduction for medically necessary concomitant medication and consider changing any medically required concomitant medication known to be hepatotoxic to a suitable alternative.

When IMP is stopped due to PDILI (as described in Section 6.4.2), IMP must be permanently discontinued unless a subsequent alternative diagnosis fully explains the hepatic findings. If a subsequent alternative diagnosis fully explains the hepatic findings, and the requirements provided in Section 9.2.1.2.1 are met, rechallenge with IMP may be appropriate.

Rechallenge with a substance potentially causing drug-induced liver injury is dangerous, may be fatal, and must not occur.

Table 9-6 summarizes the approach to investigate PDILI.

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Table 9-6: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms [a] of hepatitis or hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
≥3xULN	≥2xULN [b]	NA	Hepatology consult.[c] Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and study participant discussed with Medical Monitor ASAP.	Immediate, permanent IMP discontinuation.	Essential: Must have repeat liver chemistry values and additional testing completed ASAP (see Section 9.2.1.3); recommended to occur at the site with HCP.	Monitoring of liver chemistry values at least twice per week until values normalize, stabilize, or return to within Baseline values.[d]
≥3xULN	NA	Yes		Immediate, temporary or permanent, IMP discontinuation.		
≥3xULN (and ≥2x Baseline) and <5xULN	<2xULN	No	Discussion with Medical Monitor required if the criterion that allows for IMP continuation is met.	Further investigation – immediate IMP discontinuation not required (see Section 9.2.1.2).	Not required unless otherwise medically indicated (at discretion of investigator).	
≥5xULN (and ≥2x Baseline)	<2xULN	No	Discussion with Medical Monitor required. Hepatology consult required if ALT or AST ≥8xULN	Immediate, permanent IMP discontinuation.	Essential: Every attempt must be made to have repeat liver chemistry values and additional testing completed within 48 hours at the site with HCP (see Section 9.2.1.3).	Monitoring of liver chemistry values at least twice per week until values normalize, stabilize, or return to within Baseline values.[d]

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Table 9-6: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms [a] of hepatitis or hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**

ALP=alkaline phosphatase; ALT=alanine aminotransferase; ASAP=as soon as possible; AST=aspartate aminotransferase; HCP=healthcare practitioner; IMP=investigational medicinal product; NA=not applicable; PDILI=potential drug-induced liver injury; ULN=upper limit of normal

[a] Hepatitis symptoms include fatigue, nausea, vomiting, and right upper quadrant pain or tenderness; hypersensitivity symptoms include eosinophilia (>5%), rash, and fever (without clear alternative cause).

[b] If the study participant also has ≥2xULN ALP, the possibility of an indication of biliary obstruction should be discussed with the Medical Monitor.

[c] Details provided in Section 9.2.1.1. The local hepatologist is the expert usually consulted by the treating physician for assessment and management of potential hepatic disease. This would usually be a hepatologist, but may be a gastroenterologist.

[d] Unless an alternative monitoring schedule is agreed by the investigator and UCB responsible physician. Determination of stabilization is at the discretion of the investigator in consultation with the hepatologist (as applicable) and UCB responsible physician, as needed.

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9.2.1.1 Consultation with Medical Monitor and local hepatologist

Potential drug-induced liver injury events require notification of the Medical Monitor within 24h (eg, by laboratory alert), and the study participant must be discussed with the Medical Monitor as soon as possible. If required, the study participant must also be discussed with the local hepatologist. The local hepatologist is the expert usually consulted by the treating physician for assessment and management of potential hepatic disease. This would usually be a hepatologist, but may be a gastroenterologist. If determined necessary, this discussion should be followed by a full hepatology assessment (see Section 9.2.1.3) and SAE report (if applicable).

9.2.1.2 Immediate action: determination of IMP discontinuation

All PDILI events require immediate action, testing, and monitoring.

The immediate action is dependent on the laboratory values and symptoms of hepatitis or hypersensitivity and ranges from continuation of IMP (followed by immediate investigation) to immediate and permanent discontinuation (see Section 6.4.1 and Table 9-6 for details).

When IMP is discontinued, all concomitant medications and herbal supplements that are not medically necessary should also be discontinued. The investigator should also consider dose reduction for medically necessary concomitant medication and consider changing any medically required concomitant medication known to be hepatotoxic to a suitable alternative.

9.2.1.2.1 IMP restart/rechallenge (if applicable)

Rechallenge with a substance potentially causing drug-induced liver injury is dangerous, may be fatal, and must not occur.

Study participants who are immediately discontinued from IMP due to having met certain criteria for PDILI (as described in Section 6.4.1 and Table 9-6), but for whom an alternative diagnosis is confirmed, can rarely restart IMP. Rechallenge with IMP can occur only if ALL of the following requirements are met:

- The results of additional testing and monitoring described in Section 9.2.1.3 and Section 9.2.1.4 confirm a nondrug-related cause for the abnormal hepatic laboratory parameters and any associated symptoms (ie, a subsequent alternative diagnosis fully explains the hepatic findings).
- No alternative treatment options are available to the study participant.
- The study participant has shown clear therapeutic benefit from the IMP.
- Study participant's ALT or AST elevations do not exceed ≥3xULN.
- Study participant's total bilirubin is <1.5xULN.
- Study participant has no signs or symptoms of hypersensitivity.
- The rechallenge is approved by the UCB responsible physician, DMC, and a hepatologist. The hepatologist must be external to UCB but may be a member of the DMC. It is recommended that the hepatologist be a local hepatology expert or the hepatologist treating the study participant.
- Study participant agrees to the investigator-recommended monitoring plan.

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9.2.1.3 Testing: identification/exclusion of alternative etiology

The measurements and additional information required for the assessment of PDILI events when there is a reasonable possibility that they may have been caused by the IMP are detailed in Table 9-7 (laboratory measurements) and Table 9-8 (additional information). Results of the laboratory measurements and information collected are to be submitted to the sponsor on the corresponding eCRF. If the medical history of the study participant indicates a requirement for other assessments not included below, these additional assessments should be completed and submitted, as applicable.

All blood samples should be stored, if possible. If tests are done locally for more rapid results, a concurrent sample must also be sent to the central laboratory.

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The following measurements are to be assessed:

Table 9-7: PDILI laboratory measurements

Virology-related	Hepatitis A IgM antibody
	HBsAg
	Hepatitis E IgM antibody
	HBcAb-IgM
	Hepatitis C RNA
	Cytomegalovirus IgM antibody
	Epstein-Barr viral capsid antigen IgM antibody (if unavailable, obtain heterophile antibody or monospot testing)
Immunology	Anti-nuclear antibody (qualitative and quantitative)
	Anti-smooth muscle antibody (qualitative and quantitative)
	Type 1 anti-liver kidney microsomal antibodies (qualitative and quantitative)
Hematology	Eosinophil count
Urinalysis	Toxicology screen
Chemistry	Amylase
	If total bilirubin ≥1.5xULN, obtain fractionated bilirubin to obtain % direct bilirubin
	Serum CPK and LDH to evaluate possible muscle injury causing transaminase elevation
Additional	Prothrombin time/INR [a]
	Serum pregnancy test
	PK sample

ALT=alanine aminotransferase; CPK=creatine phosphokinase; HBcAb-IgM=hepatitis B core antibody-IgM; HBsAg=hepatitis B surface antigen; IgM=immunoglobulin M; INR=international normalized ratio; LDH=lactate dehydrogenase; PDILI=potential drug-induced liver injury; PK=pharmacokinetic; RNA=ribonucleic acid; ULN=upper limit of normal

[a] Measured only for study participants with ALT >8xULN, elevations in total bilirubin, and symptoms of hepatitis or hypersensitivity. Hepatitis symptoms include fatigue, nausea, vomiting, and right upper quadrant pain or tenderness; hypersensitivity symptoms include eosinophilia (>5%), rash, and fever (without clear alternative cause).

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The following additional information is to be collected:

Table 9-8: PDILI information to be collected

New or updated information
Concomitant prescription and over-the-counter medications (eg, acetaminophen, herbal remedies, vitamins); dosages and dates should be included.
Pertinent medical history, including the following: • History of liver disease (eg, autoimmune hepatitis, nonalcoholic steatohepatitis or other "fatty liver disease") • Adverse reactions to drugs • Allergies • Relevant family history or inheritable disorders (eg, Gilbert's syndrome, alpha-1 antitrypsin deficiency) • Recent travel • Progression of malignancy involving the liver (Note: Metastatic disease to the liver, by itself, should not be used as an explanation for significant AST and/or ALT elevations.)
The appearance or worsening of clinical symptoms of hepatitis or hypersensitivity (eg, fatigue, nausea, vomiting, right upper quadrant pain or tenderness, decreased appetite, abdominal pain, jaundice, fever, or rash)
Recent clinically significant hypotension or hypoxemia with compromised cardiopulmonary function
Alcohol and illicit drug use
Results of liver imaging or liver biopsy, if done
Results of any specialist or hepatology consult, if done
Any postmortem/pathology reports

ALT=alanine aminotransferase; AST=aspartate aminotransferase; PDILI=potential drug-induced liver injury

9.2.1.4 Follow-up evaluation

Potential drug-induced liver injury events require follow-up monitoring as described in Table 9-6. Monitoring should continue until liver chemistry values normalize, stabilize, or return to Baseline. Determination of stabilization is at the discretion of the investigator in consultation with the hepatologist (as applicable) and UCB responsible physician, as needed.

9.3 Other safety measurements

9.3.1 Pregnancy testing

Pregnancy testing will consist of serum testing at the Screening Visit (only for study participants with a gap period between the parent study and entry in CIDP04) and Baseline, if serum pregnancy test is not older than 5 weeks prior to entry into CIDP04. Pregnancy testing will consist of urine testing at dosing visits during the Treatment Period and each visit during the Observation Period as indicated in the schedule of study assessments (Table 5-1). The Screening Visit serum pregnancy testing results must be negative and should be confirmed by a negative urine pregnancy test prior to first dose of IMP. The urine pregnancy test will be performed

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locally. A negative urine pregnancy test result should be obtained prior to each dose of IMP. A positive urine pregnancy test must be confirmed using a serum pregnancy test. Pregnancy tests should be administered to all female study participants of childbearing potential, regardless of their use of birth control.

9.3.2 Vital signs

Vital signs will be measured at all visits as indicated in the schedule of study assessments (Table 5-1).

Vital signs to be assessed are as follows:

- Pulse rate (PR)
- Systolic/diastolic blood pressure (BP)
- Temperature (oral preferred, ear or axillary allowed)

Study participants should be sitting for 5 minutes prior and during the collection of BP and PR measurements. During site Visits 2, 3, and 4, vital signs will be measured prior to IMP administration, at the end of the infusion, and 2 and 4h after the end of the infusion. From Visit 5 to Visit 25, vital signs will be measured predose, at the end of the infusion and 2h after the end of the infusion only. During Treatment Period Part 2, vital signs will be measured predose, and at the end of the infusion. At nondosing visits, vital signs need only be taken once during the visit.

For study participants requiring additional assessments due to AEs (see Table 5-2), additional vital signs measurements may be taken based on the timing of the assessments.

9.3.3 Physical examination

9.3.3.1 Full physical examination

A physical examination will be performed at the visits specified in the schedule of study assessments (Table 5-1) and findings will be recorded in the eCRF. A full physical examination will be performed at Screening or Baseline, and the FV (Visit 29). At all other visits (where physical examination is performed), an abbreviated (brief) physical examination will be conducted.

Clinically important abnormal changes in subsequent physical examinations will be recorded as AEs. Physical examinations must be documented in source documentation.

The following body systems will be examined as a part of the complete physical examination: (1) General appearance; (2) Ear, nose, and throat; (3) Eyes; (4) Hair and skin; (5) Respiratory; (6) Cardiovascular; (7) Musculoskeletal; (9) Gastrointestinal; (10) Hepatic; (11) Neurological examination (see also Section 9.3.4); and (12) Mental status.

9.3.3.2 Brief physical examination

The following body systems will be examined at the visits specified in the schedule of study assessments (Table 5-1) and findings will be recorded in the eCRF. The following body systems will be examined as a part of the brief physical examination: (1) General appearance; (2) Ear, nose, and throat; (3) Eyes; (4) Skin; (5) Respiratory; (6) Gastrointestinal; and (7) Neurological (focused assessment of sensitivity and power).

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9.3.4 Neurological examination

In addition to the Screening or Baseline, and FV (Visit 29), a full neurological examination should be performed for any study participant who experiences severe headache (see Section 9.1.10 and Table 5-2). A full neurological assessment will include: (1) General appearance, including posture, motor activity and meningeal signs and, if indicated, following assessments to be done; (2) Cranial nerves examination; (3) Motor system examination, including muscle tone and power and sensory system examination – light touch; (4) Reflexes, including deep tendon reflexes; (5) Coordination, gait (if possible); and (6) Fundoscopy.

A brief neurological assessment will include a selected assessment of the following: cognition, general, reflexes, muscle strength, and coordination/cerebellar function.

9.3.5 12-lead ECG

A standard 12-lead ECG will be performed at the visits specified in the schedule of study assessments (Table 5-1). Care should be taken to assure proper lead placement and quality ECG recordings. Study participants should rest in a supine position in a controlled, calm environment for at least 15 minutes prior to the recording and should be motionless during the recording. The ECG will be performed in triplicate prior to blood collection for assessment of laboratory parameters.

The ECGs will be read at a central site. The PR, RR, QRS, QT, and corrected QT (QTc) intervals and heart rate will be recorded. All ECG readings from an individual study participant should be read by the same reader, if possible. Findings will be recorded in the eCRF.

For the QTc, the following correction formula will be applied:

$$\text{Fridericia's correction: } QTc = QT/RR^{0.33}$$

9.3.6 Assessment and management of TB and TB risk factors

With the currently available data, TB is not considered as an important potential or identified risk for treatment with rozanolixizumab. As immunomodulation may carry risk of new or activation of LTBI, UCB has conservatively developed TB detection and management procedures taking into account the most current recommendations of international guidelines (2010 WHO) and most recent literature, covering any infection by the mycobacteria TB complex.

Appropriate rigorous precautions are being taken within this protocol to monitor the risk of TB infection in this study (see Section 6.2.1 Exclusion Criterion 20 and Section 6.4 Withdrawal Criteria). The following are the key considerations of these procedures:

TB tests at Screening

The IGRA and Tuberculosis Questionnaire are required as indicated in schedule of assessments (Table 5-1).

- TB screening is mandatory both before study entry and during the conduct of the study. The preferred screening test is the IGRA performed at a central laboratory.
  - The IGRA result must be negative for study participants to enroll in this study.

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  - Study participants who test positive for IGRA test should be excluded from the study and referred for appropriate medical evaluation according to the local medical practice guidelines.
  - If the result of the IGRA test is indeterminate, the particular IGRA test previously performed may be repeated once; if positive or indeterminate on retest, the study participant may not be treated with study drug and, if already enrolled, must undergo appropriate study specified withdrawal procedures. The retest must be done during the protocol-defined Screening window.

- In addition to IGRA test, study participants will be evaluated for signs and symptoms of latent or active TB infection and for risk factors of exposure to TB, using the TB Questionnaire, at Screening. Study participants with known TB, at a high risk of acquiring TB or with LTBI should be excluded from this study as described in Exclusion Criteria (Section 6.2.1). For study participants directly enrolling in CIDP04, no new TB assessment will be performed and values of TB assessment performed at Visit 17 and/or FV (Visit 21) of CIDP01will be used.

Monitoring for TB during the study

Study participants will be monitored for signs/symptoms of TB using routine pharmacovigilance measures for AEs. Study participants reporting AEs related to signs/symptoms of TB will be evaluated for LTB and active TB according to the local medical practice guidelines.

Study participants with confirmed LTB or active TB or NTMB infection will be immediately withdrawn from the study as described in Section 6.4 Withdrawal Criteria. Confirmed LTB, active TB, and NTMB must be reported to the Sponsor immediately regardless of seriousness using the SAE data collection tool. Additional information received by the investigator should be provided to the Sponsor within 24 hours of awareness.

Once withdrawn from study treatment, study participants should return for the POET, complete all early withdrawal assessments, and complete the follow-up visits.

TB tests at Final Visit

Study participants will be evaluated for signs and symptoms of latent or active TB infection and for risk factors of exposure to TB, using the Tuberculosis Questionnaire, at the Final /PEOT Visit. See the 'Tuberculosis Signs and Symptoms Questionnaire' section for further instructions on using the questionnaire.

Signs and symptoms of TB

The investigator should consider all potential sites of infection when assessing for TB during the physical examination, and other evaluations, and based on the study participant's history.

Common symptoms with which the study participant may present with include cough, blood in sputum, night sweats, lymphadenitis, joint pain/swelling, spinal deformity, headache/confusion, abdominal pain mimicking inflammatory bowel disease, frequent or painful urination, scrotal mass in men and pelvic inflammatory disease in women as well as other symptoms, or nonspecific symptoms. This is not an exhaustive list and unusual presentations should always be considered.

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TB Signs and Symptoms Questionnaire

The questionnaire "Evaluation of signs and symptoms of tuberculosis" should be used as a source document. The questionnaire will assist with the identification of study participants who may require therapy for TB. A study participant who answers "Yes" to the question "[redacted]" at Screening is excluded. A "Yes" response to any of the other questions within the questionnaire at Screening should trigger further careful assessment to determine if study participant has latent or active TB. A "Yes" response to any of the questions at the end of the study should trigger further assessments as per local medical guidelines to determine if the study participant has either LTB or active TB infection.

LTB infection, active TB or other NTBM identified during study

During the study, study participants who develop evidence of LTB infection or active TB or NMTB must immediately stop further administration of study drug and will be referred to an appropriate medical specialist for further evaluation.

Confirmed LTB or active TB or NTMB must be reported to the Sponsor immediately as described above.

10 ASSESSMENT OF EFFICACY

10.1 iRODS

The iRODS Questionnaire should be completed by the study participant prior to dosing and before any discussion of their current health status with the treating physician or any other study assessments. The questionnaire will be given to the study participant to complete and will then be recollected and checked, for completeness only, by study personnel other than the treating physician. Study participants should complete the questionnaires themselves, unaided, in a quiet location.

The iRODS is a linearly weighted PRO measure (questionnaire) that specifically captures activity and social participation limitations in patients with CIDP. The iRODS scale was constructed based on the World Health Organization (WHO) International Classification of Functioning, Disability and Health, literature search, and patient interviews (van Nes et al, 2011). All 24 items of iRODS meet Rasch model expectations. The questionnaire consists of 24 items (including eating, taking a shower, walking a flight of stairs, standing for hours, etc) and assesses a patient's perception of their ability to perform daily and social activities. Patients have 3 response options: 0=impossible to perform; 1=performed with difficulty; and 2=easily performed, performed without difficulty (van Nes et al, 2011). The raw sum scores of iRODS (range: 0 to 48) will be translated to log odds units (logits), placing patients' estimates on the same logit scale. For easier interpretation, the person locations can be translated to values changing from 0 (most severe activity and social participation restrictions) to 100 (no activity and social participation limitations).

Study participants will be assessed for the change from Baseline to Week 25 in their iRODS score and for change from Baseline in iRODS scores at each scheduled assessment during the Treatment and Observation Periods. Other efficacy variables will also include study participant experienced CIDP relapse (iRODS), defined as a clinically important deterioration, ie, an MCID-SE ≤-1.96, and time to CIDP relapse (iRODS) during the Treatment Period.

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Study participants will complete the iRODS Questionnaire at the time points detailed in the schedule of study assessments (Table 5-1).

10.2 INCAT

The INCAT disability scale is a 10-point clinician-reported ordinal measure capturing problems in daily arm and leg activities and mobility. The measure captures daily activities such as dressing the upper part of the body, doing and undoing buttons and zips, washing and brushing hair, and handling coins. Each item is scored as being "not affected," "affected but not prevented," or "prevented." The leg scale measures problems with walking, taking into account the use of aids. The INCAT scale ranges from 0 (no signs of disability) to 10 (most severe disability score) (Breiner et al, 2014; Léger et al, 2013; Hughes et al, 2008). For the purposes of the present study, the adjusted INCAT disability score will be used. The adjusted score is identical to the INCAT disability score except for the exclusion of changes in upper limb function from 0 (normal) to 1 (minor symptoms) or from 1 to 0.

The investigator (or qualified personnel) will record the study participants' adjusted INCAT score at the time points detailed in the schedule of study assessments (Table 5-1). It is recommended that the rater of the scale remains the same throughout the duration of the study to ensure consistency of the rating.

Study participant experienced CIDP relapse (adjusted INCAT) (defined as an increase from Baseline of at least 1 point in their adjusted INCAT score) up to Week 25 after first treatment and time to CIDP relapse (adjusted INCAT) during the Treatment Period will be assessed together with the change from Baseline in adjusted INCAT score at each scheduled assessment during the Treatment and Observation Periods.

10.3 Clinician-reported grip strength

Grip strength will be assessed by qualified site personnel according to the schedule of study assessments (Table 5-1). Qualified site personnel will be trained regarding obtaining and recording measurements. At each scheduled visit, the grip strength, generated by the study participant, and measured using a standardized tool, will be evaluated 3 times in the dominant hand. All 3 assessments will be recorded in the eCRF. For analyses, UCB will utilize the maximum of the 3 assessments. Efficacy will be assessed as change from Baseline in maximum grip strength score at each scheduled assessment during the Treatment and Observation Periods.

Study participant experienced CIDP relapse (maximum grip strength) (defined as a clinically important deterioration from Baseline in grip strength, ie, a decline of >14kPa) up to Week 25 after first treatment and time to CIDP relapse (maximum grip strength) during the Treatment Period will be assessed together with the change from Baseline in maximum grip strength score at each scheduled assessment during the Treatment and Observation Periods.

10.4 Patient-reported outcomes

The PRO assessments should be administered in the following order: iRODS, CIDP PRO instrument, fatigue, PGIS, and PGIC. Refer to Section 10.1 for details on iRODS.

Study participants will complete PROs at the time points detailed in the schedule of study assessments (Table 5-1). Study personnel other than the treating physician should administer the PROs. The PROs should be completed by the study participant themselves in a quiet place.

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10.4.1 CIDP PRO instrument

Neuropathic Symptoms will be assessed at the time points detailed in the schedule of study assessments (Table 5-1). The CIDP PRO instrument consists of 2 domain scales; (1) Pain Severity numeric rating scale and (2) Neuropathy scale. Pain Severity consisting of 4 items assessing pain severity in the past 7 days and at the time of completion of the instrument, using 0 to 10 numeric rating scales. Summed total raw score will range between 0 to 40 with higher scores reflecting higher levels of pain severity. The Neuropathy scale consists of 17 items rated within a 7-day recall period on a 6-point Likert severity scale ranging from "none" to "very severe." The summed total raw score will range from 17 to 102 with higher scores reflecting higher levels of pain and physical sensations severity. Following psychometric evaluation and refinement (eg, reduction in items) of these domains scales by using data generated in CIDP01, transformed interval 0 to 100 scoring will be provided for both domain scores with higher score reflecting higher severity.

10.4.2 Fatigue

Fatigue will be assessed at the time points detailed in the schedule of study assessments (Table 5-1). The Fatigue instrument consists of 3 domain scales; Physical Fatigue comprising 16 items; Mental Fatigue comprising 18 items and Fatigability comprising 21 items. All 55 items across the 3-domain scales are rated within a 7-day recall period on a 5-point Likert frequency scale ranging from "none of the time" to "all of the time." The summed total raw scores for each of the 3 scales will range between 16 and 80; 18 to 90 and 21 to 105 points for the Physical, Mental, and Fatigability scales, respectively, with a potential for an exploratory total overall score ranging from 55 to 275. Higher scores reflect higher levels of fatigue across all domain scale scores. Following psychometric evaluation and refinement (eg, reduction in number of items) of these domain scales by using data generated in CIPD01, transformed interval 0 to 100 scoring will be provided for each domain score with higher scores reflecting higher levels of fatigue.

10.4.3 Patient Global Impressions

Patient global impressions will be assessed at the time points detailed in the schedule of study assessments (Table 5-1). Both PGI-C and PGI-S will be used as anchors to determine a meaningful change threshold for CIDP PRO and fatigue scores.

Study participants will rate their global impression of CIDP symptom severity and fatigue severity respectively, on a 5-point Likert severity scale ranging from 'none" to "very severe."

Study participants will rate their global impression of change (if at all) in CIDP symptom and fatigue respectively, on a 7-point Likert severity scale ranging from "very much improved" to "very much worse" from Baseline/start of clinical study treatment to the scheduled visits.

10.5 RT-MRC

The RT-MRC will be assessed by qualified site personnel according to the schedule of study assessments (Table 5-1).

The RT-MRC sum score is a summation of the RT-MRC grades in integers of the following muscles on each side: upper arm abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and foot dorsal flexors.

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The RT-MRC sum score was developed based on a Rasch analysis of the original MRC grading system (Vanhoutte et al, 2012; Merkies et al, 2010; Merkies et al, 2002). The MRC grades were rescored from 6 to 4 response options (0, paralysis; 1, severe weakness; 2, slight weakness; 3, normal strength) for the RT-MRC in order to acceptably fulfill Rasch model expectations. Sum scores range from 36 "normal" to 0 "quadriplegic."

Efficacy will be assessed as a change from Baseline in RT-MRC sum score at each scheduled assessment during the Treatment and Observation Periods.

11 ASSESSMENT OF PHARMACOKINETIC/ PHARMACODYNAMIC VARIABLES

11.1 Pharmacokinetic variable

The plasma concentration of rozanolixizumab will be characterized. Blood samples will be drawn by qualified personnel according to the schedule in Table 11-1. All blood samples collected before dosing with rozanolixizumab at the dosing visits will be drawn at the same time as the sampling for standard clinical laboratory tests. The time and date of collection will be recorded in the eCRF.

Table 11-1: Serial blood sampling for rozanolixizumab concentration

Matrix	Time after start of sc infusion
Plasma	Predose and postdose at 4h after finishing the [redacted] on Visits 2, 4, and 8. Predose samples will be taken at Visits 14, 18, 22 and quarterly at site visits during Treatment Period Part 2.
	Nondosing Visit 26, samples to be taken once during the visit

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study.

11.2 Pharmacodynamic variables

Pharmacodynamic variables are defined in Section 4.2.4.

For all PD assessments blood samples will be collected predose (at dosing visits) by qualified site personnel at the same time that samples are collected for standard clinical laboratory assessments. Blood samples for PD analyses will be drawn according to the schedule of study assessments (Table 5-1). The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study.

12 ASSESSMENT OF IMMUNOLOGICAL VARIABLES

The following immunological assessments will be performed according to the schedule of study assessments (Table 5-1).

- Serum immunoglobulin concentration over time: IgA, IgE, and IgM
- Serum complement levels over time: C3 and C4

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- Plasma complement levels over time: C3a and C5a
- Plasma ADA (anti-rozanolixizumab antibodies)
- Serum cytokines

For all immunological assessments, blood samples will be collected predose (at dosing visits) by qualified site personnel at the same time that samples are collected for standard clinical laboratory. Serum complement (C3, C4), plasma complement (C3a, C5a), and serum cytokine samples will also be taken 4h postdose at Visits 3, 8, 10, 14, 18, 22 and Weeks 25 and 73 during Treatment Period Part 2. Additional samples may be collected in case of infusion reactions (see Table 5-2). The time and date of the blood draws will be recorded in the eCRF. Anti-drug antibodies samples will also be taken predose at Visits 2, 4, 8, 14, 18, 22, and at Weeks 25, 37, 49, and 61 during Treatment Period Part 2 and at Visit 26.

A tiered ADA approach will be used for the study. Samples will first be evaluated in the screening assay using a false positivity rate of 5% (reported as negative screen or positive screen), followed by analysis of screened positive samples in the confirmatory assay (which is a drug depletion assay) to confirm the true positivity of the samples (reported as negative immunodepletion or positive immunodepletion). Samples that are confirmed as positive will be evaluated in a titration assay to quantify the ADA level and will be reported as titer (reciprocal dilution factor including MRD).

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study.

12.1 Assessment of exploratory biomarkers

Collection of these samples will occur according to the schedule of study assessments (Table 5-1). Blood samples will be drawn prior to dosing (on dosing visits) at the same time as the sampling for clinical laboratory tests. Exploratory samples may be collected 4h postdose in case of AE of interest (Table 5-2). The time and date of collection will be recorded in the eCRF. For each protein and metabolite exploratory biomarker blood sample, a volume of 8mL of whole blood is needed (4mL for serum and 4mL for plasma).

If not used immediately, these samples will be stored at -80°C for up to 20 years for later exploratory analyses. Any exploratory biomarker will only ever be related to the exploration of the underlying causes of CIDP in patients, related biology, and drug response. The nature and format of these tentative additional analyses will be determined at a later time. Details on the collection, storage, preparation, and shipping of samples will be presented in the Laboratory Manual provided separately. Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study. Detailed information on sample analyses will be provided in a bioanalytical report.

13 STUDY MANAGEMENT AND ADMINISTRATION

13.1 Adherence to protocol

The investigator should not deviate from the protocol. However, the investigator should take any measure necessary in deviation from or not defined by the protocol in order to protect clinical

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study participants from any immediate hazard to their health and safety. In this case, this action should be taken immediately, without prior notification of the regulatory authority, IRB/IEC, or sponsor.

After implementation of such measure, the investigator must notify the Clinical Project Manager of the sponsor within 24 hours and follow any local regulatory requirements.

13.2 Monitoring

UCB (or designee) will monitor the study to meet the sponsor's monitoring SOPs, ICH-GCP guideline, and applicable regulatory requirements, and to ensure that study initiation, conduct, and closure are adequate. Monitoring of the study may be delegated by UCB to a CRO or a contract monitor.

The investigator and his/her staff are expected to cooperate with UCB (or designee) and to be available during the monitoring visits to answer questions sufficiently and to provide any missing information. The investigator(s)/institution(s) will permit direct access to source data/documents for study-related monitoring, audits, IRB/IEC review, and regulatory inspection(s).

The investigator will allow UCB (or designee) to periodically review all CRFs and corresponding source documents (eg, hospital and laboratory records for each study participant). Monitoring visits will provide UCB (or designee) with the opportunity to evaluate the progress of the study, verify the accuracy and completeness of CRFs, ensure that all protocol requirements, applicable authorities' regulations, and investigator's obligations are being fulfilled, and resolve any inconsistencies in the study records.

13.2.1 Definition of source data

All source documents must be accurate, clear, unambiguous, permanent, and capable of being audited. They should be made using some permanent form of recording (ink, typing, printing, optical disc). They should not be obscured by correction fluid or have temporary attachments (such as removable self-stick notes). Photocopies and/or printouts of CRFs are not considered acceptable source documents.

Source documents are original records in which raw data are first recorded. These may include hospital/clinic/general practitioner records, charts, diaries, x-rays, laboratory results, printouts, pharmacy records, care records, ECG or other printouts, completed scales, or quality of life questionnaires, for example. Source documents should be kept in a secure, limited access area.

Source documents that are computer generated and stored electronically must be printed for review by the monitor (eg, ECG reports). Once printed, these copies should be signed and dated by the investigator and become a permanent part of the study participant's source documents. The investigator will facilitate the process for enabling the monitor to compare the content of the printout and the data stored in the computer to ensure all data are consistent.

Electronic data records, such as Holter monitor records or electroencephalogram records, must be saved and stored as instructed by UCB (or designee).

13.2.2 Source data verification

Source data verification ensures accuracy and credibility of the data obtained. During monitoring visits, reported data are reviewed with regard to being accurate, complete, and verifiable from

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source documents (eg, study participant files, recordings from automated instruments, tracings [ECG], x-ray films, laboratory notes). All data reported on the eCRF should be supported by source documents, unless otherwise specified in Section 13.2.1.

13.3 Data handling

13.3.1 Case Report form completion

This study is performed using remote data capture. The investigator is responsible for prompt reporting of accurate, complete, and legible data in the eCRFs and in all required reports.

Any change or correction to the eCRF after saving must be accompanied by a reason for the change.

Corrections made after the investigator's review and approval (by means of a password/electronic signature) will be reapproved by the investigator.

The investigator should maintain a list of personnel authorized to enter data into the eCRF.

Detailed instructions will be provided in the eCRF Completion Guidelines.

13.3.2 Database entry and reconciliation

Case Report forms/external electronic data will be entered/loaded into a validated electronic database using a clinical data management system (CDMS). Computerized data cleaning checks will be used in addition to manual review to check for discrepancies and to ensure consistency of the data. Case Report form data are entered into the clinical database using independent, double-data entry, with the exception of comment fields, which are verified by a second person. The data are entered into the electronic CRFs once and are subsequently verified if the study is performed using electronic data capture.

An electronic audit trail system will be maintained within the CDMS to track all data changes in the database once the data have been saved initially into the system or electronically loaded. Regular backups of the electronic data will be performed.

13.3.3 Study participant Screening and Enrollment log/Study participant Identification Code list

The study participant's screening and enrollment will be recorded in the Study participant Screening and Enrollment Log.

The investigator will keep a Study participant Identification Code list. This list remains with the investigator and is used for unambiguous identification of each study participant.

The study participant's consent and enrollment in the study must be recorded in the study participant's medical record. These data should identify the study and document the dates of the study participant's participation.

13.4 Termination of the study

UCB reserves the right to temporarily suspend or prematurely discontinue this study either at a single site, multiple sites, or at all sites at any time for reasons including, but not limited to, safety or ethical issues, inaccurate or incomplete data recording, noncompliance, or unsatisfactory enrollment with respect to quality or quantity.

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If the study is prematurely terminated or suspended, UCB (or its representative) will inform the investigators/institutions and the regulatory authority(ies) of the termination or suspension and the reason(s) for the termination or suspension, in accordance with applicable regulatory requirement(s). The IRB/IEC should also be informed and provided with reason(s) for the termination or suspension by the sponsor or by the investigator/institution, as specified by the applicable regulatory requirement(s). In addition, arrangements will be made for the return of all unused IMP and other material in accordance with UCB procedures for the study.

13.5 Archiving and data retention

The investigator will maintain adequate records for the study, including CRFs, medical records, laboratory results, Informed Consent documents, drug dispensing and disposition records, safety reports, information regarding participants who discontinued, and other pertinent data.

All essential documents are to be retained by the investigator 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 at least 2 years have elapsed since the formal discontinuation of clinical development of the IMP/investigational device. These documents should be retained for a longer period, however, if required by the applicable regulatory requirement(s) or by an agreement with UCB (Committee for Proprietary Medicinal Products [CPMP]/ICH/135/95, 2002 [Section 4.9.5]). The investigator will contact UCB for authorization prior to the destruction of any study records or in the event of accidental loss or destruction of any study records. The investigator will also notify UCB should he/she relocate or move the study-related files to a location other than that specified in the sponsor's trial master file.

13.6 Audit and inspection

The investigator will permit study-related audits mandated by UCB, after reasonable notice, and inspections by domestic or foreign regulatory authorities.

The main purposes of an audit or inspection are to confirm that the rights and well-being of the study participants enrolled have been protected, that enrolled study participants (ie, signing consent and undergoing study procedures) are appropriate for the study, and that all data relevant for the evaluation of the IMP/investigational device have been processed and reported in compliance with the planned arrangements, the protocol, investigational site, and IRB/IEC SOPs, ICH GCP, and applicable regulatory requirements.

The investigator will provide direct access to all study documents, source records, and source data. If an inspection by a regulatory authority is announced, the investigator will immediately inform UCB (or designee).

13.7 Good Clinical Practice

Noncompliance with the protocol, ICH-GCP, or local regulatory requirements by the investigator, institution, institution staff, or designees of the sponsor will lead to prompt action by UCB to secure compliance. Continued noncompliance may result in the termination of the site's involvement in the study.

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14 STATISTICS

A description of statistical methods follows and will be described in more detail in SAP which will be finalized and approved prior to database lock.

14.1 Definition of analysis sets

14.1.1 Enrolled Set

The Enrolled Set (ES) will consist of all study participants who have signed the ICF.

14.1.2 Safety Set

The Safety Set (SS) will consist of all enrolled study participants who were administered at least 1 dose of rozanolixizumab.

Safety variables will be analyzed using the SS.

14.1.3 Full Analysis Set

The Full Analysis Set (FAS) will consist of all study participants in the SS who have a Baseline and least 1 post-Baseline iRODS measurement.

The FAS is the primary analysis set for efficacy analyses.

14.1.4 Pharmacokinetic Per-Protocol Set

The Pharmacokinetic Per-Protocol Set (PK-PPS) is a subset of the SS, consisting of those study participants who had no important protocol deviation affecting the plasma concentration of rozanolixizumab. Post-Baseline deviations will not necessarily lead to total exclusion of a study participant from the PK-PPS but may lead to exclusion of specific data.

14.1.5 Pharmacodynamic Per-Protocol Set

The Pharmacodynamic Per-Protocol Set (PD-PPS) is a subset of the FAS, consisting of those study participants who had no important protocol deviation affecting the serum concentrations of total IgG or IgG subclasses. Post-Baseline deviations will not necessarily lead to total exclusion of a study participant from the PD-PPS but may lead to exclusion of specific data.

14.2 General statistical considerations

All analyses will be performed using SAS® version 9.2 or later (SAS Institute, Cary, NC, USA). Continuous variables will be summarized by visit (where applicable) with the statistics mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized by visit (where applicable) with frequency counts and percentages.

Data listings containing all documented data and all calculated data will be generated.

Baseline will be the last nonmissing data collected prior to the first dose of IMP, and measurement-specific Baseline values will be defined in the SAP.

14.3 Planned safety analyses

14.3.1 Safety analyses

The incidence of study participants with TEAEs will be determined. Furthermore, the absolute and relative frequencies for study participants with a given TEAE with respect to the preferred term according to the latest available version of the Medical Dictionary for Regulatory Activities

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(MedDRA®), will be determined within each system organ class. Additional tables will summarize TEAEs by maximum severity and causal relationship with rozanolixizumab, as judged by the investigator. Adverse events will be categorized by severity according to the National Institutes for Health CTCAE version 5.0 grading (National Institutes for Health, 2017). In case the CTCAE grading is not available, the intensity (mild/moderate/severe) will be utilized. The TEAEs leading to discontinuation of IMP and the serious TEAEs will also be summarized. The action taken, time of onset relative to dosing, actual dose received, and duration of each AE will be listed only.

For the continuous laboratory variables, the values and changes from Baseline will be descriptively summarized at each time point. For categorized values according to the reference range, shift tables from Baseline to each post-Baseline time point will be presented for selected variables to be defined in the SAP. Values outside the reference range will be flagged in the data listings.

Descriptive statistics will be presented for ECG value and changes from Baseline over time based on the mean of the triplicate assessments at each time point. Categorical analyses for QTc, eg, QTc increase >60msec, will also be performed.

Descriptive statistics will be reported for all vital sign measurements (including BP, PR, temperature, and body weight). Measured values and changes from Baseline will be summarized by time point.

Physical and neurological examination findings and the results of any pregnancy testing will be presented in listings only. Results will be listed for any study participants who complete a headache questionnaire, undergo stool sampling, or lumbar puncture, etc.

14.4 Other analyses

14.4.1 Efficacy analyses

For CIDP relapse (iRODS, adjusted INCAT, and maximum grip strength as assessed by site personnel) (Yes/No) point estimates the proportion of patients relapsing will be presented along with 95% confidence intervals (CIs).

For time to CIPD relapse (iRODS, adjusted INCAT and maximum grip strength as assessed by site personnel), Kaplan Meier estimates and corresponding 95% CIs will be constructed using the asymptotic standard error (asymptotic Wald confidence limits).

Statistical methods for time to rescue mediation administration during treatment period will be the same as for time to CIPD relapse.

For other efficacy variables, including change from Baseline to Week 25 in iRODS score, change from Baseline in adjusted INCAT score and change from Baseline in RT-MRC sum score, appropriate summary and descriptive statistics will be provided at each time point where the data are recorded.

A sensitivity analysis will be performed excluding any study participant who received a mean dose more than ±10% from the intended dose. Additional sensitivity analyses may be carried out and will be fully detailed in the SAP.

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14.4.2 Pharmacokinetic analyses

Pharmacokinetic variables of rozanolixizumab like AUC (area under the curve from 0 to infinity) and C_{max} (maximum observed plasma concentration) cannot be derived, due to the sparse blood sampling scheme. Thus, PK is restricted to concentration data.

In contrast to the general descriptive display, concentration data will be summarized by actual dose received and time point using the number of available observations, mean, median, SD, minimum, maximum, geometric mean (and associated 95% CIs), and geometric coefficient of variation (assuming log-normally distributed data). Values below the lower limit of quantification (LLOQ) will be reported with a clear sign indicating that they were below the LLOQ. Descriptive statistics of concentrations will be calculated if at least two-thirds of the individual data points are quantifiable (≥LLOQ). Individual concentrations of rozanolixizumab will also be displayed graphically.

14.4.3 Pharmacodynamic analyses

For all PD variables, descriptive statistics for the value, change from Baseline, and/or percentage change from Baseline will be tabulated by actual dose received and time point.

The PD variables will include serum IgG and IgG subclass and NF-L.

14.4.4 Immunological analyses

All immunologic variables including concentrations of immunoglobulins (IgA, IgE, and IgM), and serum (C3 and C4) and plasma (C3a and C5a) complement levels, and serum cytokines will be summarized and visit using descriptive statistics.

The ADA status (negative or confirmed positive) and the changes in confirmed positive titer at each scheduled assessment during Treatment and Observation Periods will be summarized by visit to inform on incidence and emergence of ADA; figures will also be presented.

Further details will be provided in the SAP.

14.5 Handling of protocol deviations

Important protocol deviations are identified as part of the data cleaning process in the Protocol Deviation Specification (PDS). Ongoing data cleaning meetings will be held throughout the duration of the study. Objectives of these meetings include to review and update (if necessary) the important protocol deviations in the PDS and discuss criteria for exclusion of study participants from analysis populations. Furthermore, overall trends in protocol deviations will be discussed at the Data Evaluation Meeting. Through this ongoing data cleaning and evaluation process, all decisions regarding important protocol deviations and exclusions from analysis populations are made on an ongoing basis and will be finalized before database lock.

14.6 Handling of dropouts or missing data

For study participants who prematurely withdraw from the study, no imputation of missing efficacy data will be performed.

Details of how missing or partial dates for safety assessments will be handled will be provided in the SAP.

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14.7 Planned interim analysis and data monitoring

A DMC will systematically monitor and report on the progress, safety, and/or critical efficacy endpoints of this study by convening to review the ongoing program safety and efficacy data. The DMC will also review the impact of infusion rate on local and systemic tolerability during the first 2 doses.

A DMC charter will define the composition, roles, and responsibilities of the DMC, specify the data to be reviewed and determine the procedures to be followed. Ad hoc DMC meetings can be held for reasons determined appropriate by the sponsor.

The deliberations and decisions of the DMC will be formally documented.

A detailed description of the DMC composition, processes, and responsibilities will be provided in a separate DMC charter.

Two interim analyses will be conducted. Firstly at the time of the lock of the parent study CIPD01 and additionally once all study participants have completed Part 1 of the Treatment Period in CIDP04 and have either entered into the Treatment Period Part 2 or the Observation Period. Details of the planned analyses will be fully outlined in the respective SAPs.

14.8 Determination of sample size

No formal sample size calculation can be performed. All study participants from the parent study (eg, CIDP01, with a maximum of ■ study participants to be randomized) eligible for the OLE will be included.

15 ETHICS AND REGULATORY REQUIREMENTS

15.1 Informed consent

Study participant's informed consent must be obtained and documented in accordance with local regulations, ICH-GCP requirements, and the ethical principles that have their origin in the principles of the Declaration of Helsinki.

Prior to obtaining informed consent, information should be given in a language and at a level of complexity understandable to the study participant in both oral and written form by the investigator (or designee). Each study participant will have the opportunity to discuss the study and its alternatives with the investigator.

Prior to participation in the study, the ICF should be signed and personally dated by the study participant, or his/her legal representative, and by the person who conducted the informed consent discussion (investigator or designee). The study participant or his/her legal representative must receive a copy of the signed and dated ICF. As part of the consent process, each study participant must consent to direct access to his/her medical records for study-related monitoring, auditing, IRB/IEC review, and regulatory inspection.

If the ICF is amended during the study, the investigator (or the sponsor, if applicable) must follow all applicable regulatory requirements pertaining to the approval of the amended ICF by the IRB/IEC and use of the amended form.

All studies conducted at centers in the United States must include the use of a Health Insurance Portability and Accountability Act Authorization form.

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The study participant may withdraw his/her consent to participate in the study at any time. A study participant is considered as enrolled in the study when he/she has signed the ICF. An eCRF must not be started, nor may any study specific procedure be performed for a given study participant, without having obtained his/her written consent to participate in the study.

Any data already generated on the samples will be retained and used, but no further laboratory analysis will occur.

15.2 Study participant identification cards

Upon signing the Informed Consent and Assent form (as applicable), the study participant or legal representative will be provided with a study participant identification card in the language of the study participant. The investigator will fill in the study participant identifying information and medical emergency contact information. The investigator will instruct the study participant to keep the card with him/her at all times.

15.3 Institutional Review Boards and Independent Ethics Committees

The study will be conducted under the auspices of an IRB/IEC, as defined in local regulations, ICH-GCP, and in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

The investigator/UCB will ensure that an appropriately constituted IRB/IEC that complies with the requirements of the current ICH-GCP version or applicable country-specific regulations will be responsible for the initial and continuing review and approval of the clinical study. Prior to initiation of the study, the investigator/UCB will forward copies of the protocol, ICF, IB, investigator's curriculum vitae (if applicable), advertisement (if applicable), and all other study participant-related documents to be used for the study to the IRB/IEC for its review and approval.

Before initiating a study, the investigator will have written and dated full approval from the responsible IRB/IEC for the protocol.

The investigator will also promptly report to the IRB/IEC all changes in the study, all unanticipated problems involving risks to human study participants or others, and any protocol deviations, to eliminate immediate hazards to study participants.

The investigator will not make any changes in the study or study conduct without IRB/IEC approval, except where necessary to eliminate apparent immediate hazards to the study participants. For minor changes to a previously approved protocol during the period covered by the original approval, it may be possible for the investigator to obtain an expedited review by the IRB/IEC as allowed.

As part of the IRB/IEC requirements for continuing review of approved studies, the investigator will be responsible for submitting periodic progress reports to the IRB/IEC (based on IRB/IEC requirements), at intervals appropriate to the degree of study participant risk involved, but no less than once per year. The investigator should provide a final report to the IRB/IEC following study completion.

UCB (or its representative) will communicate safety information to the appropriate regulatory authorities and all active investigators in accordance with applicable regulatory requirements.

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The appropriate IRB/IEC will also be informed by the investigator or the sponsor, as specified by the applicable regulatory requirements in each concerned country. Where applicable, investigators are to provide the sponsor (or its representative) with evidence of such IRB/IEC notification.

15.4 Study participant privacy

UCB staff (or designee) will affirm and uphold the study participant's confidentiality. Throughout this study, all data forwarded to UCB (or designee) will be identified only by the study participant number assigned at Screening.

The investigator agrees that representatives of UCB, its designee, representatives of the relevant IRB/IEC, or representatives of regulatory authorities will be allowed to review that portion of the study participant's primary medical records that directly concerns this study (including, but not limited to, laboratory test result reports, ECG reports, admission/discharge summaries for hospital admissions occurring during a study participant's study participation, and autopsy reports for deaths occurring during the study).

15.5 Protocol amendments

Protocol changes may affect the legal and ethical status of the study and may also affect the statistical evaluations of sample size and the likelihood of the study fulfilling its primary objective.

Significant changes to the protocol will only be made as an amendment to the protocol and must be approved by UCB, the IRB/IEC, and the regulatory authorities (if required), prior to being implemented.

16 FINANCE, INSURANCE, AND PUBLICATION

Insurance coverage will be handled according to local requirements.

Finance, insurance, and publication rights are addressed in the investigator and/or CRO agreements, as applicable.

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18 APPENDICES

18.1 Suggested management guidelines for infusion reactions

Table 18-1: Suggested management guidelines for infusion reactions

Type of reaction	Sponsor recommendations for management
Acute – Mild eg, flushing, dizziness, headache, sweating, palpitations, nausea	Slow [redacted] [redacted] Administer antihistamine iv/im. Administer paracetamol 1g orally. Monitor vital signs every 10 minutes until back to Baseline. [redacted] as tolerated until intended dose has been given.
Acute – Moderate eg, flushing, chest tightness, dyspnea, hypo/hypertension (change >20mmHg in systolic blood pressure), raised temperature, palpitations, urticaria	Stop infusion. [redacted] Administer antihistamine iv/im. Administer paracetamol 1g orally. Monitor vital signs every 5 minutes until back to Baseline. [redacted] following this suggested regimen: [redacted]), as tolerated until intended dose has been given.
Acute – Severe eg, hypo/hypertension (change >40mmHg in systolic blood pressure), raised temperature with rigors, chest tightness, dyspnea with wheezing, stridor	Stop infusion definitively. Alert crash team. Maintain airway, ensure oxygen is available. If wheezing, give epinephrine 0.5mg im (0.5mL 1:1000 epinephrine). Administer antihistamine iv/im. Administer corticosteroids iv. Monitor vital signs every 2 minutes until back to Baseline.

im=intramuscular; iv=intravenous

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18.2 Diagnosis of anaphylactic reactions

Anaphylaxis is highly likely when any of the following 3 criteria is fulfilled (Sampson et al, 2006):

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING

a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow [PEF], hypoxemia)

b. Reduced blood pressure [BP] or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)

2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):

a. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips tongue-uvula)

b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)

c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)

d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

Reduced blood pressure after exposure to known allergen for that study participant (minutes to several hours): Systolic BP of less than 90mmHg or greater than 30% decrease from the study participant's Baseline systolic BP value.

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18.3 Protocol amendment 1

Rationale for the amendment

The current protocol has been locally amended to align with CIPD01 Protocol Amendment 1.1, modifying the timeframe for use of contraception post study completion, and the final urinary pregnancy test of the study.

The following shows the changes made in Protocol Amendment 1 compared to the original Protocol, dated 14 Dec 2018.

Modifications and changes

Specific changes

Change #1

5.2 Schedule of study assessments

Table 5-1 Schedule of study assessments; footnote k

In case of immediate entry from the parent study, the serum pregnancy test from the parent study should not be older than 5 weeks prior to entry into this CIDP04 study and the urine pregnancy test done at Visit 2 must both be negative before dosing. In case of gap period between the parent study and entry in CIDP04, a serum test will be performed at Visit 1 (Screening). Note that the final urine pregnancy test of the study should be no longer than 60 days after the final dose of IMP.

Has been changed to:

In case of immediate entry from the parent study, the serum pregnancy test from the parent study should not be older than 5 weeks prior to entry into this CIDP04 study and the urine pregnancy test done at Visit 2 must both be negative before dosing. In case of gap period between the parent study and entry in CIDP04, a serum test will be performed at Visit 1 (Screening). Note that the final urine pregnancy test of the study should be no longer than ~~60~~**90** days after the final dose of IMP.

Change #2

6.1 Inclusion criteria

4. Female subjects of child-bearing potential must have the results of a negative serum pregnancy test from either the parent study (not older than 5 weeks) or the Screening Visit available at the CIDP04 Baseline (Visit 2), and a urine pregnancy test must be negative when subject enters CIDP04 and prior to further dosing at each study visit thereafter.

   Female subjects of childbearing potential must agree to use a highly effective method of birth control, during the study and for a period of 2 months after their final dose of IMP. Highly effective forms of birth control are methods that achieve a failure rate of less than 1% per year when used consistently and correctly. According to the International Council for Harmonisation (ICH) M3 R2, highly effective methods of birth control include:

   – Combined (estrogen- and progesterone-containing) hormonal contraception (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at

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least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).

- Progesterone-only hormonal contraceptives (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).
- Progesterone-releasing intrauterine systems or the TCu 380A intrauterine device.
- Vasectomized partner (provided sole partner and partner has medical proof of surgical success).
- True heterosexual sexual abstinence is an acceptable form of contraception when this is in line with the preferred and usual lifestyle of the person. Periodic abstinence (eg, calendar, ovulation, symptothermal, postovulation methods), declaration of abstinence for the duration of the study, and withdrawal are not acceptable methods of contraception.
- Women not agreeing to use birth control must be of nonchildbearing potential, defined as being:
- Postmenopausal (for at least 2 years before the Screening Visit of CIDP04 or the parent study if no Screening Visit is scheduled in CIDP04), verified by serum follicle-stimulating hormone level >40mIU/mL at the Screening Visit, or
- Permanently sterilized (eg, bilateral tubal occlusion, hysterectomy, bilateral salpingectomy), or
- Congenitally sterile

Has been changed to:

4. Female subjects of child-bearing potential must have the results of a negative serum pregnancy test from either the parent study (not older than 5 weeks) or the Screening Visit available at the CIDP04 Baseline (Visit 2), and a urine pregnancy test must be negative when subject enters CIDP04 and prior to further dosing at each study visit thereafter.

   Female subjects of childbearing potential must agree to use a highly effective method of birth control, during the study and for a period of ~~2~~**3** months after their final dose of IMP. Highly effective forms of birth control are methods that achieve a failure rate of less than 1% per year when used consistently and correctly. According to the International Council for Harmonisation (ICH) M3 R2, highly effective methods of birth control include:

   - Combined (estrogen- and progesterone-containing) hormonal contraception (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).
   - Progesterone-only hormonal contraceptives (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening

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[Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).

- Progesterone-releasing intrauterine systems or the TCu 380A intrauterine device.
- Vasectomized partner (provided sole partner and partner has medical proof of surgical success).
- True heterosexual sexual abstinence is an acceptable form of contraception when this is in line with the preferred and usual lifestyle of the person. Periodic abstinence (eg, calendar, ovulation, symptothermal, postovulation methods), declaration of abstinence for the duration of the study, and withdrawal are not acceptable methods of contraception.
- Women not agreeing to use birth control must be of nonchildbearing potential, defined as being:
- Postmenopausal (for at least 2 years before the Screening Visit of CIDP04 or the parent study if no Screening Visit is scheduled in CIDP04), verified by serum follicle-stimulating hormone level >40mIU/mL at the Screening Visit, or
- Permanently sterilized (eg, bilateral tubal occlusion, hysterectomy, bilateral salpingectomy), or
- Congenitally sterile

Change #3

9.2 Laboratory measurements

Table 9-3 Laboratory measurements; footnote e

Urine pregnancy test (dipstick) for women of childbearing potential performed prior to dosing (and confirmed negative) at dosing visits and each visit of the Observation Period. Note that the final urinary pregnancy test of the study should be no longer than 60 days after the final dose of IMP.

Has been changed to:

Urine pregnancy test (dipstick) for women of childbearing potential performed prior to dosing (and confirmed negative) at dosing visits and each visit of the Observation Period. Note that the final urinary pregnancy test of the study should be no longer than ~~60~~**90** days after the final dose of IMP.

18.4 Protocol amendment 2

Rationale for the amendment

The purpose of this substantial protocol amendment is to provide clarification on the dose of investigational product administered (including an allowance of ±10% compared to the [redacted] target dose arm), as well as a flexible infusion rate. Sensitivity analyses were introduced to account for deviation outside the 10% target dosage and the descriptive analyses will inform

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about actual doses administered to the subjects. Updates to the status of the other rozanolixizumab studies have been included. The predominance of objective criteria over the investigator's judgement has been confirmed for the assessment of CIDP relapse. The timeframe of expected use of contraception post-study completion has been extended to 90 days in view of the probable half-life of rozanolixizumab. Exclusion criterion #14 has been extended to prediabetic condition. The expectation with regards to the use of cannabidiols and medicinal marijuana has been clarified in the concomitant medication section. The protocol amendment confirms the expectation of a single rater for the INCAT assessment to ensure consistency of the rating during the course of the study. The exit interview assessment has been removed from the follow-up study; this will allow UCB to confirm the adequacy of this tool using data collected in CIDP01 before extending its use in another study. Safety reporting procedures have been updated to align with most current UCB practices.

In addition, some administrative changes have been made.

Modifications and changes

Global changes

Text pertaining to the exit interview has been removed from the entire protocol and is not listed in the specific changes.

Specific changes

Change #1

1 Summary; fourth paragraph

The following sentence has been added to the end of the paragraph:

For exact doses to be administered, refer to Section 7.2.

Change #2

2 Introduction; fifth and sixth paragraphs

Rozanolixizumab is a humanized anti-FcRn monoclonal antibody that has been specifically designed to inhibit IgG binding to FcRn without inhibiting albumin binding to FcRn. Rozanolixizumab is being developed as an inhibitor of FcRn activity with the aim to reduce the concentration of pathogenic IgG in patients with IgG auto-antibody mediated diseases. Rozanolixizumab was derived from a rat antibody with specificity for human FcRn. To date, rozanolixizumab has been administered to healthy subjects in a completed first-in-human (FIH) study (UP0018), an ongoing Phase 2 study in subjects with primary immune thrombocytopenia (ITP) (TP0001, evaluating [redacted] by sc route across 5 cohorts), and an ongoing Phase 2 study in subjects with myasthenia gravis (MG) (MG0002, evaluating [redacted] by sc route).

Additional information on the development of rozanolixizumab, including data from UP0018 and the ongoing clinical studies in ITP subjects (TP0001) and MG subjects (MG0002), can be found in the current version of the Investigator's Brochure (IB) for rozanolixizumab.

Have been changed to:

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Rozanolixizumab is a humanized anti-FcRn monoclonal antibody that has been specifically designed to inhibit IgG binding to FcRn without inhibiting albumin binding to FcRn. Rozanolixizumab is being developed as an inhibitor of FcRn activity with the aim to reduce the concentration of pathogenic IgG in patients with IgG auto-antibody mediated diseases. Rozanolixizumab was derived from a rat antibody with specificity for human FcRn. To date, rozanolixizumab has been administered to healthy subjects in a completed first-in-human (FIH) study (UP0018), **a completed** Phase 2 study in subjects with primary immune thrombocytopenia (ITP) (TP0001, evaluating [redacted] by sc route across 5 cohorts), and **a completed** Phase 2 study in subjects with myasthenia gravis (MG) (MG0002, evaluating [redacted] by sc route).

Additional information on the development of rozanolixizumab~~, including data from UP0018 and the ongoing clinical studies in ITP subjects (TP0001) and MG subjects (MG0002),~~ can be found in the current version of the Investigator's Brochure (IB) for rozanolixizumab.

Change #3

5.1 Study description; third paragraph

The following sentence has been added to the end of the paragraph:

See Section 7.2 for details on treatment to be administered.

Change #4

5.2 Schedule of study assessments

Table 5-1 Schedule of study assessments; footnote k

In case of immediate entry from the parent study, the serum pregnancy test from the parent study should not be older than 5 weeks prior to entry into this CIDP04 study and the urine pregnancy test done at Visit 2 must both be negative before dosing. In case of gap period between the parent study and entry in CIDP04, a serum test will be performed at Visit 1 (Screening). Note that the final urine pregnancy test of the study should be no longer than 60 days after the final dose of IMP.

Has been changed to:

In case of immediate entry from the parent study, the serum pregnancy test from the parent study should not be older than 5 weeks prior to entry into this CIDP04 study and the urine pregnancy test done at Visit 2 must both be negative before dosing. In case of gap period between the parent study and entry in CIDP04, a serum test will be performed at Visit 1 (Screening). **Pregnancy testing will consist of urine testing at dosing visits during the Treatment Period and each visit during the Observation Period. A positive urine pregnancy test must be confirmed using a serum pregnancy test.** Note that the final urine pregnancy test of the study should be no longer than **90** days after the final dose of IMP.

Change #5

5.2 Schedule of study assessments

Table 5-1 Schedule of study assessments; footnote r

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At Visits 2, 4, 8, 10, 14, 18, and 22, samples for exploratory biomarkers should be taken predose. See Table 5-2 for sampling in case of AE of interest.

Has been changed to:

At Visits 2, **3**, 8, 10, 14, 18, and 22, samples for exploratory biomarkers should be taken predose. See Table 5-2 for sampling in case of AE of interest.

Change #6

5.3 Rationale for study design and selection of dose; second paragraph, fourth sentence

The dose and regimen of IMP to be used in the current study (rozanolixizumab [redacted] sc) is based on results from the FIH study UP0018, alongside the emerging safety data from the MG and ITP studies (MG0002 and TP0001).

Has been changed to:

The dose and regimen of IMP to be used in the current study (rozanolixizumab [redacted] sc) is based on results from the FIH study UP0018, alongside the ~~emerging~~ safety data from the MG and ITP studies (MG0002 and TP0001).

Change #7

6.1 Inclusion criteria; Criterion #4

Female subjects of child-bearing potential must have the results of a negative serum pregnancy test from either the parent study (not older than 5 weeks) or the Screening Visit available at the CIDP04 Baseline (Visit 2), and a urine pregnancy test must be negative when subject enters CIDP04 and prior to further dosing at each study visit thereafter.

Female subjects of childbearing potential must agree to use a highly effective method of birth control, during the study and for a period of 2 months after their final dose of IMP. Highly effective forms of birth control are methods that achieve a failure rate of less than 1% per year when used consistently and correctly. According to the International Council for Harmonisation (ICH) M3 R2, highly effective methods of birth control include:

- Combined (estrogen- and progesterone-containing) hormonal contraception (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).
- Progesterone-only hormonal contraceptives (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).
- Progesterone-releasing intrauterine systems or the TCu 380A intrauterine device.
- Vasectomized partner (provided sole partner and partner has medical proof of surgical success).

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- True heterosexual sexual abstinence is an acceptable form of contraception when this is in line with the preferred and usual lifestyle of the person. Periodic abstinence (eg, calendar, ovulation, symptothermal, postovulation methods), declaration of abstinence for the duration of the study, and withdrawal are not acceptable methods of contraception.
- Women not agreeing to use birth control must be of nonchildbearing potential, defined as being:
- Postmenopausal (for at least 2 years before the Screening Visit of CIDP04 or the parent study if no Screening Visit is scheduled in CIDP04), verified by serum follicle-stimulating hormone level >40mIU/mL at the Screening Visit, or
- Permanently sterilized (eg, bilateral tubal occlusion, hysterectomy, bilateral salpingectomy), or
- Congenitally sterile

Has been changed to:

Female subjects of child-bearing potential must have the results of a negative serum pregnancy test from either the parent study (not older than 5 weeks) or the Screening Visit available at the CIDP04 Baseline (Visit 2), and a urine pregnancy test must be negative when subject enters CIDP04 and prior to further dosing at each study visit thereafter.

Female subjects of childbearing potential must agree to use a highly effective method of birth control, during the study and for a period of **3** months after their final dose of IMP. Highly effective forms of birth control are methods that achieve a failure rate of less than 1% per year when used consistently and correctly. According to the International Council for Harmonisation (ICH) M3 R2, highly effective methods of birth control include:

- Combined (estrogen- and progesterone-containing) hormonal contraception (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).
- Progesterone-only hormonal contraceptives (oral, implant, injectable) associated with inhibition of ovulation (which must be stable for at least 1 full month prior to Screening [Visit 1], or must have remained stable during the parent study for subjects entering CIDP04 without a Screening Visit, and should remain stable during the study).
- Progesterone-releasing intrauterine systems or the TCu 380A intrauterine device.
- Vasectomized partner (provided sole partner and partner has medical proof of surgical success).
- True heterosexual sexual abstinence is an acceptable form of contraception when this is in line with the preferred and usual lifestyle of the person. Periodic abstinence (eg, calendar, ovulation, symptothermal, postovulation methods), declaration of abstinence for the duration of the study, and withdrawal are not acceptable methods of contraception.
- Women not agreeing to use birth control must be of nonchildbearing potential, defined as being:

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- Postmenopausal (for at least 2 years before the Screening Visit of CIDP04 or the parent study if no Screening Visit is scheduled in CIDP04), verified by serum follicle-stimulating hormone level >40mIU/mL at the Screening Visit, or
- Permanently sterilized (eg, bilateral tubal occlusion, hysterectomy, bilateral salpingectomy), or
- Congenitally sterile

Change #8

6.2.1 Additional exclusion criteria for subjects with a gap period between the parent study and entry in CIDP04; Criterion #14

Subject has a current diagnosis or has a history of Type 1 or Type 2 diabetes mellitus.

Has been changed to:

Subject has a current diagnosis or has a history of Type 1 or Type 2 diabetes mellitus **and/or hemoglobin A1c level >6.0%**.

Change #9

6.2.1 Additional exclusion criteria for subjects with a gap period between the parent study and entry in CIDP04; Criterion #21

Subject has a history of alcohol use disorder or other substance use disorder within 12 months of Screening Visit.

Has been changed to:

Subject has a history of alcohol use disorder or other substance use disorder **(as per Diagnostic and Statistical Manual of Mental Disorders-5 [American Psychiatric Association, 2013])** within 12 months of Screening Visit.

Change #10

6.4 Withdrawal criteria; Subjects may be discontinued from IMP section, Criterion #2

Subject experiences a severe AE of headache that is considered related to the IMP in the opinion of the investigator (Table 5 2). Following an event of a severe headache, a subject may continue participation in the study if the subject is willing to do so and the investigator, Medical Monitor, and Study Physician agree that the subject's continuation in the study poses no significant risk for the subject. The use of symptomatic headache treatment is allowed at the discretion of the investigator. The IMP dose can be reduced if the headache persists despite symptomatic treatment. The IMP dose may be reduced to [redacted] (refer to Section 9.1.10 for details on the management of headaches).

Has been changed to:

Subject experiences a severe AE of headache that is considered related to the IMP in the opinion of the investigator (**Section 9.1.10**). Following an event of a severe headache, a subject may continue participation in the study if the subject is willing to do so and the investigator, Medical Monitor, and Study Physician agree that the subject's continuation in the study poses no significant risk for the subject. The use of symptomatic headache treatment is allowed at the discretion of the investigator. The IMP dose can be reduced if the headache persists despite

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symptomatic treatment. The IMP dose may be reduced to [redacted] (refer to Section 9.1.10 for details on the management of headaches **and Section 7.2 for treatment to be administered**).

Change #11

7.2 Treatment to be administered

The initial dose administered will be based on the dose at the time of completion of the Treatment Period from the parent study (eg, CIDP01). For subjects who had a gap period between the parent study (eg, CIDP01) and CIDP04, a starting dose of [redacted] will be used. The dose used in the study may be reduced based on individual tolerability to [redacted] (eg, severe headache) but the maximum dose used will be [redacted].

Has been changed to:

The initial dose administered will be based on the dose at the time of completion of the Treatment Period from the parent study (eg, CIDP01). For subjects who had a gap period between the parent study (eg, CIDP01) and CIDP04, a starting dose of [redacted] will be used **(see Table 7-1)**. The dose used in the study may be reduced based on individual tolerability to [redacted] **(see Table 7-2)** (eg, severe headache) but the maximum dose used will be [redacted].

Change #12

7.2 Treatment to be administered

The following 2 tables have been added and the subsequent table has been renumbered sequentially:

Table 7-1: IMP doses to be administered (equivalent to approximately [redacted]) by body weight

Body weight ranges	IMP doses to be administered (equivalent to approximately [redacted][a])	IMP volume to be administered
≥40 to <49kg	[redacted]	[redacted]
≥49 to <63kg	[redacted]	[redacted]
≥63 to <77kg	[redacted]	[redacted]
≥77 to <91kg	[redacted]	[redacted]
≥91 to <105kg	[redacted]	[redacted]
≥105 to <119kg	[redacted]	[redacted]
≥119 to <133kg	[redacted]	[redacted]
≥133 to <147kg	[redacted]	[redacted]
≥147 to <161kg	[redacted]	[redacted]
≥161 to 170kg	[redacted]	[redacted]

IMP= investigational medicinal product

[a] Doses administered will be ±10% of the intended dose, except for subjects with a body weight of 47 to 50kg and 63kg.

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Table 7-2: IMP doses to be administered (equivalent to approximately [redacted]) by body weight

Body weight ranges	IMP doses to be administered (equivalent to approximately [redacted])	IMP volume to be administered
≥40 to <49kg	[redacted]	[redacted]
≥49 to <69kg	[redacted]	[redacted]
≥69 to <89kg	[redacted]	[redacted]
≥89 to <109kg	[redacted]	[redacted]
≥109 to <129kg	[redacted]	[redacted]
≥129 to <149kg	[redacted]	[redacted]
≥149 to <169kg	[redacted]	[redacted]
≥169 to 170kg	[redacted]	[redacted]

IMP= investigational medicinal product

Change #13

7.2 Treatment to be administered; fifth paragraph

The IMP will be administered as a sc infusion using a syringe pump. [redacted].

Has been changed to:

The IMP will be administered as a sc infusion using a syringe pump. [redacted]

Change #14

7.8.1 Permitted concomitant treatments (medications and therapies)

The following paragraph has been added:

The use of cannabidiols and medicinal marijuana (prescribed by a physician) is also permitted. When applicable, the subject must be on a stable dose of cannabidiols and/or medicinal marijuana for [redacted] prior to Screening Visit and remain stable for the duration of the study.

Change #15

7.8.3 Rescue medication; first sentence

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application. Any extracts or variations thereof.

If, at any time during this OLE study, a subject relapses according to the medical judgement of the investigator supported by, eg, subject's score on iRODS, INCAT, or maximum grip strength as assessed by the site personnel, then rescue therapy must be considered and the subject withdrawn from IMP (see Section 6.4).

Has been changed to:

If, at any time during this OLE study, a subject relapses according to the **predefined criteria for relapse as specified in Section 4.2.1 using the** subject's score on iRODS, INCAT, or maximum grip strength as assessed by the site personnel **and supported by the medical judgement of the investigator,** then rescue therapy must be considered and the subject withdrawn from IMP (see Section 6.4).

Change #16

8.1 Screening, Visit 1 (Weeks -5 to -2); second sentence

The following procedures will be performed at the Screening Visit:

Has been changed to:

The following procedures will be performed at the Screening Visit **(or as close as possible to the Screening date)**:

Change #17

9.1.1.4 Adverse events of interest; second paragraph

These events should be reported to UCB within 24h, regardless of seriousness, using the fax and email details for AEs of interest and independent of SAE reporting.

Has been changed to:

These events should be reported to UCB within 24h, regardless of seriousness**, by completing the eCRF. If the electronic system is unavailable for more than 24 hours, then the site will use the paper SAE data collection tool (see Section 9.1.2.3 for the reporting process).**

Change #18

9.1.2.3 Additional procedures for reporting serious adverse events

If an SAE is reported, UCB must be informed within 24h of receipt of this information by the site (see contact information for SAE reporting listed in the Serious Adverse Event Reporting section at the front of the protocol). The investigator must forward to UCB (or its representative) a duly completed "Investigator SAE Report Form for Development Drug" (SAE report form) provided by UCB, even if the data are incomplete, or if it is obvious that more data will be needed in order to draw any conclusions. Information recorded on this form will be entered into the global safety database.

An investigator SAE report form will be provided to the investigator. The investigator SAE Report form must be completed in English.

It is important for the investigator, when completing the SAE report form, to include the assessment as to a causal relationship between the SAE and the IMP administration. This insight

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from the investigator is very important for UCB to consider in assessing the safety of the IMP and in determining whether the SAE requires reporting to the regulatory authorities in an expedited manner.

Additional information (eg, autopsy or laboratory reports) received by the investigator must be provided within 24h. All documents in the local language must be accompanied by a translation in English, or the relevant information included in the same document must be summarized in the investigator SAE report form.

The investigator is specifically requested to collect and report to UCB (or its representative) any SAEs (even if the investigator is certain that they are in no way associated with the IMP), up to 30 days from the end of the study for each subject, and to also inform participating subjects of the need to inform the investigator of any SAE within this period. Serious AEs that the investigator thinks may be associated with the IMP must be reported to UCB regardless of the time between the event and the end of the study.

Upon receipt of the SAE report form, UCB will perform an assessment of expectedness of the reported SAE. The assessment of the expectedness of the SAE is based on the IB.

Has been changed to:

If an SAE is reported, UCB must be informed within 24h of receipt of this information by the site. **The primary mechanism for reporting an SAE to UCB will be the eCRF (using the eCRF SAE page). If the electronic system is unavailable for more than 24 hours, the** investigator must forward to UCB (or its representative) a duly completed **paper SAE data collection tool** provided by UCB, even if the data are incomplete, or if it is obvious that more data will be needed in order to draw any conclusions **(see contact information for SAE reporting listed in the Serious Adverse Event Reporting section at the front of the protocol)**. **The site will enter the SAE data into the electronic system as soon as it becomes available.**

~~An investigator SAE report form will be provided to the investigator.~~ The investigator SAE Report form must be completed in English.

It is important for the investigator, when completing the SAE **data collection tool**, to include the assessment as to a causal relationship between the SAE and the IMP administration. This insight from the investigator is very important for UCB to consider in assessing the safety of the IMP and in determining whether the SAE requires reporting to the regulatory authorities in an expedited manner.

Additional information (eg, autopsy or laboratory reports) received by the investigator must be provided within 24h. All documents in the local language must be accompanied by a translation in English, or the relevant information included in the same document must be summarized in the investigator SAE **data collection tool**.

The investigator is specifically requested to collect and report to UCB (or its representative) any SAEs (even if the investigator is certain that they are in no way associated with the IMP), up to 30 days from the end of the study for each subject, and to also inform participating subjects of the need to inform the investigator of any SAE within this period. Serious AEs that the investigator thinks may be associated with the IMP must be reported to UCB regardless of the time between the event and the end of the study.

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Upon receipt of the SAE **data collection tool**, UCB will perform an assessment of expectedness of the reported SAE. The assessment of the expectedness of the SAE is based on the IB.

After the study is completed at a given site, the electronic data collection tool will be taken off-line to prevent the entry of new data or changes to existing data.

If a site receives a report of a new SAE from a subject or receives updated data on a previously reported SAE after the electronic data collection tool has been taken off-line, then the site can report this information on a paper SAE form.

Change #19

9.1.2.4 Immediate reporting of adverse events; first sentence

The following AEs must be reported immediately using the SAE Report Form according to the procedure in Section 9.1.2.3:

Has been changed to:

The following AEs must be reported immediately using the SAE **data collection tool** according to the procedure in Section 9.1.2.3:

Change #20

9.1.4 Pregnancy; final paragraph, final sentence

Those SAEs must be additionally reported using the investigator SAE Report form.

Has been changed to:

Those SAEs must be additionally reported using the investigator SAE **data collection tool**.

Change #21

9.1.6 Overdose of investigational medicinal product; first sentence

Excessive dosing (beyond that prescribed in the protocol and including overdose) should be recorded in the eCRF

Has been changed to:

Excessive dosing (beyond that prescribed in the protocol and including overdose **ie, >10% above** [redacted]) should be recorded in the eCRF.

Change #22

9.2 Laboratory measurements

Table 9-3 Laboratory measurements; footnote e

Urine pregnancy test (dipstick) for women of childbearing potential performed prior to dosing (and confirmed negative) at dosing visits and each visit of the Observation Period. Note that the final urinary pregnancy test of the study should be no longer than 60 days after the final dose of IMP.

Has been changed to:

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Urine pregnancy test (dipstick) for women of childbearing potential performed prior to dosing (and confirmed negative) at dosing visits and each visit of the Observation Period. Note that the final urinary pregnancy test of the study should be no longer than **90** days after the final dose of IMP.

Change #23

9.3.6 Assessment and management of TB and TB risk factors; Monitoring for TB during the study, second paragraph, second sentence

Confirmed LTB, active TB, and NTMB must be reported to the Sponsor immediately regardless of seriousness using the SAE Report Form.

Has been changed to:

Confirmed LTB, active TB, and NTMB must be reported to the Sponsor immediately regardless of seriousness using the SAE **data collection tool**.

Change #24

10.2 INCAT; second paragraph

The investigator (or qualified personnel) will record the subjects' adjusted INCAT score at the time points detailed in the schedule of study assessments (Table 5-1).

Has been changed to:

The investigator (or qualified personnel) will record the subjects' adjusted INCAT score at the time points detailed in the schedule of study assessments (Table 5-1). **It is recommended that the rater of the scale remains the same throughout the duration of the study to ensure consistency of the rating.**

Change #25

14.3.1 Safety analyses; first paragraph, final sentence

The action taken, time of onset relative to dosing, and duration of each AE will be listed only.

Has been changed to:

The action taken, time of onset relative to dosing, **actual dose received,** and duration of each AE will be listed only.

Change #26

14.4.1 Efficacy analyses; fifth paragraph

Additional sensitivity analyses may be carried out and will be fully detailed in the SAP.

Has been changed to:

A sensitivity analysis will be performed excluding any subject who received a mean dose more than ±10% from the intended dose. Additional sensitivity analyses may be carried out and will be fully detailed in the SAP.

Change #27

14.4.2 Pharmacokinetic analyses; second paragraph, first sentence

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In contrast to the general descriptive display, concentration data will be summarized by time point using the number of available observations, mean, median, SD, minimum, maximum, geometric mean (and associated 95% CIs), and geometric coefficient of variation (assuming log-normally distributed data).

Has been changed to:

In contrast to the general descriptive display, concentration data will be summarized by **actual dose received and** time point using the number of available observations, mean, median, SD, minimum, maximum, geometric mean (and associated 95% CIs), and geometric coefficient of variation (assuming log-normally distributed data).

Change #28

14.4.3 Pharmacodynamic analyses; first sentence

For all PD variables, descriptive statistics for the value, change from Baseline, and/or percentage change from Baseline will be tabulated by time point.

Has been changed to:

For all PD variables, descriptive statistics for the value, change from Baseline, and/or percentage change from Baseline will be tabulated by **actual dose received and** time point.

Change #29

14.5 Handling of protocol deviations; first and third sentences

Important protocol deviations are identified as part of the data cleaning process in the Data Cleaning Plan (DCP). Ongoing data cleaning meetings will be held throughout the duration of the study. Objectives of these meetings include to review and update (if necessary) the important protocol deviations in the DCP and discuss criteria for exclusion of subjects from analysis populations.

Have been changed to:

Important protocol deviations are identified as part of the data cleaning process in the **Protocol Deviation Specification (PDS)**. Ongoing data cleaning meetings will be held throughout the duration of the study. Objectives of these meetings include to review and update (if necessary) the important protocol deviations in the **PDS** and discuss criteria for exclusion of subjects from analysis populations.

Change #30

17 References

The following reference has been added:

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Association; 2013.

Change #31

18 Appendices

Table 18-1 Suggested management guidelines for infusion reactions, first 2 reactions

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Type of reaction	Sponsor recommendations for management
Acute – Mild eg, flushing, dizziness, headache, sweating, palpitations, nausea	Slow [redacted] Infuse 0.9% sodium chloride 500 to 1000mL/h iv. Administer antihistamine iv/im. Administer paracetamol 1g orally. Monitor vital signs every 10 minutes until back to Baseline. [redacted] as tolerated until intended dose has been given.
Acute – Moderate eg, flushing, chest tightness, dyspnea, hypo/hypertension (change >20mmHg in systolic blood pressure), raised temperature, palpitations, urticaria	Stop infusion. [redacted]. Administer antihistamine iv/im. Administer paracetamol 1g orally. Monitor vital signs every 5 minutes until back to Baseline. [redacted]. [redacted] following this suggested regimen: Restart [redacted] [redacted] as tolerated until intended dose has been given.

Have been changed to:

Type of reaction	Sponsor recommendations for management
Acute – Mild eg, flushing, dizziness, headache, sweating, palpitations, nausea	Slow infusion rate to [redacted] [redacted]. Administer antihistamine iv/im. Administer paracetamol 1g orally. Monitor vital signs every 10 minutes until back to Baseline. [redacted].
Acute – Moderate eg, flushing, chest tightness, dyspnea, hypo/hypertension (change >20mmHg in systolic blood pressure), raised temperature, palpitations, urticaria	Stop infusion. [redacted] Administer antihistamine iv/im. Administer paracetamol 1g orally. Monitor vital signs every 5 minutes until back to Baseline. [redacted] [redacted] following this suggested regimen: [redacted]

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Type of reaction	Sponsor recommendations for management
	[redacted] **intended dose has been given**. [redacted]

18.5 Protocol amendment 3

Rationale for the amendment

The purpose of this substantial protocol amendment is to assess the safety and key efficacy of rozanolixizumab during an optional additional treatment period (Treatment Period Part 2) of up to 52 weeks (or until an Access Program or equivalent is available for rozanolixizumab, whichever comes first) on the basis of each study participant's individual benefit-risk assessment at the end of the first 24-week Treatment Period. This amendment is the opportunity to update the new legal entity of UCB effective since December 2019. Additional wording pertaining study participants being able to self-administer IMP after appropriate training has been included. One exclusion criteria has been clarified. The management of hypogammaglobulinemia has been adjusted for better control. An additional interim analysis has been added at the time of lock of the parent study and another at the end of the first Treatment Period (24 weeks) matching the original timepoint of results availability.

The following shows the changes made in Protocol Amendment 3 compared to the Protocol Amendment 2, dated 12 Jul 2019.

Modifications and changes

Global changes

Where applicable, the sponsor company name has changed from "UCB Biopharma SPRL" to "UCB Biopharma SRL" since the name of the legal form of the entity UCB Biopharma has changed into "société à responsabilité limitée" abbreviated "SRL. This change is not listed in the specific changes.

The term "subject" has been replaced with "study participant" where it has been used in reference to an individual who participates in a clinical study and is not listed in the specific changes.

Due to the additional Treatment Period in the study, where applicable, the term "Period" has been changed to "Periods" and is not listed in the specific changes.

Where "anti-rozanolixizumab antibodies" has been used in the protocol, the abbreviation "ADA" has been added where applicable and is not listed in the specific changes.

Specific changes

Change #1

Study contact information, sponsor study physician

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Name:	[redacted]
Address:	UCB Chemin du Foriest 1420 Braine-l'Alleud BELGIUM
Phone:	[redacted]

Has been changed to:

Name:	[redacted]
Address:	UCB Chemin du Foriest 1420 Braine-l'Alleud BELGIUM
Phone:	[redacted]

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Change #2

1 Summary; third paragraph

In case the subjects have a gap period between the end of the parent study and the start of this open-label study (ie, last visit in the parent study does not take place on the same day as entry of study CIDP04), a Screening Period of 2 to 5 weeks will be applicable to confirm that the subject still meets the eligibility criteria for entry in the open-label study and allow for a smooth transition between the treatment used by the subjects during the gap period and initiation of rozanolixizumab. The CIDP04 study includes a 24-week Treatment Period followed by an 8-week Observation Period. For the 24-week Treatment Period, subjects will have weekly visits (either on site or at home) during which they will be dosed with an sc infusion of rozanolixizumab, up to [redacted] The initial dose will be based on the dose the subject has received at the completion of the parent study (eg, CIDP01). For subjects who were known to be on placebo in the parent study (eg, CIDP01), a starting dose of [redacted] will be used. Dose may be reduced to [redacted] if [redacted] is not tolerable (eg, headache). The maximum dose of rozanolixizumab in CIDP04 will be [redacted] For exact doses to be administered, refer to Section 7.2.

Has been changed to:

In case the study participants have a gap period between the end of the parent study and the start of this open-label study (ie, last visit in the parent study does not take place on the same day as entry of study CIDP04), a Screening Period of 2 to 5 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry in the open-label study and allow for a smooth transition between the treatment used by the study participants during the gap period and initiation of rozanolixizumab. The CIDP04 study includes a 24-week Treatment Period, **an optional additional maximum 52-week Treatment Period** followed by an 8-week Observation

Period. **The length of the additional Treatment and Observation Periods may be shortened adjusted in case of availability of an Access Program**. For the ~~24-week~~ Treatment Period**s**, study participants will have weekly visits (either on site or at home) during which they will be dosed with an sc infusion of rozanolixizumab, up to [redacted]. The initial dose in the study will be based on the dose the study participant has received at the completion of the parent study (eg, CIDP01). For study participants who were known to be on placebo in the parent study (eg, CIDP01), a starting dose of [redacted] will be used. Dose may be reduced to [redacted] if [redacted] is not tolerable (eg, headache) **and/or recurrent low IgG levels (Treatment Period Part 2).** The maximum dose of rozanolixizumab in CIDP04 will be [redacted] For exact doses to be administered, refer to Section**.**

Change #3

2.1.1 Rationale for this study; first paragraph

The following sentence has been added to the end of the paragraph:

An optional extension of the treatment period by a maximum of an additional 52 weeks, or until an Access Program or equivalent is in place, whichever comes first, will be allowed on the basis of each participant's individual benefit-risk assessment at the end of the first 24-weeks Treatment Period. Study participants may choose to self-administer the IMP during Treatment Period Part 2 under supervision of a nurse and after having received appropriate training.

Change #4

4.2.1 Efficacy variables; selected other efficacy variables

- Absolute change from Baseline to Week 25 in iRODS score
- Subject experienced CIDP relapse (iRODS) up to Week 25 from Baseline
- Values and absolute change from Baseline in iRODS scores at each scheduled assessment during the Treatment and Observation Periods
- Time to CIDP relapse (adjusted INCAT) during the Treatment Periods from Baseline
- Subject experienced CIDP relapse (maximum grip strength as assessed by site personnel) up to Week 25 from Baseline

Has been changed to:

- ~~Absolute change from Baseline to Week 25 in iRODS score~~
- Values and absolute change from Baseline in iRODS scores at each scheduled assessment during the Treatment and Observation Periods
- Study participant experienced CIDP relapse (iRODS) up to Week 25 **and 77 (where applicable)** from Baseline
- Study participant experienced CIDP relapse (adjusted INCAT) up to Week 25 **and 77 (where applicable)** from Baseline

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- Study participant experienced CIDP relapse (maximum grip strength as assessed by site personnel) up to Week 25 **and 77 (where applicable)** from Baseline

Change #5

4.2.2 Efficacy variables; other efficacy variables

The following variables have new wording:

- Values and change from Baseline in fatigue **domain scores** at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in CIDP PRO instrument **domain scores** at each scheduled assessment during the Treatment and Observation Periods
- Patient Global Impressions of Change (PGIC) **value** at each scheduled assessment during Treatment and Observation Periods

Change #6

5.1 Study description; third, fourth, fifth and sixth paragraph

In case the subjects have a gap period between the end of the parent study and the start of this OLE study (ie, last visit in the parent study does not take place on the same day as entry of study CIDP04), a Screening Period of 2 to 5 weeks will be applicable to confirm that the subject still meets the eligibility criteria for entry in the OLE study and allow for a smooth transition between the treatment used by the study participants during the gap period and the initiation of rozanolixizumab. The CIDP04 study includes a first 24-week Treatment Period followed by an 8-week Observation Period. For the 24-week Treatment Period, subjects will have weekly visits (either on site or at home) during which they will be dosed with an sc infusion of rozanolixizumab up to [redacted] The initial dose will be based on the dose the subject has received at the completion of the parent study (eg, CIDP01). For subjects who were known to be on placebo in the parent study, a starting dose of [redacted] will be used. The maximum dose will be [redacted] See Section 7.2 for details on treatment to be administered.

During the first 4 weeks of the Treatment Period, all visits will be on site. During Weeks 5 to 8, home visits and on-site visits will be alternating (Weeks 5 and 7 will be on site; Weeks 6 and 8 will be at home). Starting at Week 9 and through the end of the Treatment Period (Week 24), subjects will have 1 visit on site followed by 3 visits at home for every 4-week period.

Starting at Week 25, subjects will enter the 8-week Observation Period where no IMP will be administered. During the Observation Period, study participants will have on-site visits at Weeks 25, and 32, and home visits at Weeks 27 and 29). Subjects can return to their SOC during the Observation Period (Section 6.4).

At the discretion of the investigator and/or subjects, home visits can be changed to site visits (eg, for safety reasons).

Has been changed to:

In case the study participants have a gap period between the end of the parent study and the start of this OLE study (ie, last visit in the parent study does not take place on the same day as entry

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of study CIDP04), a Screening Period of 2 to 5 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry in the OLE study and allow for a smooth transition between the treatment used by the study participants during the gap period and the initiation of rozanolixizumab. The CIDP04 study includes a **first** 24-week Treatment Period **(Part 1)** followed by **a second Treatment Period (Part 2) of 52 weeks. Entry to the Treatment Period (Part 2) will be contingent to a favorable individual benefit-risk after careful individual assessment has been performed for each study participant completing Treatment Period (Part 1). An 8**-week Observation Period **will be followed in case of premature termination or after completion of the Treatment Periods (either at end of Part 1 for study participants not continuing in Part 2 or at end of Part 2),** study participants will have weekly visits (either on site or at home) during which they will be dosed with an sc infusion of rozanolixizumab up to [redacted]. The initial dose will be based on the dose the study participant has received at the completion of the parent study (eg, CIDP01) **or at the completion of CIDP04 Part 1 for study participants entering CIDP04 Part 2**. For study participants who were known to be on placebo in the parent study, a starting dose of [redacted] will be used. The maximum dose will be [redacted]. See Section 7.2 for details on treatment to be administered.

During the Treatment Periods (Part 1 and Part 2), study participants all visits will be on site. During Weeks 5 to 8, home visits and on-site visits will be alternating (Weeks 5 and 7 will be on site; Weeks 6 and 8 will be at home). Starting at Week 9 and through the end of the Treatment Period (Week 24 **and if applicable, Week 76**), study participants will have 1 visit on site followed by 3 visits at home for every 4-week period.

After the completion of the Treatment Period(s) (starting at Week 25 for study participants only completing Part 1 or from Week 77 for study participants completing both Part 1 and Part 2 or at any early timepoint in case of PEOT), study participants will enter the 8-week Observation Period where no IMP will be administered. During the Observation Period, study participants will have on-site visits at **the entry and exit of the Observation Period (**Weeks 25/**77**, and 32/**84**, and home visits at Weeks 27/**79** and 29/**81)**. Study participants can return to their SOC during the Observation Period (Section 6.4). **In case the study participant enters an Access Program, no Observation Period will be performed with the exception of the PEOT (Visit 26) Visit which will be immediately completed.**

At the discretion of the investigator and/or subject, home visits can be changed to site visits (eg, for safety reasons). **In case an on-site visit cannot performed, the next visit will be performed at site instead of at home, and all safety assessments that should have been completed at the missed visits will be performed.**

Change #7

5.1.1 Study duration per subject; first paragraph

The total duration of the study for an individual subject is up to 37 weeks; this includes a 2- to 5-week Screening Period, a 24-week Treatment Period and an 8-week Observation Period.

Has been changed to:

The total duration of the study for an individual study participant will be up to ~~37 weeks is~~ **89** weeks; this includes a 2- to 5-week Screening Period, a 24-week Treatment Period **(Part 1), an**

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optional maximum 52-week Treatment Period (Part 2) or until an Access Program or equivalent is in place whichever comes first, and an 8-week Observation Period **in case the participant does not enter in an Access Program (or equivalent).**

Change #8

5.2 Schedule of study assessments; Table 5-1

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period												8-Week Observation Period			
	Visit	**1 Scr [a]**	**2 BL**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 14 18 22**	**11 15 19 23**	**12 16 20 24**	**13 17 21 25**	**26 PEOT**	**27**	**28**	**29 FV**
	Week	**-5 to -2**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9 13 17 21**	**10 14 18 22**	**11 15 19 23**	**12 16 20 24**	**25**	**27**	**29**	**32**
Assessments	**Visit type [a]**	**S**	**S**	**S**	**S**	**S**	**S**	**H [a]**	**S**	**H [c]**	**S**	**H [c]**	**H [c]**	**H [c]**	**S**	**H [c]**	**H [c]**	**S**
Written informed consent [a]		X	X															
Demographic data [d]		X	X															
Verification of inclusion and exclusion criteria [d]		X	X															
Withdrawal criteria			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Medical history update [d]		X	X															
Prior and concomitant medication		X	X [a]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medical procedures		X	X [e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs [a]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body weight		X	X [e]												X			X
Recording of AEs		X	X [e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Query for suicidality [a]		X	X [e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period												8-Week Observation Period			
	Visit	**1 Scr [a]**	**2 BL**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10 14 18 22**	**11 15 19 23**	**12 16 20 24**	**13 17 21 25**	**26 PEOT**	**27**	**28**	**29 FV**
	Week	**-5 to -2**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9 13 17 21**	**10 14 18 22**	**11 15 19 23**	**12 16 20 24**	**25**	**27**	**29**	**32**
Assessments	**Visit type [a]**	**S**	**S**	**S**	**S**	**S**	**S**	**H [a]**	**S**	**H [c]**	**S**	**H [c]**	**H [c]**	**H [c]**	**S**	**H [c]**	**H [c]**	**S**
Fatigue scale			X [e]				X				X				X			X
CIDP PRO Instrument			X [e]				X				X				X			X
PGIS			X [e]				X				X				X			X
PGIC			X [e a]				X				X				X			X
Full physical examination		X	X [e]															X
Brief physical examination				X	X	X	X		X		X				X			
Full neurological examination [a]		X	X [e]															X
Brief neurological examination				X	X	X	X		X		X				X			
12-lead ECG		X	X [e]	X	X	X			X		X		X		X			X
Labs (hematology, chemistry, urinalysis)		X	X [e]	X	X	X	X		X		X		X		X			X
Serology for HIV, hepatitis B, and hepatitis C [a]		X																
Serum/urine pregnancy test [a]		X	X [e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period												8-Week Observation Period			
	Visit	1 Scr [a]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	25	27	29	32
Assessments	**Visit type [a]**	S	S	S	S	S	S	H [a]	S	H [c]	S	H [c]	H [c]	H [c]	S	H [c]	H [c]	S
IGRA tuberculosis test [a]		X	X [e]															X
Tuberculosis Signs and Symptoms Questionnaire		X												X [a]				X
Contact IRT		X	X	X	X	X	X	X	X	X	X	X	X	X	X			X
Administration of IMP			X	X	X	X	X	X	X	X	X	X	X	X				
Blood sampling for PK of rozanolixizumab [a]			X [e]		X				X		X [a]				X			
Anti-rozanolixizumab antibodies			X [e]		X				X		X [o]				X			X
Serum complement (C3, C4) and plasma complement (C3a, C5a) [a]			X	X					X		X							
Serum cytokines [p]			X	X					X		X							

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period												8-Week Observation Period			
	Visit	1 Scr [a]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	25	27	29	32
Assessments	**Visit type [a]**	**S**	**S**	**S**	**S**	**S**	**S**	**H [a]**	**S**	**H [c]**	**S**	**H [c]**	**H [c]**	**H [c]**	**S**	**H [c]**	**H [c]**	**S**
Vaccination-specific antibody titers (tetanus and influenza Type A)		X							X		X [a]				X			
Immunoglobulins (total IgG and IgG subclasses)		X	X [e]	X	X	X	X		X		X				X			X
NF-L			X [e]						X						X			
IgA, IgM, IgE			X [e]	X	X	X	X		X		X				X			X
CIDP-specific auto-antibodies			X [e]				X				X				X			X
Blood sampling for exploratory biomarker analysis [a]			X	X					X		X							
iRODS assessment [a]		X	X [e]	X	X	X	X		X		X				X			X
INCAT assessment		X	X [e]	X	X	X	X		X		X				X			X
Assessment of grip strength by site personnel		X	X [e]	X	X	X	X		X		X				X			X
RT-MRC assessment		X	X [e]	X	X	X	X		X		X				X			X

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period												8-Week Observation Period			
	Visit	1 Scr [a]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	25	27	29	32
Assessments	Visit type [a]	S	S	S	S	S	S	S	H [a]	S	H [c]	S	H [c]	H [c]	H [c]	S	H [c]	H [c]	S

ADA=antidrug antibody; AE=adverse event; BL=baseline; CIDP=chronic inflammatory demyelinating polyradiculoneuropathy; C-SSRS=Columbia Suicide Severity Rating Scale; ECG=electrocardiogram; FV=Final Visit; H=Home visit; HIV=human immunodeficiency virus; ICF=Informed Consent form; IgA=immunoglobulin A; IgE=immunoglobulin E; IgG=immunoglobulin G; IgM=immunoglobulin M; IGRA=interferon gamma release assay; IMP=investigational medicinal product; INCAT=Inflammatory Neuropathy Cause and Treatment; iRODS=inflammatory Rasch-built Overall Disability Scale; IRT=interactive response technology; NF-L=neurofilament light chain; PEOT=premature end of treatment; PGIC=Patient Global Impressions of Change; PGIS=Patient Global Impressions of Severity; PK=pharmacokinetic; PRO=patient-reported outcome; RT-MRC=Rasch-built, modified-interval Medical Research Council scale, S=on-site visit; Scr=Screening visit; V=visit

Note: All assessments are to be completed in the order specified in the protocol or laboratory manual if possible. The ICF should be completed before any assessment. The PROs should be conducted in the order specified in Section 10.4 immediately after ICF (where applicable). The laboratory manual will provide further guidance on the order of sample collection.

[a] Only for subjects with a gap period between the parent study and entry in CIDP04.

[b] All visits have a ±2-day window. Minimum time between doses must be at least 5 days.

[c] The following visits can be performed by a healthcare professional visiting the subject at his/her home: Visits 11 to 13, 15 to 17, 19 to 21, and 23 to 25 (Weeks 10 to 12, 14 to 16, 18 to 20, and 22 to 24). Alternately, the visits can be conducted at the site as deemed necessary by site and/or subject. Feasibility of IMP dosing in a home setting will have to be confirmed before the visit is conducted (see Section 8.2).

[d] Will not be repeated at Visit 2 if performed at Visit 1.

[e] If entry in CIDP04 (Visit 2) is done on the same day as the last visit of the parent study and in case assessment was performed at last visit of the parent study, data from the parent study will be used and corresponding assessments will not be repeated in CIDP04.

[f] During site Visits 2, 3, and 4, vital signs will be measured prior to IMP administration, at the end of the infusion, and 2 and 4h after the end of the infusion. From Visit 5, vital signs will be measured predose, at the end of the infusion and 2h after the end of the infusion only. At nondosing visits, vital signs need only be taken once during the visit. For subjects requiring additional assessments due to AEs (see Table 5-2), additional vital sign measurements may be taken based on the timing of the assessments.

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[g] A full C-SSRS assessment will be performed only when the subject has a positive response to the suicidal ideation query. If a subject has active suicidal ideation as confirmed by the answer "Yes" to Question 4 or Question 5 of the C-SSRS assessments, the subject will be excluded or withdrawn from the study and immediately referred to a Mental Healthcare Professional.

[h] Not required for subjects who had a Screening Visit.

[i] The full neurological examination includes a fundoscopy. In addition to the FV, a full neurological examination should be performed for any subject who experiences severe headache (refer to Section 5.2.1 and Table 5-2).

[j] Serology includes hepatitis C virus (HCV)-antibodies (Ab)+, hepatitis B virus antibodies (HBsAg and HBcAb), human immunodeficiency virus antibodies (HIV1 and HIV2).

[k] In case of immediate entry from the parent study, the serum pregnancy test from the parent study should not be older than 5 weeks prior to entry into this CIDP04 study and the urine pregnancy test done at Visit 2 must both be negative before dosing. In case of gap period between the parent study and entry in CIDP04, a serum test will be performed at Visit 1 (Screening). Pregnancy testing will consist of urine testing at dosing visits during the Treatment Period and each visit during the Observation Period. A positive urine pregnancy test must be confirmed using a serum pregnancy test. Note that the final urine pregnancy test of the study should be no longer than 90 days after the final dose of IMP.

[l] The IGRA test will be performed in a central laboratory.

[m] Tuberculosis signs and symptoms Questionnaire must be done at least every 12 weeks.

[n] Trough PK samples should be taken for all subjects receiving rozanolixizumab. At Visits 2, 4, and 8, PK samples should be taken predose and 4h postdose for all subjects. At Visits 14, 18, and 22, a predose sample only should be taken. At Visit 26, samples to be taken once during the visit.

[o] Does not apply to Visit 10.

[p] Serum complement (C3, C4), plasma complement (C3a, C5a), and serum cytokines should be taken predose at Visit 2 for all subjects. Samples should be taken predose and 4h postdose for all subjects at other scheduled visits (Visits 3, 8, 10, 14, 18, and 22); if an infusion reaction occurs within the first 2h, refer to Section 5.2.1 and Table 5-2.

[q] Only at Visit 14.

[r] At Visits 2, 3, 8, 10, 14, 18, and 22, samples for exploratory biomarkers should be taken predose. See Table 5-2 for sampling in case of AE of interest.

[s] Assessment to be performed before all other assessments at each visit except ICF.

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Has been changed to:

Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [ab]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [bc]	S	S	S	S	S	S	H [ed]	S	H [ed]	S	H [ed]	H [ed]	H [ed]	S	H [ed]	S	H [ed]	H [ed]	S
Written informed consent [de]		X	X																	
Demographic data [de]		X	X																	
Verification of inclusion and exclusion criteria [de]		X	X																	
Withdrawal criteria			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Medical history update [de]		X	X																	
Prior and concomitant medication		X	X [ef]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medical procedures		X	X [ef]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [ab]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [bc]	S	S	S	S	S	S	H [ed]	S	H [ed]	S	H [ed]	H [ed]	H [ed]	S	H [ed]	S	H [ed]	H [ed]	S
Vital signs [fg]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body weight		X	X [ef]												X [h]		X			X
Recording of AEs		X	X [ef]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Query for suicidality [gi]		X	X [ef]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
Fatigue scale			X [ef]				X				X				X [j]		X			X
CIDP PRO Instrument							X				X				X [j]		X			X
PGIS			X [ef]				X				X				X [j]		X			X
PGIC			X [ef hk]				X				X				X [j]		X			X
Full physical examination		X	X [ef]																	X
Brief physical examination				X	X	X	X		X		X				X		X			

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [ab]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [bc]	S	S	S	S	S	S	H [ed]	S	H [ed]	S	H [ed]	H [ed]	H [ed]	S	H [ed]	S	H [ed]	H [ed]	S
Full neurological examination [l]		X	X [ef]																	X
Brief neurological examination				X	X	X	X		X		X				X		X			
12-lead ECG		X	X [ef]	X	X	X			X		X		X		X [m]		X			X
Labs (hematology, chemistry, urinalysis)		X	X [ef]	X	X	X	X		X		X		X		X		X			X
Serology for HIV, hepatitis B, and hepatitis C [jn]		X																		
Serum/urine pregnancy test [ko]		X	X [ef]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
IGRA tuberculosis test [lp]		X	X [ef]																	X

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [ab]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [bc]	S	S	S	S	S	S	H [ed]	S	H [ed]	S	H [ed]	H [ed]	H [ed]	S	H [ed]	S	H [ed]	H [ed]	S
Tuberculosis Signs and Symptoms Questionnaire		X												X [mq]	X [q]					X
Contact IRT		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			X
Administration of IMP			X	X	X	X	X	X	X	X	X	X	X	X	X [r]	X [r]				
Blood sampling for PK of rozanolixizumab [ns]			X [ef]		X				X		X [t]				X [m]		X			
ADA (Anti-rozanolixizumab antibodies)			X [ef]		X				X		X [et]				X [m]		X			X
Serum complement (C3, C4) and plasma complement (C3a, C5a) [pu]			X	X					X		X				X					

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [ab]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [bc]	S	S	S	S	S	S	H [ed]	S	H [ed]	S	H [ed]	H [ed]	H [ed]	S	H [ed]	S	H [ed]	H [ed]	S
Serum cytokines [pu]			X	X					X		X				X					
Vaccination-specific antibody titers (tetanus and influenza Type A)		X							X		X [qv]				X [m]		X			
Immunoglobulins (total IgG and IgG subclasses)		X	X [ef]	X	X	X	X	X [w]	X	X [w]	X	X [w]	X [w]	X [w]	X	X [w]	X			X
NF-L			X [ef]						X						X [x]		X [y]			
IgA, IgM, IgE			X [ef]	X	X	X	X		X		X				X [m]		X			X
CIDP-specific auto-antibodies			X [ef]				X				X				X [x]		X [y]			X [x]

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [ab]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [bc]	S	S	S	S	S	S	H [ed]	S	H [ed]	S	H [ed]	H [ed]	H [ed]	S	H [ed]	S	H [ed]	H [ed]	S
Blood sampling for exploratory biomarker analysis [fz]			X	X					X		X									
iRODS assessment [saa]		X	X [ef]	X	X	X	X		X		X				X		X			X
INCAT assessment		X	X [ef]	X	X	X	X		X		X				X		X			X
Assessment of grip strength by site personnel		X	X [ef]	X	X	X	X		X		X				X		X			X
RT-MRC assessment		X	X [ef]	X	X	X	X		X		X				X [x]		X [y]			X [x]

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Table 5-1: Schedule of study assessments

			24-Week Treatment Period (Part 1)												52-Week Additional Treatment Period (Part 2 - Optional) [a]		8-Week Observation Period (Optional)			
	Visit	1 Scr [ab]	2 BL	3	4	5	6	7	8	9	10 14 18 22	11 15 19 23	12 16 20 24	13 17 21 25	Additional Visits numbered sequentially		26 PEOT	27	28	29 FV
	Week	-5 to -2	1	2	3	4	5	6	7	8	9 13 17 21	10 14 18 22	11 15 19 23	12 16 20 24	Every 4 weeks	Weekly in between site visits	25 or 77	27 or 79	29 or 81	32 or 84
Assessments	Visit type [bc]	S	S	S	S	S	S	H [ed]	S	H [ed]	S	H [ed]	H [ed]	H [ed]	S	H [ed]	S	H [ed]	H [ed]	S

ADA=antidrug antibody; AE=adverse event; BL=baseline; CIDP=chronic inflammatory demyelinating polyradiculoneuropathy; C-SSRS=Columbia Suicide Severity Rating Scale; ECG=electrocardiogram; FV=Final Visit; H=Home visit; HIV=human immunodeficiency virus; ICF=Informed Consent form; IgA=immunoglobulin A; IgE=immunoglobulin E; IgG=immunoglobulin G; IgM=immunoglobulin M; IGRA=interferon gamma release assay; IMP=investigational medicinal product; INCAT=Inflammatory Neuropathy Cause and Treatment; iRODS=inflammatory Rasch-built Overall Disability Scale; IRT=interactive response technology; NF-L=neurofilament light chain; PEOT=premature end of treatment; PGIC=Patient Global Impressions of Change; PGIS=Patient Global Impressions of Severity; PK=pharmacokinetic; PRO=patient-reported outcome; RT-MRC=Rasch-built, modified-interval Medical Research Council scale, S=on-site visit; Scr=Screening visit; V=visit

Note: All assessments are to be completed in the order specified in the protocol or laboratory manual if possible. The ICF should be completed before any assessment. The PROs should be conducted in the order specified in Section 10.4 immediately after ICF (where applicable). The laboratory manual will provide further guidance on the order of sample collection.

[a] **The 52-week duration can be shortened or extended in view of the availability of an access program.**

[aa] Assessment to be performed before all other assessments at each visit except ICF.

[b] Only for study participants with a gap period between the parent study and entry in CIDP04.

[c] All visits have a ±2-day window. Minimum time between doses must be at least 5 days.

[d] The following visits can be performed by a healthcare professional visiting the study participant at his/her home: Visits 11 to 13, 15 to 17, 19 to 21, and 23 to 25 (Weeks 10 to 12, 14 to 16, 18 to 20, and 22 to 24). Visits in Treatment Period Part 2 will follow the same pattern: one site visit followed by 3 visits

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conducted at the participant home. Alternately, the visits can be conducted at the site as deemed necessary by site and/or study participant. Feasibility of IMP dosing in a home setting will have to be confirmed before the visit is conducted (see Section 8.2).

[e] Will not be repeated at Visit 2 if performed at Visit 1.

[f] If entry in CIDP04 (Visit 2) is done on the same day as the last visit of the parent study and in case assessment was performed at last visit of the parent study, data from the parent study will be used and corresponding assessments will not be repeated in CIDP04.

[g] During site Visits 2, 3, and 4, vital signs will be measured prior to IMP administration, at the end of the infusion, and 2 and 4h after the end of the infusion. From Visit 5 until Visit 25, vital signs will be measured predose, at the end of the infusion and 2h after the end of the infusion only. During Treatment Period Part 2, vital signs will be measured predose, at the end of the infusion. At nondosing visits, vital signs need only be taken once during the visit. For study participants requiring additional assessments due to AEs (see Table 5-2), additional vital sign measurements may be taken based on the timing of the assessments.

[h] **Body weight is collected every 6 months during Treatment Period Part 2 starting at first visit in this period and will be used to select the correct volume for dose infusion from these timepoints**.

[i] A full C-SSRS assessment will be performed only when the study participant has a positive response to the suicidal ideation query. If a study participant has active suicidal ideation as confirmed by the answer "Yes" to Question 4 or Question 5 of the C-SSRS assessments, the study participant will be excluded or withdrawn from the study and immediately referred to a Mental Healthcare Professional.

[j] **Only performed every 24 weeks**.

[k] Not required for study participants who had a Screening Visit.

[l] The full neurological examination includes a fundoscopy. In addition to the FV, a full neurological examination should be performed for any study participant who experiences severe headache (refer to Section 5.2.1 and Table 5-2).

[m] Assessment to be performed every 12 weeks **(Weeks 25, 37, 49 and 61)**.

[n] Serology includes hepatitis C virus (HCV)-antibodies (Ab)+, hepatitis B virus antibodies (HBsAg and HBcAb), human immunodeficiency virus antibodies (HIV1 and HIV2).

[o] In case of immediate entry from the parent study, the serum pregnancy test from the parent study should not be older than 5 weeks prior to entry into this CIDP04 study and the urine pregnancy test done at Visit 2 must both be negative before dosing. In case of gap period between the parent study and entry in CIDP04, a serum test will be performed at Visit 1 (Screening). Pregnancy testing will consist of urine testing at dosing visits during the Treatment Period Part 1, monthly urine testing during Treatment Period Part 2 and at each visit during the Observation Period for women of childbearing potential. A positive urine pregnancy test must be confirmed using a serum pregnancy test. Note that the final urine pregnancy test of the study should be no longer than 90 days after the final dose of IMP.

[p] The IGRA test will be performed in a central laboratory.

[q] Tuberculosis signs and symptoms Questionnaire must be done at least every 12 weeks.

[r] **Self-administration may be performed by study participant under the supervision of the home nurse after full training.**

[s] Trough PK samples should be taken for all study participants receiving rozanolixizumab. At Visits 2, 4, and 8, PK samples should be taken predose and 4h postdose for all study participants. At Visits 14, 18, 22 and **quarterly at site visits during Treatment Period Part 2,** a predose sample only should be taken. At Visit 26, samples to be taken once during the visit.

[t] Does not apply to Visit 10.

[u] Serum complement (C3, C4), plasma complement (C3a, C5a), and serum cytokines should be taken predose at Visit 2 for all study participants. Samples should be taken predose and 4h postdose for all study participants at other scheduled visits (Visits 3, 8, 10, 14, 18, 22 and at first (Week 25) and last visit (Week 73) of Treatment Period Part 2); if an infusion reaction occurs within the first 2h, refer to Section 5.2.1 and Table 5-2.

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[v] Only at Visit 14.

[w] **In case IgG levels are below 2 and the study participant does not qualify for a withdrawal, IgG levels will be monitored weekly.**

[x] **Assessments to be performed only at the first visit after Visit 25 (ie, 1st visit of Part 2). Visit 29/FV should not performed after Treatment Period 2.**

[y] **Only performed at PEOT visit when starting Observation Period directly after Treatment Period Part 1**

[z] At Visits 2, 3, 8, 10, 14, 18, and 22, samples for exploratory biomarkers should be taken predose. See Table 5-2 for sampling in case of AE of interest.

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Change #9

5.2.1 Additional study assessments; Table 5-2; complements and cytokines, and exploratory biomarkers rows only

Table 5-2: Additional study assessments

Assessment	When applicable
For subjects who experience infusion reactions (excluding local injection site reactions):	
Complements and cytokines	Samples required for all subjects are detailed in the schedule of study assessments (Table 5-1). In subjects who experience an infusion reaction within the first 2h at Visits 2, 4, 5, and 6, samples should also be taken 2 and 4 hours postdose (see Section 9.1.9 and Section 18.1). In subjects who experience an infusion reaction within 2 hours at Visits 3, 8, 10, 14, 18, and 22, samples should be taken 2 hours postdose (see Section 9.1.9 and Section 18.1).
For subjects who experience an AE of interest, including severe headache, moderate to severe diarrhea, moderate to severe abdominal pain, or moderate to severe vomiting: If the AE is initially reported at a home visit, the subject should be reviewed at the study site as soon as is practically possible for further investigation.	
Exploratory biomarkers	Samples required for all subjects are detailed in the schedule of study assessments (Table 5-1). In subjects who experience an AE of interest (as defined in Section 9.1.14) at Visits 2, 3, 8, 10, 14, 18, and 22, samples should also be taken 4 hours postdose.
For subjects who experience severe headache:	
Headache Questionnaire	In subjects who report severe headache, this assessment will be performed daily until resolution (ie, if headache becomes moderate or mild, normal collection of AEs should apply) (see Section 9.1.10).
Full neurological examination	Assessments required for all study participants are detailed in the schedule of study assessments Table 5-1 In subjects who report severe headache at the clinic visit, a full neurological examination (including fundoscopy) should be performed (see Section 9.1.10). In subjects who report a severe headache whilst at home, a visit to the site for the full neurological examination should be arranged for as soon as is practically possible.

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Has been changed to:

Table 5-2: Additional study assessments

Assessment	When applicable
For study participants who experience infusion reactions (excluding local injection site reactions):	
Complements and cytokines	Samples required for all study participants are detailed in the schedule of study assessments (Table 5-1). In study participants who experience an infusion reaction within the first 2h at Visits 2, 4, 5, and 6, samples should also be taken 2 and 4 hours postdose (see Section 9.1.9 and Section 18.1). In study participants who experience an infusion reaction within 2 hours at Visits 3, 8, 10, 14, 18, ~~and~~ 22 **and "S" visits during Treatment Period Part 2**, samples should be taken 2 hours postdose (see Section 9.1.9 and Section 18.1).
For study participants who experience an AE of interest, including severe headache, moderate to severe diarrhea, moderate to severe abdominal pain, or moderate to severe vomiting: If the AE is initially reported at a home visit, the study participant should be reviewed at the study site as soon as is practically possible for further investigation.	
Exploratory biomarkers	Samples required for all subjects are detailed in the schedule of study assessments (Table 5-1). In subjects who experience an AE of interest (as defined in Section 9.1.14) at Visits 2, 3, 8, 10, 14, 18, ~~and~~ 22 **and "S" visits during Treatment Period Part 2**, samples should also be taken 4 hours postdose.
For study participants who experience severe **and/or serious** headache:	
Headache Questionnaire	In study participants who report severe **and/or serious** headache, this assessment will be performed daily until resolution (ie, if headache becomes moderate or mild, normal collection of AEs should apply) (see Section 9.1.10).
Full neurological examination	Assessments required for all study participants are detailed in the schedule of study assessments (Table 5-1). In study participants who report severe **and/or serious** headache at the clinic visit, a full neurological examination (including fundoscopy) should be performed (see Section 9.1.10). In study participants who report a severe headache whilst at home, a visit to the site for the full neurological examination should be arranged for as soon as is practically possible.

Change #10

5.3 Rationale for study design and selection of dose; second paragraph

The initial dose of rozanolixizumab will be based on the dose the subject has received at the completion of the parent study (eg, CIDP01). For subjects who were known to be on placebo in parent study, a starting dose of [redacted] will be used. The dose may be reduced to [redacted] if [redacted] is not tolerable (eg, severe headache, Section 9.1.10). The dose and regimen of IMP to be used in the current study (rozanolixizumab [redacted] sc) is based on results from the FIH study UP0018, alongside the safety data from the MG and ITP studies (MG0002 and TP0001). CIDP04, similar to the parent study, CIDP01, will utilize a liquid formulation at [redacted].

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Has been changed to:

The initial dose of rozanolixizumab will be based on the dose the study participant has received at the completion of the parent study (eg, CIDP01). For study participants who were known to be on placebo in parent study, a starting dose of [redacted] will be used. The dose may be reduced to [redacted] if [redacted] is not tolerable (eg, severe headache, Section 9.1.10), **or in case of IgG levels are <1g/L (see Section 6.4.1.3**). The dose and regimen of IMP to be used in the current study (rozanolixizumab [redacted] sc) is based on results from the FIH study UP0018, alongside the safety data from the MG and ITP studies (MG0002 and TP0001). CIDP04, similar to the parent study, CIDP01, will utilize a liquid formulation at [redacted]

Change #11

6.2 Exclusion Criteria, criterion #19

Subject has a history of clinically relevant ongoing chronic infections including but not limited to human immunodeficiency virus (HIV), hepatitis B, hepatitis C, or is tested positive for human immunodeficiency virus antibody 1 (HIV1), human immunodeficiency virus antibody 2 (HIV2), hepatitis B surface antigen, or hepatitis C antibody at the Screening Visit.

Has been changed to:

Study participant has a history of clinically relevant ongoing chronic infections including but not limited to human immunodeficiency virus (HIV), hepatitis B, hepatitis C, or is tested positive for human immunodeficiency virus antibody 1 (HIV1), human immunodeficiency virus antibody 2 (HIV2), hepatitis B surface antigen, **hepatitis B core antibody without hepatitis B surface antibody test positive,** or hepatitis C antibody at the Screening Visit.

Change #12

6.4.1.1 Serious infection

Treatment must be temporarily discontinued if subject has a serious infective episode requiring eg, hospitalization, or iv antibiotic therapy (including but not limited to bacteremia or sepsis, bacterial meningitis, osteomyelitis or septic arthritis, bacterial pneumonia, or visceral abscess). Upon resolution of such an event, the subject may restart treatment with IMP at the discretion of the investigator and in agreement with Medical Monitor and Study Physician, if the subject is willing and if the benefit-risk remains favorable for the subject.

Has been changed to:

Treatment must be ~~temporarily~~ discontinued if study participant has a serious infective episode requiring eg, hospitalization, or iv antibiotic therapy (including but not limited to bacteremia or sepsis, bacterial meningitis, osteomyelitis or septic arthritis, bacterial pneumonia, or visceral abscess). ~~Upon resolution of such an event, the subject may restart treatment with IMP at the discretion of the investigator and in agreement with Medical Monitor and Study Physician, if the subject is willing and if the benefit-risk remains favorable for the subject.~~

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Change #13

6.4.1.2 Hypogammaglobulinemia and non-serious persisting or recurrent infection

Treatment may be temporarily discontinued for the subject who develops an event of non-serious infection, which is persisting or recurrent, and a serum total IgG ≤2 g/L (see Section 7.9). Upon resolution of such an event, the subject may restart treatment with IMP at the discretion of the investigator and in agreement with Medical Monitor and Study Physician, if the subject is willing and if the benefit-risk remains favorable for the subject.

Has been changed to:

In the event of a non-serious infection, the Benefit-Risk of continuing treatment with IMP must be carefully evaluated by the Investigator in collaboration with the Medical Monitor and the Study Physician. Treatment may be temporarily discontinued for the subject who develops **a** ~~an event of~~ non-serious ~~infection, which is~~ persisting or recurrent **infection with a**~~,~~ ~~and a~~ serum total IgG **levels between ≥1 and <≤**2g/L (see Section 7.9). Upon resolution of ~~such an event~~ **infection and the IgG levels returning to ≥2g/L**, the study participant may restart treatment with IMP **(at the same dose for study participants in Treatment Period Part 1, or at the same dose or at the reduced dose of [redacted] for study participants in Treatment Period Part 2)** at the discretion of the investigator and in agreement with Medical Monitor and Study Physician **at a dose level of [redacted] for study participants in TP Part 2**, if the subject is willing and if the benefit-risk remains favorable for the study participant.

Change #14

6.4.1.3 Hypogammaglobulinemia irrespective of infection

Treatment may will be temporarily discontinued for the subject who develops an event of hypogammaglobulinemia with a serum total IgG <1g/L (see Section 7.9) regardless of event of infection. When the IgG level reaches ≥1g/L, the subject may be allowed to continue treatment with IMP at the discretion of the investigator and in agreement with Medical Monitor and Study Physician, if the subject is willing and if the benefit-risk remains favorable for the subject. The dose of the IMP may be reduced to [redacted] (Section 7.2)

Has been changed to:

Treatment ~~may~~ **will** be temporarily discontinued for the study participant who develops an event of hypogammaglobulinemia with a serum total IgG <1g/L (see Section 7.9) ~~regardless of event~~ **irrespective** of infection. When the IgG level reaches ≥~~1~~**2**g/L, the study participant may **be allowed to restart** ~~continue~~ treatment with IMP **(at the same dose for study participants in Treatment Period Part 1, or at the same dose or at the reduced dose of [redacted] for study participants in Treatment Period Part 2)** at the discretion of the investigator and in agreement with Medical Monitor and Study Physician, **at a dose level of [redacted] for study participants in Treatment Period Part 2**, if the study participant is willing and if the benefit-risk remains favorable for the study participant.

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Change #15

7.2 Treatment to be administered; first, second and sixth paragraph

The initial dose administered will be based on the dose at the time of completion of the Treatment Period from the parent study (eg, CIDP01). For subjects who had a gap period between the parent study (eg, CIDP01) and CIDP04, a starting dose of [redacted] will be used (see Table 7-1). The dose used in the study may be reduced based on individual tolerability to [redacted] (see Table 7-2) (eg, severe headache) but the maximum dose used will be [redacted].

Eligible subjects will receive rozanolixizumab [redacted] by sc infusion for 24 weeks during Treatment Period Part 1 (from Visit 2 to Visit 25) and during an additional 52 weeks during Treatment Period Part 2.

The subject's body weight at entry into CIDP04 (either at Screening [Visit 1] or Baseline [Visit 2]) will be used for the dose calculation throughout the duration of the study.

Has been changed to:

The initial dose administered will be based on the dose at the time of completion of the Treatment Period from the parent study (eg, CIDP01). For study participants who had a gap period between the parent study (eg, CIDP01) and CIDP04, a starting dose of [redacted] will be used (see Table 7-1). The dose used in the study may be reduced based on individual tolerability to [redacted] (see Table 7-2) (eg, severe headache) but the maximum dose used will be [redacted] **The dose used during Treatment Period Part 2 may be reduced to [redacted] in case of recurrent low observed IgG levels for a participant. Treatment temporary halt may also be implemented in some situation (see Section 6.4.1).**

Eligible study participants will receive rozanolixizumab [redacted] by sc infusion for 24 weeks **during Treatment Period Part 1 (**from Visit 2 to Visit 25**) and during an additional 52 weeks during Treatment Period Part 2. Treatment Period Part 2 may be shortened depending on availability of an Access Program or equivalent.**

Study participants may choose to self-administer the IMP during Treatment Period Part 2 under supervision of a nurse and after having received appropriate training.

The study participant's body weight at entry into CIDP04 (either at Screening [Visit 1] or Baseline [Visit 2]) will be used for the dose calculation throughout ~~the duration of the study~~ **Treatment Period Part 1. Body weight will be reevaluated at start of the Treatment Period Part 2, and again 6 months later, and will be used to select the correct volume for dose infusion from these timepoints.**

Change #16

7.5 Handling and storage requirements; second paragraph

Appropriate storage conditions must be ensured either by controlling the temperature (eg, room, refrigeration unit) or by completion of a temperature log in accordance with local requirements on a regular basis (eg, once a week), showing actual and minimum/maximum temperatures reached over the time interval.

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Has been changed to:

Appropriate storage conditions must be ensured either by controlling the temperature (eg, room, refrigeration unit) or by completion of a temperature log in accordance with local requirements on a regular basis (eg, ~~once a week~~ **every work day**), showing actual and minimum/maximum temperatures reached over the time interval.

Change #17

8 Study Procedures by Visit

The following paragraph has been added:

In case an on-site visit cannot be performed, the subsequent visit will be performed at the site instead of at home, and all safety assessments that should have been completed at the missed visit will be performed.

Change #18

8.2 Treatment Period, Visits 2 to 25 (Weeks 1 to 24); last paragraph

The investigator will be asked to complete a checklist confirming all criteria have been fully evaluated either at Screening (Visit 1) or Baseline (Visit 2), and be confirmed in case of changes to the subject's condition. This checklist will be shared with the UCB Study Physician and reviewed before IMP administration in a home setting can take place.

Has been changed to:

8.2 Treatment Period **Part 1**, Visits 2 to 25 (Weeks 1 to 24); last paragraph

The investigator will be asked to complete a checklist confirming all criteria have been fully evaluated ~~either at Screening (Visit 1) or Baseline (Visit 2)~~**and met before the first home dosing visit can take place,** and **will** be **re**confirmed in case of changes to the study participant's condition. This checklist will be shared with the UCB Study Physician and reviewed before IMP administration in a home setting can take place.

Change #19

The following sections have been added:

8.3 **Treatment Period Part 2 (Weeks 25 to 76)**

Entry into the Treatment Period (Part 2) will be subject to a careful individual assessment of the benefit-risk for each study participant completing Treatment Period (Part 1) following a discussion with the Sponsor's Medical Monitor and/or Study Physician. The first visit of Treatment Period Part 2 will be performed at site at Week 25 followed by 3 weekly visits at the study participant's home. This sequence will be repeated until the end of the Treatment Period Part 2. The visits during this period will be numbered sequentially.

Study participants may choose to self-administer the IMP during Treatment Period 2 under supervision of a nurse and after having received appropriate training.

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8.3.1 Additional site visits during maximum 52-week Treatment Period Part 2 (monthly starting at Week 25) or until availability of an Access Program (whichever comes first)

The first visit of Treatment Period Part 2 will be performed on site at Week 26. Site visits will be performed monthly. The following procedures will be performed at monthly frequency unless otherwise defined:

- **PROs should be conducted in the order specified in Section 10.4:**
  - **iRODS assessment – to be performed before any other assessment**
  - **Fatigue scale (every 24 weeks)**
  - **CIDP PRO instrument (every 24 weeks)**
  - **PGIS (every 24 weeks)**
  - **PGIC (every 24 weeks)**
- **Query for suicidality**
- **Tuberculosis Signs and Symptoms Questionnaire (every 12 weeks)**
- **Withdrawal criteria assessment**
- **Prior and concomitant medications**
- **Concomitant medical procedures**
- **Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)**
- **Body weight (Week 25 and Week 49)**
- **Recording of AEs**
- **Brief physical examination**
- **Brief neurological examination**
- **12-lead ECG (on-site visits only [Weeks 25, 37, 49, 61])**
- **Blood sample (all samples should be taken predose unless otherwise specified; the laboratory manual will provide guidance on the order of sample collection) for:**
  - **Clinical laboratory tests (ie, hematology and clinical chemistry)**
  - **PK of rozanolixizumab (on-site visits only [Weeks 25, 37, 49, 61])**
  - **ADA (anti-rozanolixizumab antibodies) (on-site visits only [Weeks 25, 37, 49, 61])**
  - **Serum complement (C3, C4) and plasma complement (C3a, C5a) (predose and 4h postdose) (at Weeks 25 and 73)**
  - **Serum cytokines (predose and 4h postdose) (at Weeks 25 and 73)**
  - **Vaccination-specific antibody titers (tetanus and influenza Type A) (on-site visits only [Weeks 25, 37, 49, 61])**

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- **Immunoglobulins (total IgG and IgG subclasses)**
- **IgA, IgM, IgE (on-site visits only [Weeks 25, 37, 49, 61])**
- **NF-L (only at Week 25)**
- **CIDP specific auto-antibodies (only at Week 25)**

- **Urine pregnancy test**
- **Contact IRT**
- **Administer IMP – self-administration by the study participant under the supervision of the nurse (to confirm that study participant is proceeding correctly) may be considered provided the participant is willing to do so, the participant has been adequately trained by the site personnel according to Self-administration training guidance document**
- **INCAT assessment**
- **Assessment of grip strength by site personnel**

8.3.2 Additional home visits during Treatment Period Part 2 (weekly in between site visits starting at Week 26

The following procedures will be performed during the Treatment Period Part 2 by a healthcare professional visiting the study participant at his or her home. Visits will be performed weekly in between monthly site visits (Section 8.3.1):

- **Withdrawal criteria assessment**
- **Prior and concomitant medications**
- **Concomitant medical procedures**
- **Vital signs (prior to IMP administration, at the end of the infusion, at 2h after the end of the infusion)**
- **Recording of AEs**
- **Contact IRT**
- **Administer IMP (unless IMP is temporarily discontinued (see Section 6.4.1.3) – self-administration by the study participant under the supervision of the home nurse may be considered provided the participant is willing to do it and has been adequately trained by the site personnel according to Self-administration training guidance document.**

Change #20

8.3 Observation Period, Visits 26 to 29 (Weeks 25 to 32); heading and first paragraph

Following the final dose of rozanolixizumab at Week 24 (Visit 25), 4 subsequent visits will be scheduled over 8 weeks (Visits 26 to 29) to collect safety and efficacy data for study-related outcome measures and procedures. Visit 27 and Visit 28 are home nursing visits to be conducted by a healthcare professional visiting the subject at his/her home; these visits can be conducted at the site as deemed necessary by site personnel and/or subject.

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All subjects should perform all visits of the Observation Period, including the FV (scheduled 8 weeks after the final dose of IMP). If at any time during the Observation Period the subject relapses (according to the medical judgement of the investigator supported by, eg, subject's score on iRODS, INCAT, or maximum grip strength [assessed by site personnel]), then rescue medication must be considered. The subject will return to the SOC (ie, Ig treatment) as rescue medication at the time of relapse.

Has been changed to:

8.4 Observation Period, Visits 26 to 29 (Weeks 25 **to 32 study participants completing Treatment Period Part 1 only and Weeks 77 to 84 for study participants completing Treatment Period Part 1 and Part 2**)

Following the final dose of rozanolixizumab at Week 24 (Visit 25) **or Week 76**, 4 subsequent visits will be scheduled over 8 weeks (Visits 26 to 29) to collect safety and efficacy data for study-related outcome measures and procedures **unless the study participant continues rozanolixizumab treatment under an Access Program or equivalent. In the latter case, only the PEOT Visit (Visit 26) will be performed.** Visit 27 and Visit 28 are home nursing visits to be conducted by a healthcare professional visiting the study participant at his/her home; these visits can be conducted at the site as deemed necessary by site personnel and/or study participant.

All study participants **who do not continue on rozanolixizumab in an Access Program** should perform all visits of the Observation Period, including the FV (scheduled 8 weeks after the final dose of IMP). If at any time during the Observation Period the study participant relapses (according to the medical judgement of the investigator supported by, eg, study participant's score on iRODS, INCAT, or maximum grip strength [assessed by site personnel]), then rescue medication must be considered. The study participant will return to the SOC (ie, Ig treatment) as rescue medication at the time of relapse.

Change #21

8.3.1 Visit 26 (Week 25/PEOT); first sentence and specific assessments

The following procedures will be performed at Visit 26 (Week 25/PEOT):

- Pregnancy test
  - Anti-rozanolixizumab antibodies
  - NF-L (Visit 26 [Week 25] only)
  - CIDP specific auto-antibodies (Visit 26 [Week 25] only)
- RT-MRC assessment (Visit 26 [Week 25] only)

Has been changed to:

8.~~3~~4.1 Visit 26 (Week 25 **or Week 77 or** PEOT)

The following procedures will be performed at Visit 26 (Week 25 **or Week 77 or** ~~/~~PEOT):

- **Urine** ~~P~~**p**regnancy test **for women of childbearing potential**
  - ~~Anti-~~ **ADA (anti-**rozanolixizumab antibodies**)**

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– NF-L **(Visit 26 [Week 25] only or PEOT only if Treatment Period 1 is performed)**

– CIDP specific auto-antibodies **(Visit 26 [Week 25] only or PEOT only if Treatment Period 1 is performed)**

- RT-MRC assessment **(Visit 26 [Week 25] only)**

Change #22

8.3.2 Visit 27 and 28 (Weeks 27 and 29), Home Visits; first sentence

The following procedures will be performed at Visits 27 and 28 (Weeks 27 and 29, and at 79 and 81) by a healthcare professional visiting the subject at his/her home:

Has been changed to:

8.~~3~~**4**.2 Visit 27 and 28 (Weeks 27 and 29**, and at 79 and 81**), Home Visits; first sentence

The following procedures will be performed at Visits 27 and 28 (Weeks 27 and 29**, and at 79 and 81**) by a healthcare professional visiting the subject at his/her home:

Change #23

8.3.3 Visit 29 (Week 32/FV); first sentence

The following procedures will be performed at Visit 29 (Week 32/FV):

- Urine sample for urinalysis and urine pregnancy test
  – Anti-rozanolixizumab antibodies

Has been changed to:

8.~~3~~**4**.3 Visit 29/**FV** (Week 32/~~FV~~**84**)

The following procedures will be performed at Visit 29/**FV** (Week 32/~~FV~~**84**):

- Urine sample for urinalysis ~~and urine pregnancy test~~
- **Urine pregnancy test for women of childbearing potential**
  – ~~Anti-~~**ADA (anti**-rozanolixizumab antibodies**)**

Change #24

8.5 Premature end of treatment and Final Visit

The following paragraph has been added:

A study participant entering the Access Program after completion of part or full Treatment Period 2 without any relapse will not complete the Observation Period but will only perform the PEOT/V26 one week after the last IMP dispensing for the study.

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Change #25

9.1.1.2.1 Anticipated serious adverse events

The following Anticipated SAEs are anticipated to occur in the population studied in this protocol at some frequency that is independent of drug exposure (Table 9-1).

This list does not change the investigator's obligation to report all SAEs (including Anticipated SAEs) as detailed in Section 9.1.2.3.

Table 9-1: Anticipated serious adverse events for CIDP population

Neurologic diseases [a]	Muscle weakness, numbness and pain in the extremities, impaired balance, difficulty walking

[a] The investigator should report these adverse events as serious adverse events only if they meet criteria for seriousness (see Section 9.1.1.2).

Has been changed to:

The following Anticipated SAEs, **fatigue, infection and headache** are anticipated to occur in the population studied in this protocol at some frequency that is independent of drug exposure ~~(Table 9-1)~~.

This ~~list~~ **information** does not change the investigator's obligation to report all SAEs (including Anticipated SAEs) as detailed in Section 9.1.2.3.

~~Table 9-1: Anticipated serious adverse events for CIDP population~~

~~Neurologic diseases [a]~~	~~Muscle weakness, numbness and pain in the extremities, impaired balance, difficulty walking~~

~~[a] The investigator should report these adverse events as serious adverse events only if they meet criteria for seriousness (see Section 9.1.1.2).~~

Change #26

9.1.2.1 Description of adverse events, third paragraph

For recording an AE, Common Terminology Criteria for Adverse Events (CTCAE) will be used, and only if it is impossible to assess severity using CTCAE, then AE intensity will be assessed using a scale of mild, moderate, or severe.

Has been changed to:

~~For recording an AE, Common Terminology Criteria for Adverse Events (CTCAE) will be used, and only if it is impossible to assess severity using CTCAE, then AE intensity will be assessed using a scale of mild, moderate, or severe.~~

- **Mild: An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities**
- **Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities**

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- **Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.**
- **An event is defined as 'serious' when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe (eg, a severe AE may be either serious or not serious, depending on whether these criteria are also met).**

Change #27

9.1.4 Pregnancy; first paragraph, second bullet point

The study participant should immediately stop the intake of the IMP or be down-titrated as instructed at the PEOT Visit.

Has been changed to:

The study participant should immediately stop the intake of the IMP ~~or be down-titrated~~ as instructed at the PEOT Visit.

Change #28

9.1.9 Hypersensitivity and adverse reactions; first paragraph and Table 9-2

The grading for infusion-related reactions according to the NCI Common Terminology Criteria for Adverse Events version 4.03 (Jun 2010) (Doessegger and Banholzer, 2015) is provided in Table 9-2. In the event of a severe or life-threatening (ie, Grade 3 or 4) infusion reaction, the subject must permanently discontinue IMP and be managed as described in Section 18.1.

Table 9-2: Infusion-related reaction grading according to the NCI Common Terminology Criteria for adverse events version 4.03 (Jun 2010)

Grading	Infusion-related reaction
1	Mild transient reaction: infusion interruption not indicated; intervention not indicated
2	Moderate: Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (for example, antihistamines, NSAIDs, narcotics, iv fluids); prophylactic medications indicated for ≤24h
3	Severe: Prolonged; recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae
4	Life-threatening consequences; urgent intervention indicated
5	Death

iv=intravenous; NCI=National Cancer Institute; NSAID=nonsteroidal anti-inflammatory drugs
Data source: Doessegger et al, 2015

Has been changed to:

The grading for infusion-related reactions according to the NCI Common Terminology Criteria for Adverse Events **(CTCAE)** version ~~4.03~~**5.0** (Jun ~~2010~~**2017**) ~~(Doessegger and Banholzer, 2015)~~ is provided in Table 9-2. In the event of a severe or life-threatening (ie, Grade 3 or 4)

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infusion reaction, the study participant must permanently discontinue IMP and be managed as described in Section 18.1.

Table 9-2: Infusion-related reaction grading according to the NCI Common Terminology Criteria for adverse events version ~~4.03~~**5.0** (Jun ~~2010~~**2017**)

Grading	Infusion-related reaction
1	Mild transient reaction: infusion interruption not indicated; intervention not indicated
2	Moderate: Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (for example, antihistamines, NSAIDs, narcotics, iv fluids); prophylactic medications indicated for ≤24h
3	Severe: Prolonged **(eg, not rapidly responsive to symptomatic medication and/or brief interruption of infusion)**; recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae
4	Life-threatening consequences; urgent intervention indicated
5	Death

iv=intravenous; NCI=National Cancer Institute; NSAID=nonsteroidal anti-inflammatory drugs

~~Data source: Doessegger et al, 2015~~

Change #29

9.1.10 Management of headache

Treatment of headaches should be as per national guidelines and take medical history of previous headaches, concomitant medication, and co-morbidities (eg, asthma) in consideration. In case of continued tolerance issues, and if symptomatic headache medication (eg, acetylsalicylic acid 1000mg) is not sufficient, a further step can be to reduce dose of IMP to [redacted] (see Section 7.2).

Severe headache is defined as severe pain limiting self-care activities of daily living (ADL) or new/prolonged hospitalization for management of headache or life-threatening consequences requiring urgent medical intervention. Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications. Treatment of headache will be provided as clinically indicated according to the national guidelines.

Subjects experiencing severe headache will complete the Headache Questionnaire daily until resolution (ie, if headache becomes moderate or mild, normal collection of AEs should apply). At the clinic visit when the severe headache is reported, the Headache Questionnaire will be followed by a neurological assessment (including fundoscopy). If the severe headache is initially reported at a home visit or during a telephone call, the subject should be reviewed at the study site as soon as is practically possible for further investigations. Further workup will be performed at the discretion of the investigator and may include, eg, a computed tomography scan, magnetic resonance imaging and/or a lumbar puncture for cerebral spinal fluid collection. In addition, samples for exploratory biomarkers should be taken for subjects experiencing severe headache Table 5-2). These investigations will be performed to further understand the mechanism of headache in these subjects.

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Details of neurological examination to be performed are provided in Section 9.3.4. The Headache Questionnaire will be provided in the study procedures manual.

Has been changed to:

Based on current available clinical data, headache is the most commonly reported adverse drug reaction in study participants treated with rozanolixizumab. Study participants should be well informed of this potential adverse drug reaction and should be instructed on how to manage it.

Treatment of headaches should be as per national guidelines and take medical history of previous headaches, concomitant medication, and co-morbidities (eg, asthma) in consideration. In case of continued tolerance issues, and if symptomatic headache medication (eg, acetylsalicylic acid 1000mg) is not sufficient, a further step can be to reduce dose of IMP to [redacted] (see Section 7.2).

Determination of the severity of headache will be consistent with National Cancer Institute CTCAE version 5.0. Severe headache is defined as severe pain limiting self-care activities of daily living (ADL) ~~or new/prolonged hospitalization for management of headache or life-threatening consequences requiring urgent medical intervention~~. Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications. Treatment of headache will be provided as clinically indicated according to the national guidelines.

Study participants experiencing severe **and/or serious** headache will complete the Headache Questionnaire daily until resolution (ie, if headache becomes **nonserious,** moderate or mild, **or completely resolved, whichever comes first** ~~normal collection of AEs should apply~~). At the clinic visit when the severe headache is reported, the Headache Questionnaire will be followed by a neurological assessment (including fundoscopy). If the severe **or serious** headache is initially reported at a home visit or during a telephone call, the study participant should be reviewed at the study site as soon as is practically possible for further investigations. **Study participants should be monitored for signs and symptoms suggestive of central nervous system involvement and evaluated immediately if other causes (eg, meningitis, intracranial bleeding) are suspected.** Further **neurological** workup ~~will~~**may** be performed **(if indicated)** at the discretion of the investigator and may include, ~~eg,~~ a computed tomography scan, magnetic resonance imaging and/or a lumbar puncture for cerebral spinal fluid collection. In addition, samples for exploratory safety biomarkers should be **collected**~~taken~~ for study participants experiencing severe **or serious** headache **when possible** (Table 5-2). These investigations will be performed to further understand the mechanism of headache in these study participants.

Details of neurological examination to be performed are provided in Section 9.3.4. The Headache Questionnaire will be provided in the study procedures manual.

Change #30

9.1.11 Management of moderate or severe diarrhea; first and second paragraph

Moderate or severe diarrhea is defined as an increase of ≥4 stools per day over Baseline or incontinence due to urgency of diarrhea or new/prolonged hospitalization for management of diarrhea or limiting self-care ADL or life-threatening consequences requiring urgent medical intervention.

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Stool collection and analysis will be performed for subject reporting moderate or severe diarrhea. The frequency of stool sampling will be as clinically indicated in the opinion of the investigator. Analysis of stool samples will be performed locally.

Has been changed to:

Moderate or severe diarrhea is defined as an increase of ≥4 stools per day over Baseline or incontinence due to urgency of diarrhea or new/prolonged hospitalization for management of diarrhea or limiting self-care ADL or life-threatening consequences requiring urgent medical intervention. **Determination of the severity of diarrhea will be consistent with CTCAE version 5.0.**

Stool collection and analysis will be performed for subjects reporting moderate or severe diarrhea. The frequency of stool sampling will be as clinically indicated in the opinion of the investigator **and assessed per local guidance**. Analysis of stool samples will be performed locally. **In addition, collection of blood samples for the assessment of exploratory safety biomarkers is required for study participants with severe GI disturbances including diarrhea.**

Change #31

9.3.2 Vital signs, second paragraph

Subjects should be sitting for 5 minutes prior and during the collection of BP and PR measurements. During site Visits 2, 3, and 4, vital signs will be measured prior to IMP administration, at the end of the infusion, and 2 and 4h after the end of the infusion. From Visit 5, vital signs will be measured predose, at the end of the infusion and 2h after the end of the infusion only. At nondosing visits, vital signs need only be taken once during the visit.

Has been changed to:

Study participants should be sitting for 5 minutes prior and during the collection of BP and PR measurements. During site Visits 2, 3, and 4, vital signs will be measured prior to IMP administration, at the end of the infusion, and 2 and 4h after the end of the infusion. From Visit 5 **to Visit 25**, vital signs will be measured predose, at the end of the infusion and 2h after the end of the infusion only. **During Treatment Period Part 2, vital signs will be measured predose, and at the end of the infusion.** At nondosing visits, vital signs need only be taken once during the visit.

Change #32

10.4.3 Patient Global Impressions

The following sentence has been added:

Both PGI-C and PGI-S will be used as anchors to determine a meaningful change threshold for CIDP PRO and fatigue scores.

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Change #33

11.1 Pharmacokinetic variable; Table 11-1

Table 11-1: Serial blood sampling for rozanolixizumab concentration

Matrix	Time after start of sc infusion
Plasma	Predose and postdose at 4h after finishing the [redacted] on Visits 2, 4, and 8. Predose samples will be taken at Visits 14, 18, 22.
	Nondosing Visit 26, samples to be taken once during the visit

Has been changed to:

Table 11-1: Serial blood sampling for rozanolixizumab concentration

Matrix	Time after start of sc infusion
Plasma	Predose and postdose at 4h after finishing the [redacted] on Visits 2, 4, and 8. Predose samples will be taken at Visits 14, 18, ~~and~~ 22 **and monthly at site visits during Treatment Period Part 2**.
	Nondosing Visit 26, samples to be taken once during the visit

Change #34

12 Assessment of immunological variables; second and third paragraph

For all immunological assessments, blood samples will be collected predose (at dosing visits) by qualified site personnel at the same time that samples are collected for standard clinical laboratory. Serum complement (C3, C4), plasma complement (C3a, C5a), and serum cytokine samples will also be taken 4h postdose at Visits 3, 8, 10, 14, 18, and 22. Additional samples may be collected in case of infusion reactions (see Table 5-2).

Has been changed to:

For all immunological assessments, blood samples will be collected predose (at dosing visits) by qualified site personnel at the same time that samples are collected for standard clinical laboratory. Serum complement (C3, C4), plasma complement (C3a, C5a), and serum cytokine samples will also be taken 4h postdose at Visits 3, 8, 10, 14, 18, ~~and~~ 22 **and quarterly at site visit during Treatment Period Part 2**. Additional samples may be collected in case of infusion reactions (see Table 5-2). The time and date of the blood draws will be recorded in the eCRF. **Anti-drug antibodies samples will also be taken predose at Visits 2, 4, 8, 14, 18, 22, monthly at site visits during Treatment Period Part 2 and at Visit 26.**

A tiered ADA approach will be used for the study. Samples will first be evaluated in the screening assay using a false positivity rate of 5% (reported as negative screen or positive screen), followed by analysis of screened positive samples in the confirmatory assay (which is a drug depletion assay) to confirm the true positivity of the samples (reported as negative immunodepletion or positive immunodepletion). Samples that are confirmed as positive

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will be evaluated in a titration assay to quantify the ADA level and will be reported as titer (reciprocal dilution factor including MRD).

Change #35

14.3.1 Safety analyses; first paragraph

The incidence of subjects with TEAEs will be determined. Furthermore, the absolute and relative frequencies for subjects with a given TEAE with respect to the preferred term according to the latest available version of the Medical Dictionary for Regulatory Activities (MedDRA®), will be determined within each system organ class. Additional tables will summarize TEAEs by maximum severity and causal relationship with rozanolixizumab, as judged by the investigator. Adverse events will be categorized by severity according to the National Institutes for Health CTCAE version 4.03 grading (National Institutes for Health, 2009). In case the CTCAE grading is not available, the intensity (mild/moderate/severe) will be utilized. The TEAEs leading to discontinuation of IMP and the serious TEAEs will also be summarized. The action taken, time of onset relative to dosing, actual dose received, and duration of each AE will be listed only.

Has been changed to:

The incidence of study participants with TEAEs will be determined. Furthermore, the absolute and relative frequencies for study participants with a given TEAE with respect to the preferred term according to the latest available version of the Medical Dictionary for Regulatory Activities (MedDRA®), will be determined within each system organ class. Additional tables will summarize TEAEs by maximum severity and causal relationship with rozanolixizumab, as judged by the investigator. Adverse events will be categorized by severity according to the National Institutes for Health CTCAE version **5.0** ~~4.03~~ grading (National Institutes for Health, ~~2009~~**2017**). In case the CTCAE grading is not available, the intensity (mild/moderate/severe) will be utilized. The TEAEs leading to discontinuation of IMP and the serious TEAEs will also be summarized. The action taken, time of onset relative to dosing, actual dose received, and duration of each AE will be listed only.

Change #36

14.4.2 Pharmacokinetic variables, first paragraph

Pharmacokinetic variables of rozanolixizumab like AUC (area under the curve from 0 to infinity) and C_{max} (maximum observed plasma concentration) cannot be derived, since blood sampling will be performed at 1 time point post dosing per visit only. Thus, PK is restricted to concentration data.

Has been changed to:

Pharmacokinetic variables of rozanolixizumab like AUC (area under the curve from 0 to infinity) and C_{max} (maximum observed plasma concentration) cannot be derived, ~~since~~ **due to** blood sampling ~~will be performed at 1 time point post dosing per visit only~~ **scheme**. Thus, PK is restricted to concentration data.

Change #37

14.7 Planned interim analysis and data monitoring

The following paragraph has been added:

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Two interim analyses will be conducted. Firstly at the time of the lock of the parent study CIPD01 and additionally once all study participants have completed Part 1 of the Treatment Period in CIDP04 and have either entered into the Treatment Period Part 2 or the Observation Period. Details of the planned analyses will be fully outlined in the respective SAPs.

Change #38

14.8 Determination of sample size

No formal sample size calculation can be performed. All subjects from the parent study (eg, CIDP01) eligible for the OLE will be included.

Has been changed to:

No formal sample size calculation can be performed. All study participants from the parent study (eg, CIDP01**, with a maximum of [redacted] study participants to be randomized**) eligible for the OLE will be included

Change #39

17 References

The following reference has been removed:

~~Doessegger L, Banholzer ML. Clinical development methodology for infusion-related reactions with monoclonal antibodies. Clin Transl Immunology. 2015;4(7):e39.~~

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19 DECLARATION AND SIGNATURE OF INVESTIGATOR

I confirm that I have carefully read and understood this protocol and agree to conduct this clinical study as outlined in this protocol, according to current Good Clinical Practice and local laws and requirements.

I will ensure that all subinvestigators and other staff members read and understand all aspects of this protocol.

I have received and read all study-related information provided to me.

The objectives and content of this protocol as well as the results deriving from it will be treated confidentially, and will not be made available to third parties without prior authorization by UCB.

All rights of publication of the results reside with UCB, unless other agreements were made in a separate contract.

Investigator:

Printed name	Date/Signature

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20 SPONSOR DECLARATION

I confirm that I have carefully read and understand this protocol and agree to conduct this clinical study as outlined in this protocol and according to current Good Clinical Practice.

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Approval Signatures

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Document Approvals	
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Approval Verdict: Approved	Name: [redacted] Capacity: Clinical Date of Signature: 17-Mar-2020 10:24:26 GMT+0000