AN OPEN-LABEL EXTENSION STUDY TO EVALUATE ROZANOLIXIZUMAB IN STUDY PARTICIPANTS WITH GENERALIZED MYASTHENIA GRAVIS

PROTOCOL MG0007 AMENDMENT 3

PHASE 3

SHORT TITLE:

A Phase 3, open-label extension (OLE) study to evaluate 6-week treatment cycles of rozanolixizumab in study participants with gMG.

Sponsor:
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Regulatory agency identifying number(s):

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PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

Document History		
Document	**Date**	**Type of amendment**
Protocol Amendment 3	03 Oct 2022	Substantial
Protocol Amendment 2	30 Jun 2022	Substantial
Protocol Amendment 1	03 Mar 2021	Substantial
Protocol Amendment 0.2 (France)	28 Jan 2021	Substantial
Protocol Amendment 0.1 (France)	25 Jan 2021	Substantial
Original Protocol Addendum A (UK)	19 Oct 2020	Not applicable
Original Protocol	31 Jul 2020	Not applicable

Amendment 3 (03 Oct 2022)

Overall Rationale for the Amendment

The primary reason for this protocol amendment is to provide an update on the safety information in line with the updated Investigator's Brochure (IB) dated Sep 2022 and updates on the adverse events of special monitoring (AESM). The criteria for study medication discontinuation due to coronavirus disease 2019 (COVID-19) and the requirements for male contraception were also updated.

This amendment is considered to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.

Section # and Name	Description of Change	Brief Rationale
Global	Minor editorial and formatting changes have been made.	To provide clarity and remain consistent with remainder of protocol.
1.3 Schedule of activities, Table 1-2, Table 1-3	New footnotes "k" (Table 1-2) and "h" (Table 1-3): Added to clarify that a full neurological examination should be performed in the event of severe and/or serious headache or suspected aseptic meningitis. Subsequent footnotes have been reordered.	The accumulated safety data on rozanolixizumab led to an update of the adverse events requiring special monitoring. As of the cut-off date of the IB (13 Jul 2022), the following serious adverse events (SAEs) Headache and Meningitis

Section # and Name	Description of Change	Brief Rationale
1.3 Schedule of activities, Table 1-2, Table 1-3 8.9 Biomarkers	Footnote q (now r, Table 1-2), footnote m (now n, Table 1-3), and text (Section 8.9): Updated to remove the former AESM of severe GI disorders, to add the new AESM of suspected aseptic meningitis, and to further detail the sampling time.	Aseptic (PT terms) suggest a possible causal relationship to rozanolixizumab; based on both their temporal association with investigational medicinal product (IMP) infusion (primarily initial infusion) and given the events have occurred more than once in the rozanolixizumab clinical development program.
1.3.1 Additional study assessments	New section added to detail additional study assessments in case of AESM of severe and/or serious headache or the new AESM of suspected aseptic meningitis.	
2.3 Benefit/Risk assessment	Revised text on most common adverse drug reactions, safety concerns, and other safety topics of interest.	
8.3.7 Adverse events of special monitoring	The AESM have been updated to delete severe GI disorders and opportunistic infections and to add suspected aseptic meningitis.	
10.2 Appendix 2: Clinical Laboratory Tests, Table 10-1	Added cross-reference to Table 1-6 for additional assessments that may be required in case of AESM.	
1.1 Synopsis, Objectives and endpoints 3 Objectives and endpoints	The other endpoint specific to Change from Baseline (Day 1) in [redacted] has been updated to delete "AESM of severe headache".	The sampling of complement for severe headache was removed to align with a new guidance on biomarker collection.
1.3 Schedule of activities, Table 1-2, Table 1-3 8.9.1 Immunological assessments 9.4.2.3 Immunological analyses	Footnote s (now t, Table 1-2), footnote n (now o, Table 1-3), and text (Section 8.9.1 and Section 9.4.2.3): Updated to delete "severe headache".	
1.1 Synopsis, Objectives and endpoints	The collection and analysis of cytokines has been removed from the protocol.	The endpoint was removed as the analysis of cytokines is not required in this protocol as samples have been collected in other rozanolixizumab studies

Section # and Name	Description of Change	Brief Rationale
1.3 Schedule of activities, Table 1-2, Table 1-3 3 Objectives and endpoints 9.4.2.3 Immunological analyses		and no additional information is expected from this study, and the scientific value is limited.
1.3 Schedule of activities, Table 1-2	Scheduled visits have been removed from the full physical activity and additional visits have been added to the brief physical activities.	Updated to match the correct procedures at sites.
1.3 Schedule of activities, Table 1-3	For QMG scale, visits specific to treatment with no rozanolixizumab (every 12 weeks) was updated to replace footnote "m" with "o" (now p). Footnote b: Updated to remove “minus (-)” from the visit window.	Updated to correct an error in protocol amendment 2. To provide clarity and remain consistent with the study design.
2.2 Background	Text on the other studies with rozanolixizumab has been updated in line with the current studies status at the time of this amendment.	Updated in line with studies status at the time of this amendment.
5.1 Inclusion criteria 10.12 Appendix 12: Gap Period Eligibility Criteria (Gap Period Inclusion Criteria) 10.4 Appendix 4: Contraceptive Guidance and Collection of Pregnancy Information	Criterion #3a (now 3b, Section 5.1) and criterion #2 (now 2a, Section 10.12) have been updated to delete the requirements for male contraception. Contraception guidance for male participants has been deleted.	To update male contraception requirements with current guidelines, after completion of the required reproductive toxicity studies and considering that rozanolixizumab has not genotoxic potential and potential exposure through seminal fluid is expected to be negligible.
7.1.3 Temporary IMP discontinuation	The temporary IMP discontinuation criteria in relation to COVID-19 infection have been updated.	To adapt the withdrawal criteria to the evolution of the medical practices and local guidelines with regards to COVID-19 management.
7.1.3 Temporary IMP discontinuation	Added a new criterion (#3) on the temporary discontinuation of IMP in the event of suspected drug-induced aseptic meningitis.	The accumulated safety data on rozanolixizumab led to an update of the discontinuation criteria which is in line with the

Section # and Name	Description of Change	Brief Rationale
7.1.4 Study medication permanent discontinuation criteria	Added a new criterion (#10) on the permanent discontinuation of study medication in the event of recurrence of aseptic meningitis. Deleted criterion #7 on the permanent discontinuation of study medication in the event of serious or recurrent (ie, second occurrence) severe AE of headache which is considered related to the study medication.	revisions to adverse events requiring special monitoring.
8.2.1 Physical examination	The text has been updated to add the details of the full neurological assessment in the event of severe and/or serious headache or suspected aseptic meningitis.	Added to provide clear guidance to Investigators on the management of AESM.
8.2.2 Vital signs	Wording on the requirement to collect vital signs for participants switching to manual push has been updated to replace "3 infusions" with "2 infusions".	Updated to be consistent with the study design and schedule of activities.
10.6 Appendix 6: Liver Safety – Suggested Actions and Follow-up Assessments	The literature reference Le Gal et al, 2005 has been moved to Section 11 References.	General update.
10.8 Appendix 8: Country-specific Requirements, Japan	Clarified that country-specific requirements for Japan aligned with Japan GCP will be provided separately in Protocol Exhibit.	Clarification.
10.9 Appendix 9: Abbreviations and Trademarks	Additions have been made to the list of abbreviations.	General update.
10.10 Appendix 10: Protocol Amendment History	Details of the previous amendment (protocol amendment 2) have been added. Some updates and corrections have been made to the summary of changes table.	General update.
10.13 Appendix 13: Management of headaches, diarrhea, and infections and hypogammaglobulinemia	The title of Appendix 13 has been updated to *Management of infections and hypogammaglobulinemia and infusion reactions or hypersensitivity reactions*.	The accumulated safety data on rozanolixizumab led to an update of the adverse events requiring special monitoring and to a revision of protocol guidance.

Section # and Name	Description of Change	Brief Rationale
10.13.1 Management of headache	The protocol guidance for the management of headache has been updated and moved to Section 10.14 (Appendix 14).	
10.13.2 Management of diarrhea	The protocol guidance for the management of diarrhea has been deleted. Subsequent subsections have been renumbered.	
10.14 Appendix 14: Management of adverse event of special monitoring	New appendix: Added to provide guidance on the management of AESM. Subsequent appendix has been renumbered.	
10.13.1 Management of infections and hypogammaglobulinemia	The text has been updated to add "during a treatment period".	Clarification.
11 References	Additions have been made to the list of references.	General update.

SERIOUS ADVERSE EVENT REPORTING

Serious adverse event reporting (24h)	
Fax	**Europe and Rest of the World:** +32 2 386 24 21 **US and Canada:** +1 800 880 6949 or +1 866 890 3175
Email	**Global:** DS_ICT@ucb.com (for interventional clinical studies)

Serious adverse event (investigational device) and device deficiency reporting (24h)	
Fax:	**Japan:** +81 3 6864 7400
Email:	**Japan:** UCBJ-Safety@ucb.com

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1 PROTOCOL SUMMARY

1.1 Synopsis

Protocol title:

An open-label extension study to evaluate rozanolixizumab in study participants with generalized myasthenia gravis.

Short Title:

A Phase 3 open-label extension study to evaluate 6-week treatment cycles of rozanolixizumab in study participants with generalized myasthenia gravis (gMG).

Rationale:

Myasthenia gravis (MG) is a serious, sometimes life threatening, debilitating condition associated with numerous symptoms including muscular weakness and fatigue. The major pathophysiology leading to MG is the abnormal production of immunoglobulin (Ig)G autoantibodies directed toward nicotinic acetylcholine receptor (AChR), or muscle-specific kinase (MuSK) protein. Several commonly prescribed treatments act, at least in part, by reducing the quantity of such circulating IgG autoantibodies. While the standard of care for MG involves the utilization of a variety of therapeutic agents including cholinesterase inhibitors, immunomodulators, corticosteroid, biologics, high dose intravenous immunoglobulin (IVIg), plasmapheresis or immunoadsorption, there remains a need for a safe and effective treatment devoid of significant side effects to conveniently treat patients with MG.

By blocking the activity of neonatal Fc receptor (FcRn), rozanolixizumab accelerates the catabolism of antibodies and reduces the serum IgG concentration, including pathogenic IgG in MG patients, thus offering a potentially [redacted], effective, and convenient alternative to existing treatments. This Phase 3 study will provide the required data to establish the safety and efficacy of rozanolixizumab in anti-AChR or anti-MuSK autoantibody-positive patients with generalized MG who experience moderate to severe symptoms and are being considered for additional treatment such as IVIg or plasma exchange (PEX).

MG0007 is a Phase 3, 2-arm, randomized, open-label extension (OLE) study to evaluate the long-term safety, tolerability, and efficacy of repeated 6-week treatment cycles of rozanolixizumab based on MG worsening in study participants with gMG. This OLE study will provide the opportunity for study participants who participated in MG0003 and MG0004 to benefit from long-term rozanolixizumab treatment based on their MG symptom needs.

Objectives and Endpoints

Objectives	Endpoints/Estimands
Primary	
• To assess the safety and tolerability of additional 6-week treatment cycles with rozanolixizumab in study participants with gMG	The primary safety endpoints are: • Occurrence of treatment-emergent adverse events (TEAEs) • TEAEs leading to withdrawal of investigational medicinal product (IMP) The other safety endpoints are: • Occurrence of serious TEAEs • Occurrence of treatment-emergent adverse events of special monitoring (AESM) • Vital sign values and changes from Baseline (Day 1) (systolic and diastolic blood pressure [BP] and pulse rate at each scheduled assessment during Treatment and Observation Periods) • 12-lead electrocardiogram (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)
Secondary	
• To assess the efficacy of 6-week treatment cycles with rozanolixizumab in study participants with gMG	The secondary efficacy endpoints are: For each of the first 3 x 6-week treatment cycle, change from Baseline (Day 1) to Day 43[a]: • In MG-Activities of Daily Living (ADL) score within one treatment cycle • In Quantitative MG (QMG) score within one treatment cycle • In MG-Composite (MG-C) score within one treatment cycle

	• In MG Symptoms patient-reported outcomes (PRO) 'Muscle Weakness Fatigability' score within one treatment cycle • In MG Symptoms PRO 'Physical Fatigue' score within one treatment cycle • In MG Symptoms PRO 'Bulbar symptoms' score within one treatment cycle • In MG-ADL responder (≥2.0-point improvement within one treatment cycle • Time to MG-ADL response (≥2.0-point improvement from Baseline [Day 1]) within one treatment cycle For consecutive treatment cycles: • Time between consecutive treatment cycles
	The other efficacy endpoints are: For each 6-week treatment cycle and Observation Period (where applicable), improvement from Baseline (Day 1)] to each scheduled assessment: • MG-ADL responder (≥2.0-point) within one treatment cycle • QMG responder rate (≥3.0-point) within one treatment cycle • MG-C responder rate (≥3.0-point) within one treatment cycle • Time to MG-ADL response (≥2.0-point) within one treatment cycle • Minimal symptom expression (MG-ADL score of 0 or 1) at any time during Treatment and Observation Periods For each 6-week treatment cycle and Observation Period (where applicable), change from Baseline (Day 1) to each scheduled assessment:

	• In MG-ADL score within one treatment cycle • In QMG score within one treatment cycle • In MG-C score within one treatment cycle • In MG Symptoms PRO 'Muscle Weakness Fatigability' score within one treatment cycle • In MG Symptoms PRO 'Physical Fatigue' score within one treatment cycle • In MG Symptoms PRO 'Bulbar symptoms' score within one treatment cycle For each 6-week treatment cycle and Observation Period (where applicable), change from Baseline (Day 1) to Day 43[a]: • In 5-level European quality of life 5 dimension (EQ-5D-5L) within one treatment cycle • In Myasthenia Gravis-Quality of Life (MG-QOL)15r within one treatment cycle
Other	
• To assess the pharmacokinetics (PK) of rozanolixizumab	• Plasma concentrations of rozanolixizumab at each scheduled assessment
• To evaluate the incidence and emergence of antidrug antibody (ADA) of rozanolixizumab	• ADA at each scheduled assessment
• To assess the pharmacodynamics (PD) of rozanolixizumab	For each 6-week treatment cycle and Observation Period (where applicable): • Minimum value and maximum decrease from Baseline (Day 1) in total serum immunoglobulin (Ig) G and IgG subclasses concentration over time • Change from Baseline (Day 1) in serum IgG subclasses concentration over time • Change (absolute and percentage) from Baseline (Day 1) in MG-specific autoantibodies at each scheduled

	assessment during the Treatment and Observation Periods
• To assess the effects of rozanolixizumab on the concentration of [redacted] and [redacted]	• Change from Baseline (Day 1)[b] in [redacted] in participants experiencing infusion reactions For initial fixed treatment cycle only: • Change from Baseline (Day 1) in serum Ig concentrations ([redacted]) at each scheduled assessment during Treatment and Observation Periods
• To assess the need for gMG medications including changes in type and doses	• Use of rescue therapy (yes/no) • Time to rescue therapy • Healthcare resource utilization, including hospitalization (type: intensive care unit [ICU]/non-ICU and duration)
• To assess the effect of rozanolixizumab on [redacted]	• Change in [redacted]

[a] Day 43 = Visit 8 for the initial fixed cycle and Visit 7 for the subsequent cycles.
[b] Baseline will be used from the sample collected at Day 1 (Visit 2) in MG0003. Other exploratory safety biomarkers may be assessed (Section 8.9).

Overall Design

This is a Phase 3, multicenter, 2-arm, OLE study to evaluate 6-week treatment cycles of rozanolixizumab in study participants with gMG. MG0007 is an extension study of MG0003.

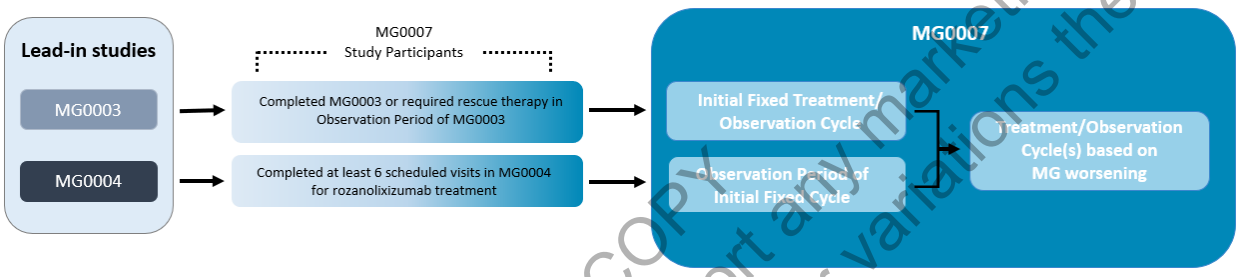
Eligible study participants from the lead-in study, MG0003, will be randomized to receive an initial fixed 6-week treatment cycle of a subcutaneous (sc) dose of rozanolixizumab equivalent to approximately 7mg/kg or 10mg/kg weekly (QW) (Table 1-1 and Figure 1-2), followed by an Observation Period that begins after the last dose of the current treatment cycle as per assessments described in the Schedule of Activities (Section 1.3).

Eligible study participants from MG0004 who have completed at least 6 scheduled visits in the Treatment Period and the premature end of treatment (PEOT) visit can move directly into the Observation Period in MG0007 of the initial fixed cycle. Additionally, eligible study participants from MG0004 who are in the Observation Period and have completed the EOS visit can move directly into the Observation Period in MG0007 of the initial fixed cycle (Figure 1-1 and Figure 1-2). If IMP treatment was withheld for low IgG in MG0004, study participant's missed dose(s) can be counted as part of the total 6 visits for completion of MG0004 and meet eligibility

requirements for MG0007. These study participants will undergo their first MG0007 treatment with rozanolixizumab upon worsening of gMG symptoms. For the first MG0007 treatment with rozanolixizumab, participants will continue on their last treatment dose from MG0004. Dose adjustments may be applied in future cycles as per description below.

The rollover into MG0007 must be completed within 4 weeks after the End of Study (EOS) visit from MG0003, or the PEOT or EOS (as appropriate) visit from MG0004. In the event a study participant has a gap period (>4 weeks) between the EOS or PEOT visit from the lead-in study and the start of MG0007, a Screening Period (see Appendix 11 [Section 10.11]) of up to 4 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry into MG0007 (see Appendix 12 [Section 10.12]).

Figure 1-1: MG0007 entry schema



MG=myasthenia gravis

In case of symptom worsening (eg, an increase of 2.0 points on the MG-ADL or 3.0 points on the QMG scale) between assessments, resulting in a need for additional treatment, study participants will undergo another 6-week treatment cycle followed by an Observation Period, based on the Investigator's discretion. The dose may be adjusted to 7mg/kg or 10mg/kg at the beginning of each treatment cycle based on the Investigator's discretion. The minimal time to start the next treatment cycle is 4 weeks following the last dose of the Treatment Period of the previous cycle. If a study participant requires treatment earlier than 4 weeks, IgG levels from the previous cycle should be considered and discussed with the Medical Monitor. A new treatment cycle **should not** be initiated until total IgG level is ≥2g/L.

Participants in MG0007 will remain on their gMG background medications. With the exception of steroids and acetylcholinesterase (AChE) inhibitors, all gMG medication doses should be maintained during each respective 6-week treatment cycle and efforts should be made to maintain a stable dose during the first 8 weeks of the Observation Period.

Study participants who receive rescue therapy (intravenous immunoglobulin [IVIg], plasma exchange [PEX], subcutaneous immunoglobulin [SCIg], or iv corticosteroid) during the Treatment Period are not eligible to receive any further treatment with rozanolixizumab. Study participants must complete the first 8 weeks of the Observation Period after the last dose of rozanolixizumab prior to completing the EOS visit assessments, and subsequently will be withdrawn from the study (Section 4.4).

Those patients who received rescue therapy (IVIg, PEX, SCIg, or iv corticosteroid) during the observation or no treatment with rozanolixizumab periods may continue in the study at the Investigator's discretion and after discussion with Medical Monitor and/or UCB Study

Physician. The following cycle of rozanolixizumab should in general not start earlier than 4 weeks following the last dose of IVIg, SCIg, or iv corticosteroids or the last PEX session, unless there is a medical reason, and an earlier treatment initiation is being considered [redacted] for the study participant as agreed upon with the Medical Monitor and/or UCB Study physician.

Study participants (not withdrawn from the study) will continue in MG0007 until product approval or until transition to a managed access program (MAP), if available, as indicated per the Sponsor, and according to local guidance. For country-specific requirements, see Appendix 8, Section 10.8.

Number of Participants

No formal sample size calculation can be performed. All eligible study participants from MG0003 and MG0004 will be invited to participate in MG0007. It will be assumed that approximately 200 study participants will be enrolled into MG0007.

Treatment Groups and Duration

Fixed unit doses across body weight tiers and study arms will be employed in MG0007. This OLE study will continue treatment with rozanolixizumab sc fixed doses equivalent to approximately 7mg/kg and 10mg/kg administered QW for 6-week treatment cycles.

Table 1-1: MG0007 dose levels and weight tiers

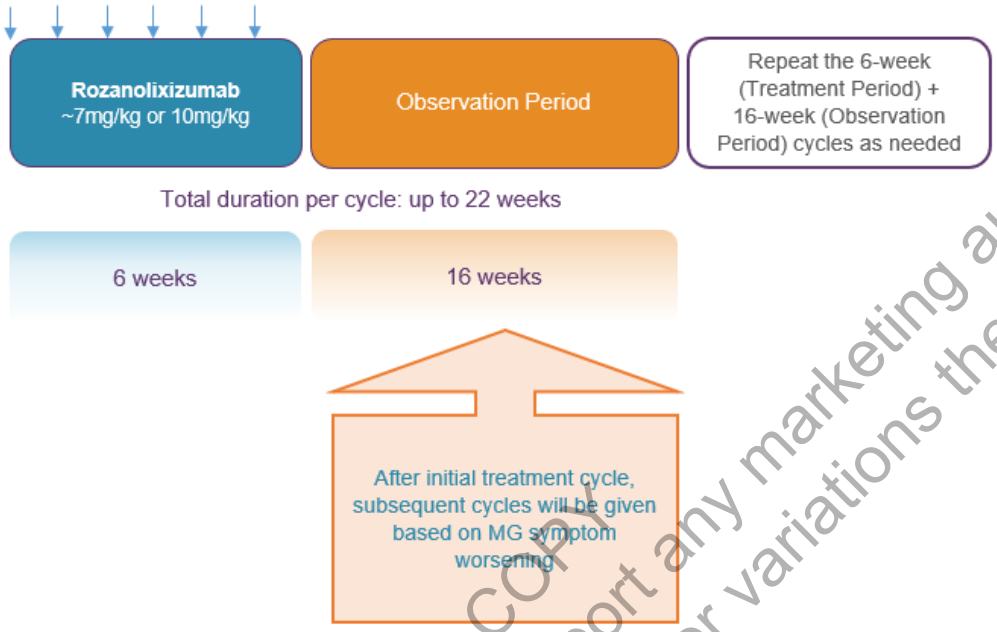
Bodyweight	Rozanolixizumab dose eqv	
	7mg/kg Dose 1	10mg/kg Dose 2
≥35 to <50kg	280mg	420mg
≥50 to <70kg	420mg	560mg
≥70 to <100kg	560mg	840mg
≥100kg	840mg	1120mg

eqv=equivalent

If a dose arm is determined to be futile and is discontinued after the interim analysis in MG0003, then that dose arm will be dropped from MG0007, and study participants in the affected dose arm will be transferred to the continuing dose arm. An independent Data Monitoring Committee (IDMC) will monitor the ongoing safety and efficacy of the study. Further details of the IDMC will be provided in an IDMC charter.

1.2 Schema

Figure 1-2: MG0007 study schema



MG=myasthenia gravis

1.3 Schedule of activities

Table 1-2: Schedule of activities (initial fixed cycle)

Procedure	**Gap Period**[a]	**Treatment Period**								**Observation Period**				**No treatment with rozanolixizumab**		
Visit	**Scr**[a]	**V1 (BL)**[b,c]	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8 (PEOT)**	**V9**	**V10**	**V11**	**V12**	**-**	**-**	**EOS**
Visit type	**S**	**S**	**H**[d]	**S**	**S**	**S**	**H**[d]	**S**	**S**	**S**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window)[e]	**-28 to -1**	**1**	**3 (±1)**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
Written informed consent	X	X								X[f]						
Demographic and Baseline characteristics	X	X								X[f]						
Verification of inclusion/exclusion criteria	X[g]	X[h]								X[f]						
Medical history update		X								X[f]						
Prior and concomitant medications and medical procedures	X	X	X	X	X	X	X	X	X	X	X		X		X	X
Body weight	X	X														
Psychiatric history/C-SSRS	X															
Query for suicidality[i]		X		X	X	X	X	X	X		X		X		X	X
IGRA TB test[j]	X															X
TB Signs and Symptoms questionnaire	X	X							X				X		X	X
12-lead ECG	X	X		X												X
Full physical examination[k]	X	X														
Brief physical examination[k]				X	X	X		X	X	X			X		X	X

Procedure	**Gap Period** [a]	**Treatment Period**								**Observation Period**				**No treatment with rozanolixizumab**		
Visit	**Scr** [a]	**V1 (BL)** [b,c]	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8 (PEOT)**	**V9**	**V10**	**V11**	**V12**	**-**	**-**	**EOS**
Visit type	**S**	**S**	**H** [d]	**S**	**S**	**S**	**H** [d]	**S**	**S**	**S**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window) [e]	**-28 to -1**	**1**	**3 (±1)**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
Vital signs[l]	X	X	X	X	X	X	X	X	X	X	X		X		X	X
Call or enter IRT to register the visit	X	X		X	X	X	X	X	X[m]							X[n]
Study participants identification card assigned		X														
Recording of AEs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (serum)	X															
Pregnancy test (urine)[o]		X														X
PTT and INR	X															
Hematology, serum chemistry	X	X		X		X		X	X		X		X		X	X
Serology (HIV, Hepatitis B, and Hepatitis C)	X															
Urinalysis	X	X				X			X				X			
Blood sampling for PK[p]		X	X[q]			X			X		X					X
Blood sampling for ADA		X				X			X		X					X
Blood sampling for total IgG and IgG subclasses	X	X		X	X	X	X[q]	X	X		X					X
[redacted]																
Blood sampling for exploratory safety biomarker analysis		X[r]														

Procedure	Gap Period [a]	Treatment Period								Observation Period				No treatment with rozanolixizumab		
Visit	**Scr [a]**	**V1 (BL)[b,c]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8 (PEOT)**	**V9**	**V10**	**V11**	**V12**	**-**	**-**	**EOS**
Visit type	**S**	**S**	**H[d]**	**S**	**S**	**S**	**H[d]**	**S**	**S**	**S**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window)[e]	**-28 to -1**	**1**	**3 (±1)**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
MG-specific autoantibodies[s]		X				X			X		X					X
[redacted]																
MGFA classification	X															X
QMG scale	X	X		X	X	X		X[u]	X	X[u]	X		X		X[u]	X
MG-C scale	X	X		X	X	X		X	X	X	X		X		X	X
MG-ADL	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
MG Symptoms PRO	X	X				X			X		X				X	X
EQ-5D-5L		X							X						X	X
MG-QOL15r		X							X						X	X
Study drug administration[v]		X		X	X	X	X	X								
Study drug discontinuation criteria		X		X	X	X	X	X								
Study withdrawal criteria	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Procedure	Gap Period [a]	Treatment Period								Observation Period				No treatment with rozanolixizumab		
Visit	**Scr [a]**	**V1 (BL)[b,c]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8 (PEOT)**	**V9**	**V10**	**V11**	**V12**	**-**	**-**	**EOS**
Visit type	**S**	**S**	**H[d]**	**S**	**S**	**S**	**H[d]**	**S**	**S**	**S**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window)[e]	**-28 to -1**	**1**	**3 (±1)**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**

AChR=acetylcholine receptor; ADA=antidrug antibody; AE=adverse event; BL=Baseline; C-SSRS=Columbia Suicide Severity Rating Scale; ECG=electrocardiogram; EQ-5D-5L=5-level European quality of life 5 dimension; EOS=End of Study; H=home; HIV=human immunodeficiency virus; [redacted]; IgG=immunoglobulin G; [redacted] IGRA=interferon-gamma release assay; IMP=investigational medicinal product; INR=international normalized ratio; IRT=interactive response technology; MG=myasthenia gravis; MG-ADL=myasthenia gravis-Activities of Daily Living; MG-C=Myasthenia Gravis Composite; MG-QOL15r=Myasthenia Gravis Quality of Life; MuSK=muscle-specific kinase; PEOT=premature end of treatment; PK=pharmacokinetics; PRO=patient-reported outcome; PTT=partial thromboplastin time; QMG=Quantitative Myasthenia Gravis; S=site; TB=tuberculosis; V=visit; VR=virtual

[a] Only applicable to study participants with a gap period, defined as any study participant who does not enroll in MG0007 within 4 weeks (or ≤32 days) of the EOS or PEOT visit from the lead-in study (see gap period screening assessments, Appendix 11, Section 10.11).

[b] For any study participant enrolling from MG0003, the EOS visit in MG0003 (Visit 14) will serve as the Baseline Visit in MG0007. All activities should be completed predose at Visit 1 (+1 week). For any activities not completed at the EOS or PEOT visit in the lead-in study, these activities should be completed at V1. For study participants with a gap period (>4 weeks), see footnote a and Section 4.1. For any study participant enrolling from MG0004, see footnote b in Table 1-3 (subsequent cycle).

[c] All MG0003 study participants will be assessed for worsening of MG symptoms (eg, an increase of 2.0 points on the MG-ADL or 3.0 points on the QMG scale) prior to first dose at the initial Baseline.

[d] For all study participants, home visits are optional and can be conducted at the site as deemed necessary by site personnel and/or the study participant (Section 6.7).

[e] A visit window of ±1 day is allowed for V2. A visit window of ±2 days is allowed for all other dosing visits. The visit window of ±2 days is relative to the first dosing visit date. However, there should be a minimum interval of 5 days and maximum interval of 9 days as compared to the previous dose. A visit window of ±7 days is allowed for V9 to V12.

[f] Only applicable to study participants enrolling from MG0004.

[g] Only applicable to study participants with a gap period (see gap period eligibility criteria, Appendix 12, Section 10.12).

[h] For criteria pertaining to laboratory measures, the last value from MG0003, or MG0004 will be used for evaluation of study participant eligibility, as long as the measurement was taken within the last 4 weeks prior to MG0007 Baseline (Day 1).

[i] A full C-SSRS assessment will be performed only when a study participant has a positive response to Question 1 of 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] The Screening visit in MG0003, and the final visit in MG0004 (Visit 52 [PEOT] or Visit 53 [EOS]) will serve as Baseline in MG0007. An IGRA test will be performed in a central laboratory. Study participant should not be dosed in case of any positive IGRA or two indeterminate (Section 8.2.6).

[k] A full neurological examination should be performed for any study participant who experiences severe and/or serious headache and for any study participant who experiences suspected aseptic meningitis. For details of the assessments included in these examinations see Section 8.2.1. For additional assessments that may be required in case of AESM, see Section 1.3.1 (Table 1-6).

[l] In case of switching to manual push administration, for the first 2 infusions vital signs will be measured prior to IMP administration, at the end of the infusion (±15 minutes), and 1 hour after the end of the infusion (±15 minutes). For the subsequent infusions all assessments will be performed prior to any blood sampling and IMP administration (see Section 8.2.2).

[m] Only applicable if study participants require PEOT.

[n] Required for study withdrawal or study completion visit (Section 4.4).

[o] For UK-specific requirements on additional pregnancy test, see Appendix 8, Section 10.8.

[p] At dosing visits, PK samples should be taken predose for all study participants.

[q] Blood samples may be collected by a healthcare professional visiting the study participant at their home. Alternately, home visits can be conducted at the site as deemed necessary by site personnel and/or the study participant or if home visits are not feasible.

[r] Baseline (Day 1, Visit 2) from MG0003 will serve as Baseline in MG0007. In study participants who experience severe and/or serious headaches or suspected aseptic meningitis, samples should be collected 4 hours after the onset of the event, or otherwise as soon as possible within 72 hours after the onset of the event. For additional assessments that may be required in case of AESM, see Section 1.3.1 (Table 1-6).

[s] For study participants entering from MG0003, MuSK and AChR antibodies will be tested at Baseline. All subsequent testing will be limited to the positive antibody.

[redacted]

[u] This assessment is optional; however, every effort should be made to capture the study participant's QMG score.

[v] Study participants must be observed at site postdose for at least 4 hours following the first 2 infusions, and then 1 hour thereafter for subsequent infusions of the initial cycle (see Section 8.2.2).

All study participants will be assessed for the worsening of gMG symptoms during the Observation Period and the no treatment with rozanolixizumab visits. In case of symptom worsening (eg, an increase of 2.0 points on the MG-ADL or 3.0 points on the QMG scale) between assessments, resulting in a need for additional treatment, study participants will undergo another 6-week treatment cycle followed by an Observation Period, based on the Investigator's discretion.

Table 1-3: Schedule of activities (subsequent cycles)

Procedure	**Treatment Period**							**Observation Period**				**No treatment with rozanolixizumab**		
Visit	**V1 (BL)[a,b]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7 (PEOT)**	**V8**	**V9**	**V10**	**V11**	**-**	**-**	**EOS**
Visit type	**S**	**H[c]**	**S**	**H[c]**	**S**	**H[c]**	**S**	**VR**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window) [d]	**1**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
Concomitant medications and medical procedures	X	X	X	X	X	X	X	X	X	X	X		X	X
Medical history update	X													
Query for suicidality [e]	X	X	X	X	X	X	X		X		X		X	X
IGRA TB test [f]														X
TB Signs and Symptoms questionnaire	X						X						X	X
Body weight [g]	X													
12-lead ECG	X						X							X
Full physical examination [h]	X													
Brief physical examination [h]			X		X		X		X		X		X	X
Vital signs [i]	X	X	X	X	X	X	X		X		X		X	X
Call or enter IRT to register the visit	X	X	X	X	X	X	X [j]							X [k]
Recording of AEs	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Procedure	**Treatment Period**							**Observation Period**				**No treatment with rozanolixizumab**		
Visit	**V1 (BL)[a,b]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7 (PEOT)**	**V8**	**V9**	**V10**	**V11**	**-**	**-**	**EOS**
Visit type	**S**	**H[c]**	**S**	**H[c]**	**S**	**H[c]**	**S**	**VR**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window) [d]	**1**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
Pregnancy test (urine) [l]	X													X
Hematology, serum chemistry	X		X				X		X		X		X	X
Urinalysis	X		X				X				X			
Blood sampling for PK [m]	X						X							X
Blood sampling for ADA	X						X							X
Blood sampling for total IgG and IgG subclasses	X			X			X		X					X
Blood sampling for exploratory safety biomarker analysis	X [n]													
MG-specific autoantibodies	X						X							X
[redacted]														
MGFA classification	X													X
QMG scale	X		X [p]		X [p]		X		X		X		X [p]	X
MG-C scale	X		X		X		X		X		X		X	X
MG-ADL	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MG Symptoms PRO	X						X						X	X
EQ-5D-5L	X						X						X	X

Procedure	**Treatment Period**							**Observation Period**				**No treatment with rozanolixizumab**		
Visit	**V1 (BL)[a,b]**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7 (PEOT)**	**V8**	**V9**	**V10**	**V11**	**-**	**-**	**EOS**
Visit type	**S**	**H[c]**	**S**	**H[c]**	**S**	**H[c]**	**S**	**VR**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window) [d]	**1**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
MG-QOL15r	X						X						X	X
Study drug administration [q]	X	X	X	X	X	X								
Study drug discontinuation criteria	X	X	X	X	X	X								
Study withdrawal criteria	X	X	X	X	X	X	X	X	X	X	X	X	X	X

ADA=antidrug antibody; AE=adverse event; BL=Baseline; ECG=electrocardiogram; EQ-5D-5L=5-level European quality of life 5 dimension; EOS=End of Study; H=home; IgG=immunoglobulin G; IGRA= interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; MG=myasthenia gravis; MG-ADL=myasthenia gravis-Activities of Daily Living; MG-C=Myasthenia Gravis Composite; MG-QOL15r=Myasthenia Gravis Quality of Life; PEOT=premature end of treatment; PK=pharmacokinetics; PRO=patient-reported outcome; QMG=Quantitative Myasthenia Gravis; S=site; TB=tuberculosis; V=visit; VR=virtual

[a] All study participant will be assessed for worsening of MG symptoms. In case of symptom worsening (eg, an increase of 2.0 points on the MG-ADL or 3.0 points on the QMG scale) between assessments, resulting to additional treatment, study participants will undergo another 6-week treatment cycle followed by an Observation Period, based on the Investigator's discretion.

[b] For any study participant enrolling from MG0004, the final visit in MG0004 (Visit 52 [PEOT] or Visit 53 [EOS]) will serve as the Baseline Visit in MG0007. All activities should be completed at Visit 1 (+1 week). For study participants with a gap period (>4 weeks), see Section 4.1.

[c] For all study participants, home visits are optional and can be conducted at the site as deemed necessary by site personnel and/or the study participant (Section 6.7).

[d] A visit window of ±2 days is allowed for V2 to V7. The visit window of ±2 days is relative to the first dosing visit date. However, there should be a minimum interval of 5 days and maximum interval of 9 days as compared to the previous dose. A visit window of ±7 days is allowed for Visit 8 to Visit 11.

[e] A full C-SSRS assessment will be performed only when a study participant has a positive response to Question 1 of 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.

[f] An IGRA test will be performed in a central laboratory. Additional IGRA TB testing will be done at least 12 months since last test. Study participant should not be dosed in case of any positive IGRA or two indeterminate IGRAs.

[g] Weight-based dose adjustments are limited to a maximum of every 6 months.

[h] A full neurological examination should be performed for any study participant who experiences severe and/or serious headache and for any study participant who experiences suspected aseptic meningitis. For details of the assessments included in these examinations see Section 8.2.1. For additional assessments that may be required in case of AESM, see Section 1.3.1 (Table 1-6).
[i] In case of switching to manual push administration, for the first 2 infusions vital signs will be measured prior to IMP administration, at the end of the infusion (±15 minutes), and 1 hour after the end of the infusion (±15 minutes). For the subsequent infusions all assessments will be performed prior to any blood sampling and IMP administration (see Section 8.2.2).
[j] Only applicable if study participants require PEOT.
[k] Required for study withdrawal or study completion visit (Section 4.4).
[l] For UK-specific requirements on additional pregnancy test, see Appendix 8, Section 10.8.
[m] At dosing visits, PK samples should be taken predose for all study participants.
[n] In study participants who experience severe and/or serious headaches or suspected aseptic meningitis, additional samples should be collected 4 hours after the onset of the event, or otherwise as soon as possible within 72 hours after the onset of the event. For additional assessments that may be required in case of AESM, see Section 1.3.1 (Table 1-6).
[redacted]
[p] After the first subsequent cycle, this assessment is optional, however every effort should be made to capture the study participant's QMG score.
[q] Study participants must be observed at site or home postdose for at least 1 hour following the first 2 infusions, and then a minimum 15 minutes thereafter for subsequent infusions. The observation time should be prolonged for the individual participants if required (see Section 8.2.2).

Table 1-4: Schedule of activities (initial fixed cycle - study participants who receive full[a] COVID-19 vaccination before or during the study)

Procedure		Treatment Period								Observation Period				No treatment with rozanolixizumab		
Visit	**Scr**	**V1 (BL)**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8 (PEOT)**	**V9**	**V10**	**V11**	**V12**	**-**	**-**	**EOS**
Visit type	**S**	**S**	**H**	**S**	**S**	**S**	**H**	**S**	**S**	**S**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window)	**-28 to -1**	**1**	**3 (±1)**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
COVID-19 post-vaccination biomarkers sampling [a]		X[b]							X		X[c]					X

BL=Baseline; COVID-19=coronavirus disease 2019; EOS=end of study; H=home; PEOT=premature end of treatment; S=site; V=visit; VR=virtual
[a] A full COVID-19 vaccination should be defined according to current regional recommendations.
[b] To be collected prior to study drug administration.
[c] If subsequent treatment cycle starts before Visit 9, or any time during the Observation period, the sample must be collected prior to study drug administration.

Table 1-5: Schedule of activities (subsequent cycles - study participants who receive full[a] COVID-19 vaccination before or during the study)

Procedure	Treatment Period							Observation Period				No treatment with rozanolixizumab		
Visit	**V1 (BL)**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7 (PEOT)**	**V8**	**V9**	**V10**	**V11**	**-**	**-**	**EOS**
Visit type	**S**	**H**	**S**	**H**	**S**	**H**	**S**	**VR**	**S**	**VR**	**S**	**VR**	**S**	**S**
Day (visit window)	**1**	**8 (±2)**	**15 (±2)**	**22 (±2)**	**29 (±2)**	**36 (±2)**	**43 (±2)**	**71 (±7)**	**99 (±7)**	**127 (±7)**	**155 (±7)**	**Every 4 weeks (±7)**	**Every 12 weeks (±7)**	**- (±2)**
COVID-19 post-vaccination biomarkers sampling [a]	X[b]						X		X[c]					X

BL=Baseline; COVID-19=coronavirus disease 2019; EOS=end of study; H=home; PEOT=premature end of treatment; S=site; V=visit; VR=virtual

[a] A full COVID-19 vaccination should be defined according to current regional recommendations.

[b] To be collected prior to study drug administration.

[c] If subsequent treatment cycle starts before Visit 8, or any time during the Observation Period, the sample must be collected prior to study drug administration.

1.3.1 Additional study assessments

In addition to those detailed in Table 1-2 to Table 1-5, the assessments in Table 1-6 may be required in case of adverse events of special monitoring (AESM) (severe and/or serious headache, or suspected aseptic meningitis, see Section 8.3.7). Note that additional vital sign measurements and/or additional investigations may be taken at the discretion of the Investigator.

Table 1-6: Additional study assessments

Assessment	When applicable
For study participants who experience severe and/or serious headache and for study participants with suspected aseptic meningitis	
Headache or suspected aseptic meningitis follow-up questionnaire	Headache follow-up questionnaire which sites will receive after reporting AESM of severe and/or serious headache should be completed promptly and returned to the Sponsor via the SAE reporting process. Suspected aseptic meningitis follow-up questionnaire which sites will receive after reporting AESM of suspected aseptic meningitis should be completed promptly and returned to the Sponsor via the SAE reporting process.
Full neurological examination	In study participants who report/are diagnosed with severe and/or serious headache or with a suspected aseptic meningitis at the clinic visit, a full neurological examination (including fundoscopy) should be performed (see Appendix 14 [Section 10.14]). In study participants who report a severe and/or serious headache while at home or features suggestive of aseptic meningitis, a visit to the site for the full neurological examination should be arranged for as soon as is practically possible.
Blood analysis	Blood sample collection for exploratory analysis.
Other	In study participants who report severe and/or serious headache, other diagnostic procedures including but not limited to CT scan, MRI (Gadolinium-enhanced preferred) and/or lumbar puncture for CSF collection are to be performed if indicated at the discretion of the Investigator.
For study participants who experience suspected aseptic meningitis	
Lumbar puncture	In study participants who reported signs and/or symptoms of meningitis which required a lumbar puncture, results of the CSF analysis should be recorded in the eCRF, and preliminary data should be included on the SAE form used for reporting the event as an AESM within 24 hours (ie, preliminary data reported on the first reporting may not have CSF results yet, but the reporting should occur as soon as there is a suspected diagnosis. Full results should be communicated in subsequent exchanges with UCB).
Additional analysis	Results of all investigations should be recorded in the eCRF, and preliminary data should be included on the SAE form used for reporting the event as an AESM. Please include details on all investigations results including but not limited to blood or CSF cultures and analysis/ PCR test (including list of microorganisms tested) / MRI scans +/- gadolinium.

AESM=adverse event of special monitoring; CSF=cerebrospinal fluid; CT=computed tomography; eCRF=electronic case report form; MRI=magnetic resonance imaging; PCR=polymerase chain reaction; SAE=serious adverse event

The frequency of the collection of samples for exploratory biomarker sample collection after severe and/or serious headache or suspected aseptic meningitis are described in Table 1-2 (footnote r) and Table 1-3 (footnote n).

2 INTRODUCTION

Rozanolixizumab is a humanized IgG4 monoclonal antibody that is being developed as an inhibitor of the activity of the FcRn for IgG.

By blocking the activity of FcRn, rozanolixizumab accelerates the catabolism of IgG antibodies, including IgG pathogenic autoantibodies. The aim is to reduce the concentration of pathogenic IgG in patients with autoimmune diseases mediated by the action of IgG autoantibodies.

The FcRn recycles IgG and albumin and transports it bidirectionally across epithelial barriers. Recent studies have shown that FcRn rescues both IgG and albumin from intracellular lysosomal degradation by recycling it from the sorting endosome to the cell surface (Roopenian and Akilesh, 2007). FcRn may also mediate transcytosis of IgG to facilitate its distribution within tissues. Rozanolixizumab has been specifically designed to block IgG binding to FcRn without blocking the binding and recycling of albumin.

Rozanolixizumab binds with high affinity to FcRn at both neutral and acidic pH. Immunoglobulin G that is constitutively taken up by pinocytosis into cells fails to bind to FcRn, even at the acidic pH found in the endosome. It is therefore not recycled and is trafficked to the lysosomes for degradation.

Production of pathogenic IgG autoantibodies is the major pathophysiology leading to a number of autoimmune diseases, which include MG, pemphigus vulgaris, [redacted], Goodpasture's syndrome, neuromyelitis optica, Guillain-Barré Syndrome, and chronic inflammatory demyelinating polyradiculoneuropathy.

As individual disease entities, IgG autoantibody-mediated conditions are relatively rare. Treatment of these disorders remains a difficult clinical problem, requiring in many of these conditions the long-term use of corticosteroids alone or combined with other immunomodulatory therapy. These therapeutic approaches are not effective in all patients and conditions and have broad immunosuppressive effects causing considerable toxicity and treatment-related morbidity.

Treatments aimed at reducing the quantity of circulating IgG autoantibodies, including plasmapheresis, immunoadsorption, or high dose IVIg, are being used for primary and secondary therapy of autoimmune diseases. The therapeutic approach of these treatments is thought in part to be based on lowering levels of pathogenic autoantibodies, which represents rational and effective treatment modalities of autoimmune diseases.

Therefore, specific removal of the IgG autoantibodies by FcRn blockade may provide an effective therapeutic option for IgG autoantibody-mediated autoimmune disorders.

More detailed information regarding the nonclinical and clinical development programs for rozanolixizumab, including all completed and ongoing studies, can be found in the latest version of the Investigator's Brochure (IB).

2.1 Study rationale

MG0007 will complement the ongoing Phase 3 study, MG0003, and replace the open-label extension (OLE) study, MG0004. The study will evaluate the safety, tolerability, and efficacy of rozanolixizumab over the initial 6-week treatment cycle and subsequent treatment cycles when given as needed based on worsening of gMG symptoms. The study will gather information on the efficacy response of subsequent treatment cycles and the duration until next treatment is needed. The study will support the intended use of rozanolixizumab in study participants with gMG, (ie, repeated 6-week treatment cycles based on worsening of symptoms).

MG0003 is a Phase 3 study of rozanolixizumab in anti-acetylcholine receptor (AChR) or anti-muscle-specific kinase (MuSK) autoantibody-positive participants with gMG who experience moderate to severe symptoms and are being considered for additional treatment such as IVIg or PEX. The primary objective is to demonstrate the clinical efficacy of rozanolixizumab in study participants with gMG. The study consists of a Screening Period of up to 4 weeks, followed by a 6-week double blind Treatment Period, and a blinded Observation Period of 8 weeks. MG0003 will provide the core data to support marketing authorization application globally. The current OLE study, MG0004, is a Phase 3, randomized study to evaluate the long-term safety, tolerability, and efficacy of rozanolixizumab in study participants with gMG.

The MG0007 study has been designed with the following considerations:

1. Double-blind placebo-controlled data will be collected on a single cycle as part of the MG0003 study. MG0007 will provide data on subsequent treatment cycles when given as needed based on worsening of gMG symptoms.
2. An open-label design is deemed appropriate since a placebo controlled long-term extension study may raise ethical concerns
3. The dose and treatment regimen for rozanolixizumab (equivalent to approximately 7mg/kg or 10mg/kg QW for 6-week treatment cycle) in MG0007 are identical to that used in MG0003.
4. For comprehensive data collection, an extended 16-week Observation Period was chosen to investigate maintenance of effect after a 6-week treatment cycle.

2.2 Background

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 autoantibody-mediated diseases.

To date, rozanolixizumab has been administered to human study participants in 8 completed clinical studies (UP0018, UP0060, MG0002, MG0003, MG0004, CIDP01, CIDP04, TP0001) and 6 ongoing studies (UP0106, TP0003, TP0006, TP0004, MOG001, and AIE001). UP0018 is a completed first-in-human study, MG0002 is a completed Phase 2 study in study participants with gMG, and [redacted] is a completed Phase 2 study in study participants with primary [redacted], and UP0060 is a completed Phase 1 study comparing the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of rozanolixizumab in Chinese, Japanese and Caucasian healthy volunteers.

In MG0002, clinically relevant improvements in day-to-day functioning, as measured by change from Baseline to Day 29 in myasthenia gravis-activities of daily living (MG-ADL) (secondary endpoint), were observed following treatment with rozanolixizumab 7mg/kg compared with placebo (p=0.036). Numerical differences numerical in favor of rozanolixizumab 7mg/kg compared with placebo were observed in reductions from Baseline in quantitative myasthenia gravis (QMG) (p=0.221) and MG-C score (p=0.089). Overall, repeated administrations of rozanolixizumab at dose levels of 7mg/kg and 4mg/kg sc have been generally well tolerated, with an acceptable safety profile. No new safety concerns were identified. The treatment-emergent adverse event (TEAE) profile was similar between rozanolixizumab and placebo except for headaches where increased frequency and severity was observed in the rozanolixizumab study participants.

Final data from the proof-of-concept [redacted] demonstrated that rozanolixizumab was tolerated with an acceptable safety profile after multiple (4, 7, and 10mg/kg) and single (15 and 20mg/kg) doses.

MG0003 is a Phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of 2 doses of rozanolixizumab (equivalent to approximately 7mg/kg and 10mg/kg) in study participants with gMG who experience moderate to severe symptoms and are being considered for additional treatment such as IVIg or PEX.

MG0004 is an open-label extension study for the lead-in study, MG0003, evaluating the long-term safety, tolerability, and efficacy of rozanolixizumab in study participants with gMG. Study participants in MG0004 are randomized to receive weekly doses of rozanolixizumab (equivalent to approximately 7mg/kg and 10mg/kg, respectively) over a 52-week Treatment Period.

MG0007 is a Phase 3 OLE study to evaluate the long-term safety, tolerability, and efficacy of repeated 6-week treatment cycles of rozanolixizumab based on MG worsening in study participants with gMG. This OLE study will provide the opportunity for study participants from the MG0003 and MG0004 to receive long-term rozanolixizumab treatment based on their MG symptom needs.

Once the OLE study MG0007 is activated at sites and ongoing study participants have had the opportunity to rollover into MG0007, MG0004 will be closed.

2.3 Benefit/Risk assessment

Generalized MG is a rare, debilitating, chronic autoimmune disease driven by, in large part, IgG autoantibodies that target neuromuscular junctions (NMJs). Most current treatment approaches are not targeted treatments to the specific underlying pathology of IgG autoantibody formation, but rather they produce a broad cascade of immune suppression, which results in undesirable side effects such as those seen with high-dose chronic steroid use. Many treatments of choice often require invasive, expensive, and time-consuming inpatient procedures such as PEX, or intravenous (IV) administration of immunoglobulins at a healthcare facility.

Rozanolixizumab represents an innovative, subcutaneous (sc) anti-FcRn monoclonal antibody that may provide a novel and specific targeted therapeutic approach for the treatment of patients with MG. Data show that rozanolixizumab markedly lowers serum IgG and IgG autoantibody levels in patients with generalized MG. The completed Phase 2 study MG0002 established supportive evidence of efficacy for the treatment of MG, achieving significant and clinically

meaningful improvements to Day 29 in MG-ADL with rozanolixizumab 7mg/kg compared with placebo (p=0.036). Repeated administrations of rozanolixizumab were generally [redacted] and well tolerated, with an acceptable safety profile and in line with sc dosing in the Phase 1 program and the safety profile observed in TP0001.

In MG0003, a Phase 3 study evaluating efficacy and safety of sc rozanolixizumab in adult study participants with gMG, the [redacted] clinical efficacy of rozanolixizumab was demonstrated by improvements versus placebo in all efficacy endpoints tested in the study. There were clinically meaningful and statistically significant reductions from Baseline in the primary endpoint, MG-ADL score, at Day 43 for both rozanolixizumab dose groups versus placebo.

The identified adverse drug reactions (ADRs) associated with sc administration of rozanolixizumab are headaches, diarrhoea, pyrexia, nausea, upper respiratory tract infections, arthralgia, rash, injections site reactions, vomiting, myalgia, and herpes simplex infections. Headache is the most commonly reported ADR. Headaches were mostly mild to moderate and easily managed with over-the-counter medications. Serious infections and hypersensitivity reactions are the safety concerns with rozanolixizumab. Other safety topics of interest include effects on vaccination response, effects on the kidney, reductions in albumin and plasma proteins, drug-induced aseptic meningitis (DIAM), and [redacted]. These risks can be mitigated by careful monitoring, exclusion of at-risk study participants, and appropriate protocol withdrawal and stopping criteria. Additionally, protocol guidance for management of severe and/or serious headaches (AESM), suspected aseptic meningitis (AESM), hypersensitivity reactions, and infection is also provided as well as expedited reporting requirements of AESM to UCB.

Restrictions on use of live vaccines have been defined in the exclusion criterion 6 (Section 5.2) (exclusion criteria 7 in Gap Period Eligibility Criteria [Section 10.12]). If vaccination with non-live vaccines (including COVID-19 vaccines) is considered necessary once a study participant has started therapy with IMP, the degree of protection afforded with a vaccine may be compromised while the participant is being treated with IMP.

Based on its mechanism of action, rozanolixizumab will reduce total IgG levels including vaccine specific IgG. However, it is unlikely that the immunogenicity of the vaccine will be compromised by FcRn inhibition. Given the study population characteristics (eg, status of the underlying disease, concomitant immunosuppressive therapies, etc.) it is recommended to perform individualized benefit risk assessment for vaccination and specifically vaccination against COVID-19 infection. If COVID-19 vaccination is planned, information regarding vaccine should be recorded (Section 6.5.1). Coronavirus Disease 2019 vaccination should be scheduled, if at all possible, to allow differentiation of safety profiles of IMP and vaccine (eg, a minimum window of 72 hours between COVID-19 vaccination and IMP administration). If any AEs were to occur, they should be handled as described in (Section 8.3) with causality assessment provided for both IMP and vaccine. Additionally, to further characterize the effect of rozanolixizumab on COVID-19 vaccination response, measurement of vaccine titers are being tested in rozanolixizumab development programs.

More detailed information about the known safety profile and expected adverse events (AEs) of rozanolixizumab may be found in the IB.

3 OBJECTIVES AND ENDPOINTS

Objectives	Endpoints/Estimands
Primary	
• To assess the safety and tolerability of additional 6-week treatment cycles with rozanolixizumab in study participants with gMG	The primary safety endpoints are: • Occurrence of treatment-emergent adverse events (TEAEs) • TEAEs leading to withdrawal of investigational medicinal product (IMP) The other safety endpoints are: • Occurrence of serious TEAEs • Occurrence of treatment-emergent adverse events of special monitoring (AESM) • Vital sign values and changes from Baseline (Day 1) (systolic and diastolic blood pressure [BP] and pulse rate at each scheduled assessment during Treatment and Observation Periods) • 12-lead electrocardiogram (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)
Secondary	
• To assess the efficacy of 6-week treatment cycles with rozanolixizumab in study participants with gMG	The secondary efficacy endpoints are: For each of the first 3 x 6-week treatment cycle, change from Baseline (Day 1) to Day 43[a]: • In MG-Activities of Daily Living (ADL) score within one treatment cycle • In Quantitative MG (QMG) score within one treatment cycle • In MG-Composite (MG-C) score within one treatment cycle

	• In MG Symptoms patient-reported outcomes (PRO) 'Muscle Weakness Fatigability' score within one treatment cycle • In MG Symptoms PRO 'Physical Fatigue' score within one treatment cycle • In MG Symptoms PRO 'Bulbar symptoms' score within one treatment cycle • In MG-ADL responder (≥2.0-point improvement within one treatment cycle • Time to MG-ADL response (≥2.0-point improvement from Baseline [Day 1]) within one treatment cycle For consecutive treatment cycles: • Time between consecutive treatment cycles
	The other efficacy endpoints are: For each 6-week treatment cycle and Observation Period (where applicable), improvement from Baseline (Day 1)] to each scheduled assessment: • MG-ADL responder (≥2.0-point) within one treatment cycle • QMG responder rate (≥3.0-point) within one treatment cycle • MG-C responder rate (≥3.0-point) within one treatment cycle • Time to MG-ADL response (≥2.0-point) within one treatment cycle • Minimal symptom expression (MG-ADL score of 0 or 1) at any time during Treatment and Observation Periods For each 6-week treatment cycle and Observation Period (where applicable), change from Baseline (Day 1) to each scheduled assessment:

	• In MG-ADL score within one treatment cycle • In QMG score within one treatment cycle • In MG-C score within one treatment cycle • In MG Symptoms PRO 'Muscle Weakness Fatigability' score within one treatment cycle • In MG Symptoms PRO 'Physical Fatigue' score within one treatment cycle • In MG Symptoms PRO 'Bulbar symptoms' score within one treatment cycle For each 6-week treatment cycle and Observation Period (where applicable), change from Baseline (Day 1) to Day 43[a]: • In 5-level European quality of life 5 dimension (EQ-5D-5L) within one treatment cycle • In Myasthenia Gravis-Quality of Life (MG-QOL)15r within one treatment cycle
Other	
• To assess the pharmacokinetics (PK) of rozanolixizumab	• Plasma concentrations of rozanolixizumab at each scheduled assessment
• To evaluate the incidence and emergence of antidrug antibody (ADA) of rozanolixizumab	• ADA at each scheduled assessment
• To assess the pharmacodynamics (PD) of rozanolixizumab	For each 6-week treatment cycle and Observation Period (where applicable): • Minimum value and maximum decrease from Baseline (Day 1) in total serum immunoglobulin (Ig) G and IgG subclasses concentration over time • Change from Baseline (Day 1) in serum IgG subclasses concentration over time • Change (absolute and percentage) from Baseline (Day 1) in MG-specific autoantibodies at each scheduled

	assessment during the Treatment and Observation Periods
• To assess the effects of rozanolixizumab on the concentration of [redacted]	• Change from Baseline (Day 1)[b] in [redacted] in participants experiencing infusion reactions For initial fixed treatment cycle only: • Change from Baseline (Day 1) in serum Ig concentrations [redacted]) at each scheduled assessment during Treatment and Observation Periods
• To assess the need for gMG medications including changes in type and doses	• Use of rescue therapy (yes/no) • Time to rescue therapy • Healthcare resource utilization, including hospitalization (type: intensive care unit [ICU]/non-ICU and duration)
• To assess the effect of rozanolixizumab on [redacted]	• Change in [redacted]

[a] Day 43 = Visit 8 for the initial fixed cycle and Visit 7 for the subsequent cycles.
[b] Baseline will be used from the sample collected at Day 1 (Visit 2) in MG0003. Other exploratory safety biomarkers may be assessed (Section 8.9).

4 STUDY DESIGN

4.1 Overall design

This is a Phase 3, multicenter, 2-arm, OLE study to evaluate 6-week treatment cycles of rozanolixizumab in study participants with gMG. MG0007 is an extension study of MG0003 and will be open for study participants from MG0003and MG0004 (see Section 4.1.1).

Eligible study participants from MG0003 will be randomized to receive an initial fixed 6-week treatment cycle of a subcutaneous dose of rozanolixizumab equivalent to approximately 7mg/kg or 10mg/kg QW (see Figure 1-1 and Figure 1-2), followed by an Observation Period that begins after the last dose of that treatment cycle as per assessments described in the Schedule of Activities (Section 1.3).

Eligible study participants from MG0004 who have completed at least 6 scheduled visits for rozanolixizumab treatment and the PEOT visit can move directly into the Observation Period in MG0007. Additionally, eligible study participants from MG0004 who are in the Observation

Period can complete the EOS visit and move directly into the Observation Period in MG0007 (see Figure 1-1 and Figure 1-2). If IMP treatment was withheld for low IgG in MG0004, study participant's missed dose(s) can be counted as part of the total 6 visits for completion of MG0004 and meet eligibility requirements for MG0007. These study participants will undergo their first MG0007 treatment with rozanolixizumab upon worsening of gMG symptoms. Participants will continue on their last treatment dose from MG0004. Dose adjustments may be applied in future cycles as per description below.

The rollover into MG0007 must be completed within 4 weeks after the EOS visit from MG0003, or the PEOT or EOS (as appropriate) visit from MG0004. In the event a study participant has a gap period (>4 weeks) between the EOS or PEOT visit from the lead-in study and the start of MG0007, a Screening Period (see Appendix 11, Section 10.11) of up to 4 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry into MG0007 (see Appendix 12, Section 10.12).

In case of symptom worsening (eg, an increase of 2.0 points on the MG-ADL or 3.0 points on the QMG scale) between assessments, resulting in a need for additional treatment, study participants will undergo another 6-week treatment cycle followed by an Observation Period, based on the Investigator's discretion.

The dose may be adjusted to 7mg/kg or 10mg/kg at the beginning of each treatment cycle based on the Investigator's discretion. Rules for dose modification and temporary treatment hold are described in Section 6.6 and Section 6.7. The minimal time to start the next treatment cycle is 4 weeks following the last dose of the treatment period of the previous cycle. If a study participant requires treatment earlier than 4 weeks, IgG levels from the previous cycle should be considered and discussed with the Medical Monitor A new treatment cycle **should not** be initiated until total IgG level is ≥2g/L.

Participants in MG0007 will remain on their gMG background medications (Table 6-3). With the exception of corticosteroids and AChE inhibitors, all gMG medication doses should be maintained during each respective 6-week treatment cycle and efforts should be made to maintain a stable dose during the first 8 weeks of the Observation Period.

Study participants who receive rescue therapy (IVIg, PEX, SCIg, or iv corticosteroid) during the Treatment Period are not eligible to receive any further treatment with rozanolixizumab, must complete an additional 8 weeks of follow up after the last dose of rozanolixizumab. Study participants must complete the first 8 weeks of the Observation Period after the last dose of rozanolixizumab prior to completing the EOS visit assessments, and subsequently will be withdrawn from the study (Section 4.4).

Those patients who received rescue therapy (IVIg, PEX, SCIg, or iv corticosteroid) during the observation or no treatment with rozanolixizumab periods may continue in the study at the Investigator's discretion and after discussion with Medical Monitor and/or UCB Study Physician. The following cycle of rozanolixizumab should in general not start earlier than 4 weeks following the last dose of IVIg, SCIg, or iv corticosteroids or the last PEX session, unless there is a medical reason, and an earlier treatment initiation is being considered [redacted] for the study participant as agreed upon with the Medical Monitor and/or UCB Study physician.

Study participants (not withdrawn from the study; criteria outlined in Section 7.2) will continue in the study and until product approval or until transition to a managed access program (MAP), if

available, as indicated per the Sponsor, and according to local guidance. For country-specific requirements, see Appendix 8 (Section 10.8).

In exceptional circumstances (eg, pandemic, hurricanes, etc) where study-specific investigations may not be conducted according to study protocol, contingency measures will be in place (see Section 8).

4.1.1 Study population

Study participants will enter from MG0003, or MG0004. Participants eligible for enrollment in this study completed MG0003, required rescue therapy during the Observation Period in MG0003 (except for study participants who opted to receive IVIg or PEX in MG0003), or completed at least 6 treatment visits in MG0004.

Study participants directly enrolling from MG0003 can use the EOS assessments as the Baseline (Day 1) in MG0007.

Study participants directly enrolling from MG0004 who have completed at least 6 visits regardless of the number of infusions (due to low IgG resulting in IMP treatment hold) will complete the PEOT visit (if entering from Treatment Period of MG0004) or EOS visit (if entering from Observation Period of MG0004) assessments from MG0004 and will directly enter the Observation Period (Visit 9 [Day 71]) of the initial fixed cycle.

A study participant who had to discontinue receiving treatment under the MG0003, or MG0004 due to the coronavirus disease 2019 (COVID-19) pandemic (ie, due to logistic reasons, resolution of suspected or confirmed COVID-19 infection, or fulfillment of quarantine period due to exposure) and provided no parameter(s) meeting the protocol-defined study drug discontinuation criteria can potentially enter MG0007. The Investigator should assess all available medical information prior to the study participant joining MG0007. The Investigator must discuss the eligibility for the study participant to join the MG0007 study based on a thorough individualized benefit-risk evaluation (ie, disease status, alternative options, AE profile, laboratory assessments), the regional situation, and protocol criteria and treatment schema with the Sponsor's Study Physician. Study participants with a gap of >4 weeks between the EOS visit from the lead-in study and the start of MG0007 must have an eligibility assessment performed during a 4-week Screening Period (see Section 10.11).

No formal sample size calculation can be performed. Approximately 200 study participants will be enrolled at approximately 130 sites from North America, Europe, and Asia (including Japan).

4.1.2 Dosing

The doses and regimen selected for the rozanolixizumab Phase 3 study, MG0003, was based on data from the Phase 2 studies in the MG and [redacted]), and Phase 1 data in healthy study participants. To date, there has not been any data to indicate that the doses used in MG0003 should be modified. Therefore, this OLE study will continue treatment with rozanolixizumab sc fixed doses across body weight tiers equivalent to approximately 7mg/kg and 10mg/kg administered QW for 6 weeks (Table 1-1). Weight-based dose adjustments should be limited to a maximum of every 6 months during the study.

If one of the doses described in Table 1-1 is determined to be futile and is discontinued in MG0003, then that dose arm will be dropped from MG0007, and study participants in the

affected dose arm will be transferred to an adjusted dose. Dose modifications are allowed in this study (see Section 6.6).

4.2 Scientific rationale for study design

MG0007 will complement the ongoing Phase 3 study, MG0003, and replace the chronic treatment OLE study, MG0004. The study will evaluate the safety, tolerability, and efficacy of rozanolixizumab over the initial 6-week treatment cycle and subsequent treatment cycles when given as needed based on worsening of gMG symptoms. The study will gather information on the efficacy response of subsequent treatment cycles and the duration until next treatment is needed. The study will support the intended use of rozanolixizumab in study participants with gMG, (ie, repeated 6-week treatment cycles based on worsening of symptoms).

MG0003 is a Phase 3 study of rozanolixizumab in anti-acetylcholine receptor (AChR) or anti-muscle-specific kinase (MuSK) autoantibody-positive participants with gMG who experience moderate to severe symptoms and are being considered for additional treatment such as IVIg or PEX. The primary objective is to demonstrate the clinical efficacy of rozanolixizumab in study participants with gMG. The study consists of a Screening Period of up to 4 weeks, followed by a 6-week double blind Treatment Period, and a blinded Observation Period of 8 weeks. MG0003 will provide the core data to support marketing authorization application globally. The OLE study, MG0004, is a Phase 3, randomized study to evaluate the long-term safety, tolerability, and efficacy of rozanolixizumab in study participants with gMG.

The MG0007 study has been designed with the following considerations:

1. Double-blind placebo-controlled data will be collected on a single cycle as part of MG0003. MG0007 will provide data on subsequent treatment cycles when given as needed based on worsening of gMG symptoms.
2. An open-label design is deemed appropriate since a placebo controlled long-term extension study may raise ethical concerns
3. The dose and treatment regimen for rozanolixizumab (equivalent to approximately 7mg/kg or 10mg/kg QW and for 6-week treatment cycle) in MG0007 are identical to that used in MG0003.
4. For comprehensive data collection, a 16-week Observation Period was chosen to investigate maintenance of effect after the 6-week treatment cycle.

4.3 Justification for dose

The dose and regimen of rozanolixizumab (equivalent to approximately 10mg/kg or 7mg/kg, administered sc QW) is selected based on the results from first-in-human study UP0018, the Phase 2 clinical studies in MG and [redacted] (MG0002 and [redacted]) as well as the doses selected for use in the pivotal Phase 3 study, MG0003; fixed-unit doses equivalent to approximately 7mg/kg or 10mg/kg QW. UP0018 was a randomized, investigator- and study participant-blind, placebo-controlled, single dose-escalating study to evaluate the safety and PK and to explore the PD of rozanolixizumab doses of 1mg/kg, 4mg/kg, and 7mg/kg administered as an iv or sc infusion over [redacted] in 49 healthy male and female volunteers. Data indicate that mean absolute decreases in IgG and mean percent change from Baseline IgG were greater in the active dose groups (n=6 each) compared to the pooled iv and sc placebo group (n=12) with median maximum decreases

of 42.8% (range: 39.6% to 48.6%) observed on Day 9 postdose for a rozanolixizumab 7mg/kg sc dose. Rozanolixizumab was tolerated with an acceptable safety profile after the single administration of a 7mg/kg sc dose, and all participant reported TEAEs were mild or moderate in severity.

MG0002 was a Phase 2, multicenter, randomized, investigator- and study participant-blind, placebo-controlled, 2-arm repeat dose, treatment sequence study evaluating the safety and efficacy of rozanolixizumab sc (4mg/kg and 7mg/kg) in 43 study participants with generalized MG. Marked improvements in patient-reported MG symptoms and disability, as measured by change from Baseline to Day 29 in MG-ADL, were observed following treatment with rozanolixizumab 7mg/kg compared with placebo. The least squares (LS) mean (standard error [SE]) change from Baseline was -1.8 (0.5) for the Rozanolixizumab 7mg/kg Group and -0.4 (0.5) for the Placebo Group. The difference between treatment groups was -1.4 (p=0.036 [95% upper confidence interval (CI): -0.4]). Smaller but numerical differences in favor of rozanolixizumab 7mg/kg vs placebo were observed in reductions from Baseline in QMG on Day 29 with the LS mean (SE) change from Baseline of -1.8 (0.6) for the Rozanolixizumab 7mg/kg Group and -1.2 (0.6) for the Placebo Group. The LS mean (SE) change from Baseline in MG-C score to Day 29 was -3.1 (0.9) for the Rozanolixizumab 7mg/kg Group and -1.2 (0.9) for the Placebo Group. In general, responder rates for QMG score, MG-C score, and MG-ADL score were higher for the rozanolixizumab 7mg/kg group than the placebo group. Serum total IgG concentrations and AChR autoantibodies rapidly decreased from Baseline in the rozanolixizumab 7mg/kg group in Dosing Period 1 and continued to decline on further dosing with 7mg/kg to a mean nadir of 3.3g/L for total IgG ([redacted] reduction from Baseline). Overall, repeated administrations of rozanolixizumab at dose levels of 7mg/kg and 4mg/kg sc have been generally [redacted] and well tolerated, with an acceptable safety profile. The TEAE profile was similar between rozanolixizumab and placebo, except for headaches where increased frequency and severity was observed in the rozanolixizumab-treated study participants.

Consistent with the mechanism of action of rozanolixizumab, an increased catabolism of IgG will reduce disease-specific autoantibodies with corresponding improvements in clinical signs and symptoms. Two sc treatment arms, equivalent to individual 7mg/kg and 10mg/kg dosing, have been selected to provide maximal reduction in autoantibody concentration and result in clinically significant improvements in the primary endpoint. A dose of 7mg/kg has demonstrated clinical improvements in MG-ADL in MG0002 (as described above). Additional data from the Phase 2 study in study participants with [redacted] demonstrated that rozanolixizumab was well tolerated at 2 doses of 10mg/kg with further IgG reduction achieved. An individual equivalent dose of 10mg/kg has been included to assess if further improvements in MG-ADL (magnitude of response and time to onset of symptom relief) can be achieved at a higher dose level with greater and more rapid IgG reduction.

A population PKPD model that characterizes the dose-exposure-IgG relationship was used to guide, through simulation, the choice of fixed-unit doses at each weight bracket that achieved equivalent IgG reductions (mean and 90% prediction interval) to the weight-based (mg/kg) dosing regimens studied previously. These models-based simulations demonstrate that the proposed weekly doses of rozanolixizumab for 6 consecutive weeks are expected to produce mean maximum IgG reductions of [redacted]. These reductions will be achieved rapidly and maintained consistently over the Treatment Period.

4.4 End of study definition

A study participant is considered to have completed the study if he/she has completed all phases of the study including the first 8 weeks of the Observation Period and the EOS visit assessments.

At the time of product approval or the availability of a MAP, or study participant early withdrawal the following scenarios need to be considered:

- if the study participant is still in a treatment cycle, he/she will need to complete that cycle and the first 8 weeks of the Observation Period before completing the EOS visit assessments.
- if a study participant is in the first 8 weeks of the Observation Period in, he/she must complete the 8 weeks before completing the EOS visit assessments
- if a study participant is in the beyond the first 8 weeks of the Observation Period or in the no treatment period, he/she can complete EOS visit assessments

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

5 STUDY POPULATION

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

5.1 Inclusion criteria

Study participants are eligible to be included in the study only if all of the following criteria apply:

Type of participant and disease characteristics

1a. Study participant must meet one of the following:

- completed MG0003,
- required rescue therapy (except IVIg or PEX) during the Observation Period in MG0003 or
- completed at least 6 visits in MG0004.

Weight

2. Body weight ≥35kg at Baseline (Day 1).

Sex

3b. Study participants may be male or female:

- Removed.
- A female participant is eligible to participate if she is not pregnant (see Appendix 4), not breastfeeding, and at least one of the following conditions applies:
  - Not a woman of childbearing potential (WOCBP) as defined in Appendix 4

    OR
  - A WOCBP who agrees to follow the contraceptive guidance in Appendix 4 during the treatment period and for at least for at least 90 days after the last dose of study

treatment. The study participant must have a negative urine pregnancy test prior to the first dose of study medication at Baseline (Day 1) of the initial and subsequent treatment cycles.

Informed consent

4. Capable of giving signed informed consent as described in Appendix 1 which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol. For Japan-specific regulations, see Appendix 8 (Section 10.8).
5. Study participant is considered reliable and capable of adhering to the protocol visit schedule, or medication intake according to the judgment of the Investigator.

For France-specific inclusion criteria (criterion #6), see Appendix 8 (Section 10.8).

5.2 Exclusion criteria

For criteria pertaining to laboratory measures, the last value from MG0003, or MG0004 will be used for evaluation of study participant eligibility, as long as the measurement was taken within the last 4 weeks prior to MG0007 Baseline (Day 1).

Study participants are excluded from the study if any of the following criteria apply:

Medical conditions

1. Study participant has any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the study participant's ability to participate in this study.
2. 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 the previous 12 months.

3a. Study participant has a known hypersensitivity to any components of the study medication or other anti-FcRn medications.

4a. Study participant with a known tuberculosis (TB) infection, at high risk of acquiring TB infection, or latent tuberculosis infection (LTBI), or current/history of nontuberculous mycobacterial infection (NTMBI).

5a. Study participant met any mandatory withdrawal or mandatory study drug discontinuation criteria in MG0003, or MG0004, or permanently discontinued study drug in either study.

Prior/Concomitant therapy

6. Study participant intends to have a live vaccination during the course of the study or within 8 weeks following the final dose of rozanolixizumab.

Diagnostic assessments

7. Study participant has absolute neutrophil count <1500 cells/mm^3.
8. Study participant with severe (defined as Grade 3 on the MG-ADL scale) weakness affecting oropharyngeal or respiratory muscles, or who has myasthenic crisis or impending crisis.

9. Study participant has any laboratory abnormality that, in the opinion of the Investigator, is clinically significant, has not resolved at randomization, and could jeopardize or compromise the study participant's ability to participate in this study.
10. Study participant has renal impairment, defined as GFR less than 45mL/min/1.73m^2.
11. Study participant has 12-lead ECG with findings considered to be clinically significant upon medical review. The clinical significance of the findings needs to be assessed by the Investigator to determine eligibility, and any queries regarding continuation of the study participants will have to be addressed with the Medical Monitor.
12. Alanine transaminase (ALT), aspartate aminotransferase (AST), or alkaline phosphatase (ALP) are >3.0x upper limit of normal (ULN).
13. Bilirubin >1.5xULN (isolated bilirubin >1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin <35%).
14a. If study participant has >ULN ALT, AST, or ALP that does not meet the exclusion limit at Baseline (Day 1), 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 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). Current unstable liver or biliary disease per Investigator assessment defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, persistent jaundice, or cirrhosis. NOTE: Stable chronic hepatobiliary disease (including Gilbert's syndrome, and asymptomatic gallstones) is acceptable of the study participant otherwise meets entry criteria. For UK-specific requirements, see Appendix 8, Section 10.8.
15a. Study participant has corrected QT interval (QTcF) >450msec (for male participants) or QTc >470msec (for female participants) or QTc >480msec in participants with bundle branch block.

Other

16. A female study participant, who plans to get pregnant during the participation in the study.
17. Study participant has a lifetime history of suicide attempt (including an [redacted]), or had suicidal ideation since the last visit in MG0003 or MG0004 as indicated by a positive response (Yes) to either Question 4 or Question 5 of the Columbia Suicide Severity Rating Scale (C-SSRS).

For France-specific exclusion criteria (criterions #18 and #19), see Appendix 8 (Section 10.8).

5.3 Lifestyle restrictions

There are no lifestyle restrictions during the study unless deemed to interfere with compliance with the protocol as deemed by the Investigator.

The use of medicinal cannabidiols and medicinal marijuana (prescribed by a Physician) is permitted. For Japan-specific regulations, see Appendix 8 (Section 10.8).

5.4 Screen failures

Applicable to study participants with a gap period only (see Section 10.11).

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

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.

6 STUDY TREATMENTS

Study treatment is defined as any investigational treatment(s), intended to be administered to a study participant according to the study protocol.

6.1 Treatments administered

A description of the IMP to be administered in MG0007 is provided in Table 6-1.

Table 6-1: Study treatments administered

Intervention name	Rozanolixizumab
Type	Drug
Dose formulation	Solution for injection A glass vial, containing rozanolixizumab at a concentration of [redacted]
Dosage level(s)	See Table 6-2
Route of administration	Subcutaneous infusion via syringe driver or manual push method
Use	Experimental
IMP and NIMP	IMP
Sourcing	Provided centrally by the Sponsor or locally by the study site, subsidiary, or designee
Packaging and labelling	Rozanolixizumab is manufactured, packaged, and labeled according to Good Manufacturing Practice guidelines and applicable laws or regulations
Current/Former name(s) or alias(es)	UCB7665

IMP=investigational medicinal product; NIMP=non investigational medicinal product

Details on the preparation of study treatment for infusion, rate of infusion, administration, appropriate records handling, and site personnel roles are provided in the IMP Handling Manual. The optional onsite manual push route of administration performed by a healthcare professional should only be introduced at the beginning of a treatment cycle and may be reverted back to the standard syringe driver administration at any time. All site personnel delegated to handle study treatment storage, preparation and administration must be trained to IMP Handling Manual.

Rozanolixizumab sc doses across body weight tiers to be used in MG0007 are presented in Table 6-2.

Table 6-2: MG0007 dose levels and weight tiers

Bodyweight	Rozanolixizumab dose eqv	
	7mg/kg Dose 1	10mg/kg Dose 2
≥35 to <50kg	280mg	420mg
≥50 to <70kg	420mg	560mg
≥70 to <100kg	560mg	840mg
≥100kg	840mg	1120mg

eqv=equivalent

6.2 Preparation, handling, storage, and accountability requirements

The Investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all study treatment received and any discrepancies are reported and resolved before use of the study treatment.

Only participants enrolled in the study may receive study treatment and only authorized site staff may supply or administer study treatment. All study treatments must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions with access limited to the Investigator and authorized site staff.

The Investigator, institution, or the head of the medical institution (where applicable) is responsible for study treatment accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records).

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

Further guidance and information for the final disposition of unused study treatment are provided in the IMP Handling Manual.

6.2.1 Drug accountability

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

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 study medication 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 study medication must be reconciled and either destroyed at the site according to local laws, regulations, and UCB and/or site 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.

6.3 Measures to minimize bias: randomization and blinding

An interactive response technology (IRT) will be used for assigning eligible participants to a treatment regimen (as applicable) based on a predetermined production randomization and/or packaging schedule provided by UCB (or designee). The randomization schedule will be produced by the IRT vendor. The IRT will generate individual assignments for kits of study medication, as appropriate, according to the visit schedule. Study participants from MG0003 who complete the EOS visit will be rerandomized in MG0007. Randomization in MG0007 is to a ratio of 1:1. Study participants from MG0004 will not be rerandomized upon entering MG0007, but will continue their last treatment regimen received in MG0004 for their first treatment cycle in MG0007.

To enroll a study participant (Visit 1), the Investigator or designee will contact the IRT and provide brief details about the participant to be enrolled. Study participants will retain the same 5-digit number assigned at Screening in MG0003 that serves as the participant identifier throughout the study. The participant number will be required in all communication between the Investigator or designee and the IRT regarding a particular participant. Participant numbers and kit numbers will be tracked via the IRT.

6.3.1 Procedures for maintaining and breaking the treatment blind

6.3.1.1 Maintenance of study treatment blind

This is an OLE study and treatment details (ie, dose arm) will not be blinded.

To maintain study integrity, IgG level will remain blinded to the study sites and the UCB study team for the first 4 weeks of the study.

6.3.1.2 Breaking the treatment blind in an emergency situation

Not applicable.

6.4 Treatment compliance

Drug accountability must be recorded on the Drug Accountability form (Section 6.2.1).

Details regarding treatment compliance are outlined in the Important Protocol Deviation Specification document.

6.5 Concomitant medication(s)/treatment(s)

6.5.1 Permitted concomitant treatments (medications and therapies)

Concomitant medications listed in Table 6-3 are permitted during the study for the treatment of gMG, and dose adjustments are allowed between treatment cycles. With the exception of corticosteroids and AChE inhibitors, the dose of permitted concomitant medications should be maintained during each 6-week treatment cycle and every effort should be made to maintain a stable dose during the first 8 weeks of each Observation Period. Any violation of the permitted treatment criteria would lead to prohibited treatment and should be discussed with the Investigator, Sponsor, and Medical Monitor.

If a study participant receives a COVID-19 vaccine, the product name and date of administration(s) should be captured in the eCRF as a concomitant medication.

Table 6-3: Permitted concomitant treatments

Permitted Medications	Dose
Oral corticosteroids (eg, prednisolone)	No specific requirements
Methotrexate	≤30mg/week
Mycophenolate mofetil	≤3g/day
Cyclosporine[a]	≤5mg/kg/day for unmodified ≤4mg/kg/day for modified (microemulsion)
Azathioprine	≤3mg/kg/day
Cholinesterase inhibitors	≤600mg pyridostigmine/day
Tacrolimus[b]	≤5mg/day

[a] Doses higher than listed are permissible if trough level is ≤300ng/mL.
[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.

6.5.2 Prohibited concomitant treatments (medications and therapies)

The following concomitant medications are prohibited during the study:

- All biologics, including rituximab
- Cyclophosphamide
- Pimecrolimus
- IPP-201101 (Lupuzor™)
- Immunoadsorption
- Vinca alkaloids (vincristine, vinblastine)

Study participants can enroll in MG0007 irrespective of their background gMG medications.

If a study participant needs or takes any prohibited medication or therapy, the Investigator will (where possible) discuss with the Medical Monitor and/or the Sponsor's Study Physician and a decision will be made whether the study participant can continue in the study or be withdrawn.

6.5.3 Treatments specific to NMJ interference

Treatments could interfere with the function of the NMJ (and which therefore could impair study participants with MG), such as, but not limited to, include the following medications:

- botulinum toxin
- aminoglycoside antibiotics
- tetracycline antibiotics
- penicillamine
- magnesium

For a more detailed list please refer to the Myasthenia Gravis Foundation of America (MGFA) medication list (https://myasthenia.org/What-is-MG/MG-Management/Cautionary-Drugs). The benefit-risk of starting these medications should be carefully considered by the Investigator, and where possible, the Investigator will discuss with the Medical Monitor and/or sponsor's Study Physician prior to initiating therapy that can affect the NMJ.

6.5.4 Rescue medication

The study site will supply rescue therapy that will be obtained locally. Rescue therapy will be given as per standard of care and at the discretion of the Investigator. Study participants who continue to experience moderate to severe symptoms despite treatment with rozanolixizumab may be treated with the following as rescue therapy:

- IVIg
- SCIg
- PEX, or plasmapheresis
- iv corticosteroids at a higher dose than previous oral dose

Participants who are treated with rescue therapy during the Treatment Period are not eligible to receive any further treatment with rozanolixizumab. Study participants must complete the first 8 weeks of the Observation Period after the last dose of rozanolixizumab prior to completing the EOS visit assessments, and subsequently will be withdrawn from the study (Section 4.4).

Those patients who received rescue therapy during the observation or no treatment with rozanolixizumab periods may continue in the study at the Investigator's discretion and after discussion with Medical Monitor and/or UCB Study Physician. The following cycle of rozanolixizumab should in general not start earlier than 4 weeks following the last dose of IVIg, SCIg, or iv corticosteroids or the last PEX session, unless there is a medical reason, and an earlier treatment initiation is being considered [redacted] for the study participant as agreed upon with the Medical Monitor and/or UCB Study physician.

The date and time of rescue medication administration as well as the name and dosage regimen of the rescue medication must be recorded.

6.6 Dose modification

Dose modifications from 10mg/kg to 7mg/kg equivalent and vice versa is permitted at the beginning of the treatment cycles at the Investigator's discretion, and if the benefit-risk remains favorable for the study participant. Recommended dose modifications from 10mg/kg to 7mg/kg equivalent due to drug-related adverse events which may include but not limited to:

- Moderate to severe headaches that are considered to be related to rozanolixizumab
- Moderate to severe GI disturbances that are considered to be related to rozanolixizumab
- Moderate to severe toxicities (≥Grade 2 as defined by Common Terminology Criteria for Adverse Events [CTCAE], version 5.0) for which rozanolixizumab cannot be excluded as a cause
- Recurrent hypogammaglobulinemia with a serum total IgG level of <2g/L.

6.7 Home (or Virtual) visits

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

- The study participant is willing to be dosed and monitored at home by a home nurse.
- The study participant has shown good acute tolerability to previous administrations of IMP (namely, he or 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 Investigator should complete a checklist to confirm that criteria for home nurse and/or self-administration have been fully evaluated.

Virtual visits will be conducted with study participants during the Observation Period and between cycles (see Schedule of Activities (Section 1.3); no treatment with rozanolixizumab) by site personnel. Alternatively, these visits can be conducted at the site as deemed necessary by site personnel and/or the study participant.

6.8 Treatment after the end of the study

Study participants who complete participation in MG0007 may have the possibility to continue receiving rozanolixizumab through a MAP if available, as indicated per the Sponsor and applicable per local regulations.

In the case of prolonged hypogammaglobulinemia after treatment discontinuation, study participants must be followed up until IgG levels return to values within the normal range or to individual Baseline values.

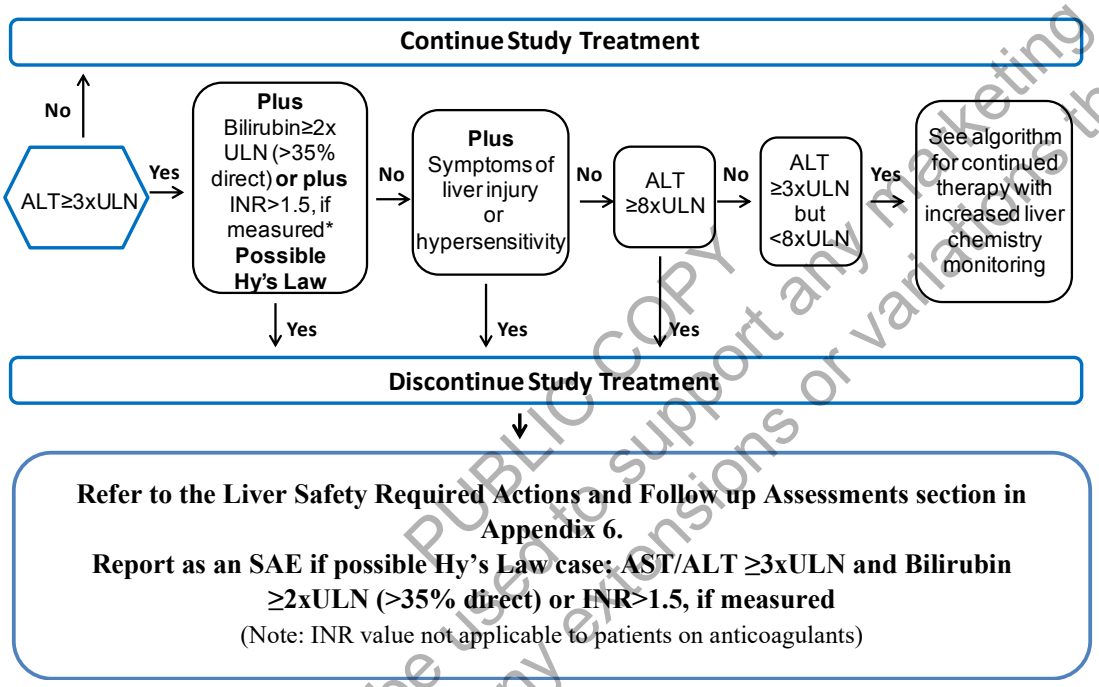
7 DISCONTINUATION OF STUDY MEDICATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 Discontinuation of study medication

7.1.1 Liver chemistry stopping criteria

Discontinuation of study treatment for abnormal liver function should be considered by the Investigator when a participant meets one of the conditions outlined Figure 7-1 and Figure 7-2 or if the Investigator believes that it is in best interest of the participant.

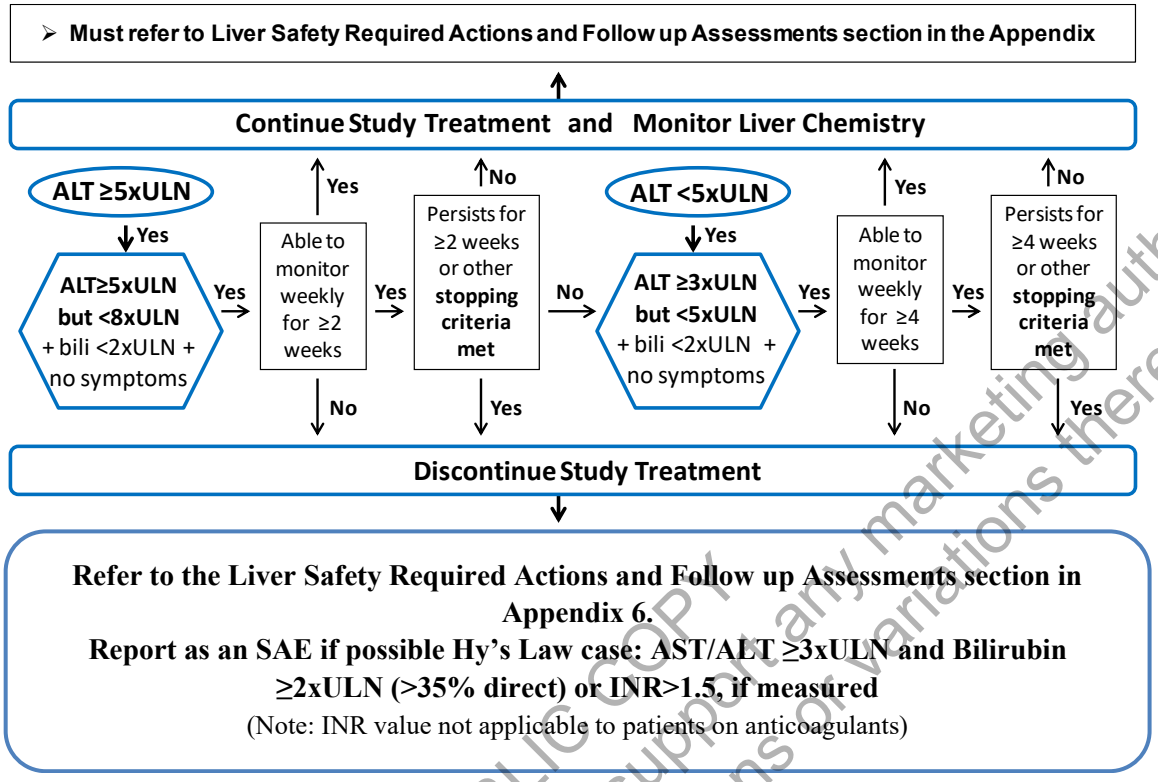
Figure 7-1: Liver Chemistry Stopping Criteria and Increased Monitoring Algorithm



ALT=alanine aminotransferase; AST=aspartate aminotransferase; INR=international normalized ratio; SAE=serious adverse event; ULN=upper limit of normal

Treatment with study medication may be continued with increased monitoring if a study participant meets one of the criteria outlined in Figure 7-2.

Figure 7-2: Liver Chemistry Increased Monitoring Algorithm with Continued Study Intervention for Participants with ALT ≥3xULN but <8xULN



ALT=alanine aminotransferase; AST=aspartate aminotransferase; bili=bilirubin; INR=international normalized ratio; SAE=serious adverse event; ULN=upper limit of normal

Specific assessments and follow up actions for potential drug-induced liver injury are provided in Appendix 6 (Section 10.6).

7.1.2 QTc stopping criteria

If a clinically significant finding is identified (including, but not limited to changes from baseline in QT interval corrected using Fridericia's formula [QTcF]) after enrollment, the Investigator or qualified designee will determine if the participant can continue in the study and if any change in participant management is needed. This review of the ECG printed at the time of collection must be documented. Any new clinically relevant finding should be reported as an AE.

A study participant who meets either bulleted criterion based on the average of triplicate ECG readings will be withdrawn from study medication and move into the Observation Period. The study participant should be referred to a specialist (ie, cardiologist) and managed as per local guidance.

- QTc >500 msec OR uncorrected QT >600msec
- Change from baseline of QTc >60msec

For participants with underlying bundle branch block, follow the discontinuation criteria listed below:

Baseline QTc with Bundle Branch Block	Discontinuation QTc Threshold with Bundle Branch Block
<450msec	>500msec
450 to 480msec	≥530msec

See the Schedule of Activities for data to be collected at the time of treatment discontinuation and follow-up and for any further evaluations that need to be completed.

7.1.3 Temporary IMP discontinuation

Study participant ***must be*** TEMPORARILY discontinued from the IMP if any of the following events occur:

1. The study participant develops an event of hypogammaglobulinemia with a serum total IgG of <1g/L irrespective of infection. When the IgG level reaches ≥2g/L, the study participant may be allowed to continue treatment with IMP (see Appendix 13; Section 10.13.1).
2. Symptomatic cases of confirmed COVID-19 infection. The IMP may be restarted if clinically appropriate when signs and symptoms have resolved and in agreement with local guidelines.
3. Study participant has a suspected DIAM. The IMP may be restarted if clinically appropriate when signs and symptoms have resolved. Refer to Section 7.1.4 for permanent discontinuation criteria (criterion #10).

Study participants ***may be*** TEMPORARILY discontinued from the IMP if the following events occur:

1. The study participant develops a nonserious persisting or recurrent infection with serum total IgG level between ≥1 and <2g/L. Upon resolution of infection and the IgG returning to level of ≥2g/L, the study participant may be allowed to resume treatment with the IMP (see Appendix 13; Section 10.13.1).
2. Asymptomatic or suspected cases of COVID-19 infection. The IMP may be restarted when clinically appropriate as deemed by the Investigator and in agreement with local guidelines.
3. Study participant has a moderate to severe infection (Grade 2 to 3) that may or may not result in hospitalization, unless the **discontinuation criterion #3** is met. Decision to start a new treatment cycle should be based on careful evaluation by the Principal Investigator of the Benefit-Risk for the individual study participant and provided a full recovery from infection has occurred, an acceptable level of total IgG (≥2g/L) has been reached and no other discontinuation criteria were met.

The Investigator should discuss with the Medical Monitor and/or Sponsor's study physician prior to reinitiating the IMP. As appropriate, virtual assessments could continue (eg, AE collection, patient-reported outcome [PRO] assessments as per contingency measures described in Section 8).

If IMP treatment is resumed, continue the next dose as previously scheduled. No "make up" dose is permitted.

The participant should subsequently follow the visit schedule as described in the protocol, and the eCRF should be completed accordingly, including the information if the visit was impacted by COVID-19 infection.

The date and reason for dose modification/hold of rozanolixizumab is to be recorded on each study participant's eCRF.

7.1.4 Study medication permanent discontinuation criteria

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

1. Study participant develops an illness that would interfere with his or her continued participation.
2. Study participant has new onset or recurrent neoplastic disease (except for superficial basal or squamous cell carcinoma of the skin not requiring targeted biological therapy, chemotherapy or radiation).
3. Study participant experiences a significant infective episode including but not limited to bacteremia/sepsis, infectious meningitis, septic arthritis, osteomyelitis, complicated pneumonia, or visceral abscess, which may or may not result in hospitalization during a treatment period. This list is not intended to be all inclusive and the investigator is expected to apply his/her judgement on continuing IMP based on the clinical situation.

   However, if a significant infective episode is reported during observation and no treatment with rozanolixizumab period, the decision to start a new treatment cycle should be based on careful evaluation by the Principal Investigator of the Benefit-Risk for the individual study participant and provided a full recovery from infection, an acceptable level of total IgG (≥2g/L) and no other discontinuation criteria were met.
4. Study participant meets potential drug-induced liver injury (PDILI) permanent discontinuation criteria.
5. Study participant has a TB test that is confirmed positive or any further evidence suggestive of potential TB infection (ie, exposure) and further examinations result in a diagnosis of active TB or latent TB infection (LTBI).
6. If a nontuberculosis mycobacterium infection (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.
7. Removed.
8. Study participant has an AE of severe or serious infusion or anaphylactic reaction requiring corticosteroid and/or epinephrine therapy (Sampson et al, 2006).
9. Study participant is treated with rescue therapy (IVIg, SCIg, PEX, or iv corticosteroids; see Section 6.5.4) during the Treatment Period. Those patients who received rescue therapy during the observation or no treatment with rozanolixizumab periods may continue in the study at the investigator's discretion and after discussion with Medical Monitor and/or UCB Study Physician. The following cycle of rozanolixizumab should in general not start earlier than 4 weeks following the last dose of IVIg, SCIg, or iv corticosteroids or the last PEX

session, unless there is a medical reason, and an earlier treatment initiation is being considered [redacted] for the study participant as agreed upon with the Medical Monitor and/or UCB Study physician.

10. Study participant has a recurrence of aseptic meningitis (see also Appendix 14 [Section 10.14]).

Study participants **may** permanently discontinue rozanolixizumab **and** move into the Observation Period 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. Study participant takes prohibited concomitant medications as defined in this protocol.

Investigators should contact the Medical Monitor, whenever possible, to discuss the withdrawal of a participant in advance. Investigators should attempt to obtain information on study participants in the event of withdrawal (eg, reason for withdrawal, any safety information).

In the event of study participant early withdrawal, the scenarios as described in Section 4.4 need to be considered.

7.2 Participant discontinuation/Withdrawal from the 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. The Sponsor or a regulatory agency requests withdrawal of the study participant.
3. There is confirmation of a pregnancy during the study, as evidenced by a positive pregnancy test.
4. 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 participants should be referred immediately to a Mental Healthcare Professional.

A participant **may** withdraw from the study at any time at his/her own request, or may be withdrawn at any time at the discretion of the Investigator for safety, behavioral, compliance, or administrative reasons.

If the study participant withdraws consent for disclosure of future information, the Sponsor may retain and continue to use any data collected before such a withdrawal of consent.

If a study participant withdraws from the study, he/she may request destruction of any samples taken and not tested, and the Investigator must document this in the site study records.

See the Schedule of Activities (Section 1.3) and Section 4.4 for data to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed.

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

7.3 Lost to follow up

A participant will be considered lost to follow-up if he or she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site must attempt to contact the participant and reschedule the missed visit as soon as possible and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain whether or not the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow up, the Investigator or designee must make every effort to regain contact with the participant (at least 1 phone call and 1 written message to the 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 participant, must be recorded in the source documents. The eCRF must document the primary reason for withdrawal.

Should the participant continue to be unreachable, he/she will be considered to have withdrawn from the study with a primary reason of lost to follow-up documented in the eCRF.

8 STUDY ASSESSMENTS AND PROCEDURES

Study procedures and their timing are summarized in the Schedule of Activities (Section 1.3).

Protocol waivers or exemptions are not allowed.

Immediate safety concerns should be discussed with the Sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study treatment.

Adherence to the study design requirements, including those specified in the Schedule of Activities (Section 1.3), is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The Investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Procedures conducted as part of the participant's routine clinical management (eg, blood count) and obtained before signing of the ICF may be utilized for Screening or Baseline purposes provided the procedures met the protocol-specified criteria and were performed within the time frame defined in the Schedule of Activities (Section 1.3).

An Unscheduled Visit can be conducted at the discretion of the Investigator (eg, due to an AE).

During the Unscheduled Visit, the following assessments will be performed:

- AE reporting
- Concomitant medications
- Review of withdrawal criteria
- Physical examination
- Vital signs

Blood samples for PK, IgG, hematology, biochemistry, other laboratory testing and assessments may be performed as clinically indicated at the discretion of the Investigator.

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

Some study-specific investigations may not be conducted according to the study protocol during a pandemic or other exceptional circumstances (eg, hurricanes) due to the need to implement safety measures and guidance from regulatory authorities. In such a situation, which may be accompanied by local or global containment or other measures, sites may need to prohibit access to study participants and study-related personnel. Study participants visits to the study site may be replaced by contingency measures. These measures are primarily established to ensure the safety of study participants during the course of the study and to maintain the study participants treatment schedule, if the Investigator considers it appropriate. These measures include but are not limited to virtual visits or home-nursing visits replacing site visits, eg, telemedicine contacts or home-nursing visits when treatment and/or blood sampling is scheduled. The contingency measures are described in a contingency plan and will be implemented as required.

8.1 Efficacy assessments

Planned timepoints for all efficacy assessments are provided in the Schedule of Activities (Section 1.3).

8.1.1 MGFA Classification

The Investigator will classify the study participant's MG using the MGFA Clinical Classification (Jaretzki et al, 2000). This is a 5-stage classification (I to V), with a higher class indicating more severe disease. To be eligible for this study, a participant with a gap period must be graded MGFA CLASS II to IVa at Visit 1, as per inclusion criteria (see Appendix 12 [Section 10.12]).

8.1.2 Quantitative Myasthenia Gravis scale

For assessment of the QMG scale, Investigators or qualified designee will follow the MGFA's QMG Manual instructions. Clinical personnel must complete mandatory training to assess study participants' QMG score (details are provided in the Study Procedures Manual). If not medically appropriate, then the treatment can be continued but the testing should be performed as best as possible at the same timeframe post last acetylcholinesterase AChE inhibitor dosing for each evaluation during the study. Study participants should not take pyridostigmine (or other AChE inhibitor medication) from midnight before testing when medically safe to do so to standardize testing (ie, if AChE inhibitors cannot be stopped). The scale tests 13 items, including ocular and facial involvement, swallowing, speech, limb strength, and forced vital capacity (FVC). For the assessment of FVC, the same spirometer should be used each time a study participant is tested, and if possible, the same person should carry out the assessment. The QMG is a validated assessment (Barnett et al, 2012), with a higher score indicating more severe disease. Scoring for each item ranges from no weakness (0) to severe weakness (3), with an overall score range from 0 to 39. A 3-point change in the total score is considered clinically relevant. Where possible, the same person should carry out the assessment at each visit.

8.1.3 MG-Composite scale

For assessment of the MG-C scale, the Investigator or qualified designee will examine the study participant to score all items, except for talking, chewing, and swallowing for which the study participant will self-assess. Study participants should not take pyridostigmine (or other AChE inhibitor medication) from midnight before testing when medically safe to do so to standardize testing. The MG-C scale is a validated assessment (Burns et al, 2010), with a higher score indicating more severe disease and a 3-point change being of clinical relevance (Muppidi et al, 2011). The scale tests 10 items, with individual items being weighted differently. The overall score ranges from 0 to 50. Clinical personnel must complete mandatory training to assess study participants' MG-C score (details are provided in the Study Procedures Manual). Where possible, the same person should carry out the assessment at each visit.

8.1.4 Patient-reported outcomes

Patient-repoted outcomes must be completed as per time points mentioned in the Schedule of Activities (Section 1.3). The PROs should be completed prior to any intrusive procedures in a quiet place.

The PROs should be completed in the following order: MG-ADL, MG Symptoms PRO, EQ-5D-5L, and MG-QOL15r. The PROs should only be checked for completeness. On dosing days, the

PROs will be completed prior to dosing. Study participants should not take pyridostigmine (or other AChE inhibitor medication) from midnight before the days when efficacy assessments are performed, when medically safe to do so to standardize testing.

8.1.4.1 MG-Activities of Daily Living

The MG-ADL is an 8-item PRO instrument developed on the basis of the QMG (Wolfe et al, 1999). The MG-ADL targets symptoms and disability across ocular, bulbar, respiratory, and axial symptoms. In a recent study, reliability, validity, and responsiveness of the MG-ADL were further assessed. The questionnaire showed strong construct validity when evaluated against the MG-C as well as against the MG-QOL15r; high test-retest reliability in a 1-week interval; and it was demonstrated that a 2-point improvement indicates clinical improvement (Muppidi, 2012; Muppidi et al, 2011). The total MG-ADL score ranges from 0 to 24, with a higher score indicating more disability.

Independently of study visit type (site, home, or virtual), the MG-ADL must be completed by study participants in a quiet place by themselves without the help of a partner or caregiver, before any clinical examination takes place. Study participants should be informed of the importance of this questionnaire and instructed to read the items and instructions carefully. They should be informed that there are no correct or incorrect answers.

Study personnel are not allowed to interpret the items for the participant. If a participant asks for guidance, study personnel should instruct him/her to respond according to their best understanding of the item. The MG-ADL should only be checked for completeness by study personnel. In the event a few questionnaire items have not been completed, study personnel should only query this with the study participant, if this results from an omission. Study personnel shall neither complete missing data nor suggest changes to participant responses. As with other study data, responses to the questionnaire should be treated as confidential information. Data privacy considerations apply.

In the specific context of virtual and home visits, paper copies of MG-ADL should be made available to study participants ahead of the visit. Site coordinators or study personnel (or an automatic alert mechanism) should remind study participants to complete MG-ADL before visit start and to record the date upon completion of the questionnaire. Once they have completed MG-ADL, study participants should transfer it electronically to site personnel. In the event study personnel finds out that MG-ADL has not been completed before the visit, study participants should be allowed some additional time to complete the questionnaire before any study related assessment is initiated.

8.1.4.2 MG Symptoms PRO

The MG Symptoms PRO instrument consists of 42 items across 5 scales: ocular symptoms (items 1-5); bulbar symptoms (items 6-15); respiratory symptoms (items 16-18); physical fatigue (items 19-33) and muscle weakness fatigability (items 34-42).

The study participant will be asked to choose the response option that best describes the severity of ocular, bulbar, and respiratory symptoms over the past 7 days using a 4-point Likert scale (“none” to “severe”) and how frequently they experience physical fatigue and muscle weakness fatigability over the past 7 days using a 5-point Likert scale (“none of the time” to “all of the

time"), respectively. A score can be obtained for each scale. All scores range from 0 to 100, with higher scores indicating more severe symptoms.

8.1.4.3 EQ-5D-5L

The 5-level EQ-5D (EQ-5D-5L) is designed to improve the instrument's sensitivity and to reduce ceiling effects.

The EQ-5D-5L essentially consists of 2 pages: the EQ-5D descriptive system and the EuroQol visual analogue scale (EQ VAS).

The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. The patient is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number that expresses the level selected for that dimension. The digits for the five dimensions can be combined into a 5-digit number that describes the patient's health state.

The EQ VAS records the patient's self-rated health on a vertical visual analogue scale, where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. The VAS can be used as a quantitative measure of health outcome that reflect the patient's own judgement.

8.1.4.4 MG-QOL15r

The MG-QOL15r is a brief survey, completed by the study participant, that is designed to assess some aspects of "quality of life" related to MG. The MG-QOL15r was designed to assess the "patient perspective" in the everyday clinic setting or in a clinical study.

When completing the 15-item MG-QOL15r, MG study participant should consider only how their MG affects these items. For example, if a study participant has no leg weakness but has a painful hip (unrelated to the MG) that causes walking trouble, the study participant should report "not at all" to the item of, "I have trouble walking." This is because any hip-related walking trouble is unrelated to the MG. One other note of clarification: if the study participant is retired (unrelated to MG), he or she should report "not at all" to the item about whether the MG negatively impacts job/occupational status.

8.2 Safety assessments

Planned time points for all safety assessments are provided in the Schedule of Activities (Section 1.3).

8.2.1 Physical examination

A complete physical examination will include, at a minimum, general appearance; ear, nose, and throat; eyes, hair, and skin; and assessments of the of the cardiovascular, respiratory, GI, neurological, and musculoskeletal systems. Height and weight will also be measured and recorded. Body weight will be measured with the study participant wearing light clothing and without wearing shoes.

A brief physical examination will include, at a minimum, assessments of the skin, respiratory system, cardiovascular system, and abdomen (liver and spleen).

A full neurological examination should be performed for any study participant who experiences severe and/or serious headache and for any study participant who experiences suspected aseptic meningitis (Appendix 14 [Section 10.14]). A full neurological assessment will include: (1) General appearance, including posture, motor activity and meningeal signs and, if indicated, the following assessments will be performed; (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.

Investigators should pay special attention to clinical signs related to previous serious illnesses.

Clinically relevant findings or worsening of previous findings will be recorded as AEs.

8.2.2 Vital signs

Oral, tympanic, temporal or axillary temperature, pulse rate, and blood pressure will be assessed.

Blood pressure and pulse measurements should be preceded by at least 5 minutes of rest for the participant in a quiet setting without distractions (eg, television, cell phones). All measurements will be assessed in a sitting position with a completely automated device. Manual techniques will be used only if an automated device is not available.

All vital signs should be taken before any blood sampling and IMP administration, unless otherwise indicated.

In case of untoward event, additional vitals (unscheduled assessment) should be taken at the discretion of the investigator and post observation time can be extended. These recommendations are applicable for dosing at site and at home.

For the initial 2 infusions after switching to manual push, vital signs will be measured prior to IMP administration, at the end of the infusion (±15 minutes), and 1 hour after the end of the infusion (±15 minutes). For the subsequent infusions, vital signs are not collected after IMP administration.

8.2.3 Electrocardiograms

Twelve-lead ECG will be obtained as outlined in the Schedule of Activities (see Section 1.3) using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and QTc intervals. Refer to Section 7.1.2 for QTc withdrawal criteria and any additional [QTc] readings that may be necessary.

All ECG recordings should be taken with the study participant resting in the supine position for at least 5 minutes before the recording.

In cases of abnormal ECG reading, triplicate ECG will be required, three individual ECG tracings should be obtained as closely as possible in succession.

8.2.4 Clinical safety laboratory assessments

See Appendix 2 (Section 10.2) for the list of clinical laboratory tests to be performed and to the Schedule of Activities (Section 1.3) for the timing and frequency.

The Investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF. The

laboratory reports must be filed with the source documents. Clinically significant abnormal laboratory findings are those which are not associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the participant's condition.

All laboratory tests with values considered clinically significantly abnormal during the 6-week treatment period or within 8 weeks after the last dose of study medication should be repeated until the values return to normal or baseline or are no longer considered clinically significant by the Investigator or Medical Monitor.

If such values do not return to normal/baseline within a period of time judged reasonable by the Investigator, the etiology should be identified, and the Sponsor notified.

All protocol-required laboratory assessments, as defined in Appendix 2 (Section 10.2), must be conducted in accordance with the laboratory manual and the Schedule of Activities (Section 1.3).

If laboratory values from non-protocol specified laboratory assessments performed at the institution's local laboratory require a change in participant management or are considered clinically significant by the Investigator (eg, SAE or AE or dose modification), then the results must be recorded in the eCRF.

8.2.5 Suicidal risk monitoring

Study participants being treated with rozanolixizumab should be monitored appropriately for suicidal ideation and behavior or any other unusual changes in behavior. Consideration should be given to discontinuing rozanolixizumab in study participants who experience signs of suicidal ideation or behavior.

Families and caregivers of study participants being treated with rozanolixizumab should be instructed to monitor participants for the emergence of unusual changes in behavior, as well as the emergence of suicidal ideation and behavior, and to report such symptoms immediately to the study Investigator.

Suicidality will be assessed by trained study personnel using the Columbia Suicide Severity Rating Scale (C-SSRS) (Columbia Univerity Medical Center, 2008). The C-SSRS will be performed at the scheduled timepoints as described in the Schedule of Activities (Section 1.3).

8.2.6 Assessment and management of TB and TB risk factors

Precautions are being taken within this protocol to monitor the risk of TB infection in this study (see Section 5.2). Any presumptive diagnosis or diagnosis of a TB infection is a reportable event. Assessment and management of TB and TB risk factors should follow local/national guidelines.

Physical Examination

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 medical or social history. Sites commonly infected by TB include: the lungs, larynx, lymph glands, pleura, GI system, genito urinary tract (including renal), bones and joints, meninges, peritoneum, pericardium, and skin. This is not an exhaustive list and unusual presentations and areas of involvement should always be considered.

Some common symptoms that the study participant may present are dependent on the primary focus of infection and may include cough, blood in sputum, night sweats, lymphadenitis, joint

pain/swelling, spinal deformity, headache/confusion, abdominal pain (mimicking inflammatory bowel disease), etc. Unusual presentations should always be considered.

Note: If available, respiratory or other specimens must also be smear and culture negative for TB (Center for Disease Control and Prevention diagnosis of LTB infection [http://www.cdc.gov/TB/topic/testing/default.htm]).

TB signs and symptoms questionnaire

In addition to a physical examination done intermittently throughout the study, study participants will be evaluated both for signs and symptoms of latent or active TB infection and for risk factors for exposure to TB using the TB questionnaire as indicated in the schedule of study assessments (cross reference to table of schedule of study assessment).

The TB questionnaire should be completed accurately and filed as a critical source document. The questionnaire will assist with the identification of study participants who may require therapy for TB.

A "Yes" response to any of the questions in the TB questionnaire during the study may trigger further assessment to determine if the study participant has either LTBI and must receive prophylactic LTBI therapy or active TB infection and must be withdrawn from the study. As an example, a study participant who answers "Yes" at Screening to the question "Has the subject been in close (eg, sleeping in the same room) contact with an individual with active TB, or an individual who has recently been treated for TB?" should not be allowed into the study pending further assessments (including TB specialist consult) as outlined previously.

TB assessment by IGRA

The TB test interferon gamma release assay (IGRA) is performed at Screening in MG0003, and the final visit in MG0004 (Visit 52 [PEOT] or Visit 53 [EOS]) will serve as Baseline in MG0007. The TB screening is mandatory both before study entry and at study completion (EOS). The preferred screening test is interferon-gamma release assay (IGRA) performed at a Central Laboratory by QuantiFERON tube test (for Japan-specific regulations, see Appendix 8 [Section 10.8]). Additional IGRA test will be performed if indicated (eg, presence of signs and symptoms suggestive of TB, recent exposure).

In high TB incidence countries, it is recommended that the IGRA be the first test performed at screening to reduce the number of unnecessary screening procedures on any IGRA positive study participants that may need to be treated for TB prophylaxis or potentially withdrawn from the study.

The test results will be reported as positive, negative, or indeterminate.

If an IGRA is positive or indeterminate the study participant must be evaluated by a TB specialist.

- Positive IGRA

The positive IGRA may represent new LTBI or active TB infection. The positive IGRA result may also reflect positivity from a recently diagnosed and adequately treated (in progress or completed within the past 12 months) LTBI or from adequately treated past TB infection. In such cases, the study participants must be evaluated by a TB specialist.

- Indeterminate IGRA

If the IGRA test result is indeterminate, the IGRA previously performed may be repeated once. If the test is positive or indeterminate on retest, the study participant must be evaluated by a TB specialist.

TB assessment by chest X-ray

A Screening chest X-ray is not required for MG0007. However, a chest X-ray or other imaging test should be performed only if indicated (eg, presence of signs and symptoms suggestive of TB, close exposure to persons with TB), and interpreted by a qualified specialist (ie, radiologist or pulmonologist).

Test Conversion

Tuberculosis test conversion is defined as a positive or indeterminate (and confirmed indeterminate on repeat) IGRA result for the current test when previous IGRA test results were negative. During the study, all study participants with positive or indeterminate IGRA test results must immediately stop study drug administration.

In case of a IGRA test conversion, the study participant must be considered as having either a suspected new latent or an active TB infection and be promptly referred to an appropriate specialist (eg, pulmonologist, infectious disease specialist) for further evaluation. If test conversion indicates LTBI, active TB, or NTMB then, TB test conversion (confirmed) should be classified adequately, either as due to LTBI, active TB infection, or NTMB, respectively. Additional assessments (eg, blood tests or IGRA, chest X-rays, or other imaging) should be performed where medically relevant and documented. Such conversions should be reported as AEs as described in the protocol. The AE term would need to be updated with final diagnosis once available.

Latent TB

Latent TB infection is defined as the absence of signs, symptoms (eg, evidence of organ specific involvement), or physical findings suggestive of TB infection with a positive IGRA test (or 2 indeterminate IGRA test results) and a chest X-ray (or other imaging) without evidence of TB infection.

LTBI must be reported as an AE and graded appropriately as described in the protocol. Follow-up reports should be completed as per protocol requirement until such time as the LTBI resolves.

Active TB or non-tuberculosis mycobacterium infection

Study participants who develop active TB or NTMB infection during the study (conversion demonstrated by IGRA) must be withdrawn from the study. The study participant must be immediately permanently discontinued from study medication and a PEOT Visit must be scheduled as soon as possible, but no later than the next scheduled visit. Treatment for active TB or NTMB should be started immediately based on local guidelines.

Confirmed active TB is always considered Serious Adverse Event. UCB's process requires that these must be captured on an SAE report form and provided to the Sponsor in accordance with SAE reporting requirements. Follow-up reports should be completed as per protocol requirement until such time as the TB infection resolves.

LTBI, active TB or other NTMB identified during study

During the study, study participants who develop evidence of LTBI, active TB or NTMB infection must immediately stop further administration of study medication and will be referred to an appropriate TB specialist (pulmonologist or infectious disease specialist) for further evaluation. Study participants diagnosed with active TB or LTBI should receive appropriate TB or prophylaxis therapy. The study participant should be transferred to the care of their Physician and managed according to the standard of care.

If infection with NTMB is identified during the study, the same procedure as for active TB acquired during the study and compliant TB treatment shall be followed.

Follow-up information of suspected and confirmed TB cases should be provided to UCB at least after 3, 9, and 12 months of the start date of anti TB treatment, including hematological and biochemical safety parameters, X-ray evolution data, and TB diagnostic procedures used to follow-up and confirm recovery of TB.

8.3 Adverse events and serious adverse events

The definitions of an AE or SAE can be found in Appendix 3 (Section 10.3). The definitions of device-related safety events, (adverse device effects [ADEs] and serious adverse device effects [SADEs]), can be found in Appendix 8 (Section 10.8). Device deficiencies are addressed in Appendix 8 (Section 10.8).

Adverse events will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative).

The Investigator and any designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible for following up AEs that are serious, considered related to the study treatment or study procedures, or that caused the participant to discontinue study treatment or MG0007 (see Section 7).

8.3.1 Time period and frequency for collecting AE and SAE information

All SAEs will be collected from the signing of the ICF until the EOS visit at the time points specified in the Schedule of Activities (Section 1.3).

All AEs will be collected from the signing of the ICF until the EOS visit at the time points specified in the Schedule of Activities (Section 1.3).

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 study medication 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.

All SAEs will be recorded and reported to the Sponsor or designee within 24 hours, as indicated in Appendix 3. The Investigator will submit any updated SAE data to the Sponsor within 24 hours of it being available.

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 study medication), up to 30 days from the end of the study for each participant, and to also inform

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 study medication must be reported to UCB regardless of the time between the event and the end of the study.

The method of recording, evaluating, and assessing causality of AE and SAE and the procedures for completing and transmitting SAE reports are provided in Appendix 3 (Section 10.3).

8.3.2 Method of detecting AEs and SAEs

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and non-leading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

8.3.3 Follow-up of AEs and SAEs

After the initial AE/SAE report, the Investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs, and non-serious AEs of special interest (AESI) or adverse events of special monitoring (AESM) (as defined in Section 8.3.6 and Section 8.3.7, respectively), will be followed until resolution, stabilization, the Investigator determines that it is no longer clinically significant, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3). Further information on follow-up procedures is given in Appendix 3 (Section 10.3).

8.3.4 Regulatory reporting requirements for SAEs

Prompt notification (24 hours) by the Investigator to the Sponsor of a SAE is essential so that legal obligations and ethical responsibilities towards the safety of participants and the safety of a study treatment under clinical investigation are met.

The Sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study treatment under clinical investigation. The Sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, Institutional Review Boards (IRB)/Independent Ethics Committees (IEC), and investigators.

Investigator safety reports must be prepared for suspected unexpected serious adverse reactions (SUSAR) according to local regulatory requirements and Sponsor policy and forwarded to investigators as necessary.

An Investigator who receives an investigator safety report describing a SAE or other specific safety information (eg, summary or listing of SAEs) from the Sponsor will review and then file it along with the IB and will notify the IRB/IEC, if appropriate according to local requirements.

8.3.5 Pregnancy

Details of all pregnancies in female participants and, if indicated, female partners of male participants will be collected after the start of study treatment and until 90 days after the last dose.

If a pregnancy is reported, the Investigator must immediately inform the Sponsor within 24 hours of learning of the pregnancy and should follow the procedures outlined in Appendix 4 (Section 10.4).

The participant should be withdrawn from the study as soon as pregnancy is known (by positive pregnancy test), and the following should be completed:

- The participant should return for an early discontinuation (PEOT) visit.

Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs.

8.3.6 Adverse events of special interest

An AESI 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. For rozanolixizumab, the following events require immediate reporting (within 24 hours regardless of seriousness) to UCB:

- Hy's Law
  - 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 (ie, without waiting for any additional etiologic investigations to have been concluded). Follow-up information should be reported if an alternative etiology is identified during investigation and monitoring of the participant.

All AESIs will follow the SAE recording and reporting procedures as indicated in Appendix 3 (Section 10.3).

8.3.7 Adverse events of special monitoring

An AE of special monitoring (AESM) is a product-specific AE, adverse reaction, or safety topic requiring special monitoring by UCB.

For rozanolixizumab, the following events require immediate reporting (within 24 hours regardless of seriousness) to UCB:

- Severe and/or serious headache
- Suspected aseptic meningitis

Procedures for the management of AESM are provided in Appendix 14 (Section 10.14).

Although infections and infusion-related reactions as well as hypersensitivity reactions or anaphylaxis are not classified as AESM, these AEs will be monitored by the Investigator. If such an event is suspected it should be managed according to the guidance provided in Appendix 13 (Section 10.13). In case of suspected anaphylaxis, the Sampson's Criteria (Sampson et al, 2006) in Appendix 15 (Section 10.15) should be completed.

All AESM will follow the SAE recording and reporting procedures as indicated in Appendix 3 (Section 10.3).

8.3.8 Treatment-emergent adverse events

Treatment-emergent AEs are defined as AEs starting after the time of first IMP administration up to and including 8 weeks after the final dose.

8.4 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 study medication so that investigators, clinical study participants, regulatory authorities, and IRBs/IECs will be informed appropriately and as early as possible.

In addition, an IDMC will periodically review and monitor safety data from this study and advise UCB. Details are provided in the IDMC Charter.

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

As appropriate for the stage of development and accumulated experience with the study medication, 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.

8.5 Treatment of overdose

For this study, any dose of increase of 10% greater than the assigned dose for each administered dose of IMP will be considered an overdose, irrespective of the weight tier band. Overdose events are only considered AEs or SAEs if there are associated clinical signs and symptoms or if the act of taking the excess IMP itself is an AE or SAE (eg, suicide attempt).

UCB does not recommend specific treatment for an overdose.

In the event of an overdose, the Investigator or treating Physician should:

1. Contact the Medical Monitor immediately.
2. Closely monitor the participant for any AE/SAE and laboratory abnormalities for at least 5 days.
3. Obtain a plasma sample for PK analysis within 3 days from the date of the last dose of study treatment if requested by the Medical Monitor (determined on a case-by-case basis).
4. Document the quantity of the excess dose as well as the duration of the overdose in the eCRF.

Decisions regarding dose interruptions or modifications will be made by the Investigator in consultation with the Medical Monitor based on the clinical evaluation of the participant.

8.6 Pharmacokinetics and antidrug antibodies

Whole blood samples will be collected for measurement of plasma concentrations of rozanolixizumab and ADA as specified in the Schedule of Activities (Section 1.3). Blood samples may be collected at additional time points during the study if warranted and agreed upon between the Investigator and the Sponsor. Instructions for the collection and handling of biological samples will be provided in the laboratory manual for this study. The actual date and time (24-hour clock time) of each sample will be recorded.

Samples will be used to evaluate the PK of rozanolixizumab and ADA and may be used for establishing assay parameters (eg, ADA cut point setting and PK selectivity assessment).

Samples collected for analyses of rozanolixizumab concentration and ADA may also be used to evaluate safety or efficacy aspects related to concerns arising during or after the study.

Participant confidentiality will be maintained. At visits during which only plasma samples for the determination of concentration of rozanolixizumab will be taken, 1 sample of sufficient volume can be used.

Any changes in the timing or addition of time points for any planned study assessments must be documented and approved by the relevant study team member and then archived in the UCB and site study files but will not constitute a protocol amendment. The IRB/IEC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the ICF.

8.7 Genetics

Genetics are not evaluated in this study.

8.8 Pharmacodynamics

Venous blood samples will be collected at time points specified in the Schedule of Activities (Section 1.3) for measurement of:

- Serum IgG and IgG sub-classes concentrations
- Serum MG-specific autoantibodies (anti-MuSK/anti-AChR) levels

For all PD assessments, blood samples will be collected predose. Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study.

8.9 Biomarkers

Collection of samples for exploratory safety biomarker research is part of this study. Baseline values from MG0003 will serve as the Baseline value for MG0007. Safety samples must be collected 4 hours after the onset of the event, or otherwise as soon as possible within 72 hours after the onset of the event in case of AESM of severe and/or serious headache or suspected aseptic meningitis.

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 cause, progression, and appropriate treatment of MG. They may also be used to develop tests/assays including diagnostic tests related to rozanolixizumab and/or FcRn inhibitor and MG.

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.

8.9.1 Immunological assessments

Blood samples for immunological testing are required and will be collected from all study participants in this study as specified in the Schedule of Activities (Section 1.3) for the

measurement of [redacted] and [redacted]. All samples should be collected predose.

For [redacted] and [redacted] Baseline values from MG0003 will serve as the Baseline value for MG0007. Additional samples should be collected 2 hours and 4 hours postevent for study participants who experience infusion reaction or hypersensitivity reaction at the site. In case the event happens at home, additional samples should be collected as soon as possible, but prior to the next dosing as specified in the Schedule of Activities (Section 1.3).

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

8.10 Medical resource utilization and health economics

Medical resource utilization and health economics will be measured for this study.

9 STATISTICAL CONSIDERATIONS

A description of statistical methods follows and will be described in more detail in the Statistical Analysis Plan (SAP).

9.1 Definition of analysis sets

The definition of analyses sets are as follows:

- The Enrolled Set: All study participants who have signed the ICF.
- Full Analysis Set (FAS): All enrolled study participants who were randomized in this study or in MG0004. Study participants enrolling from MG0004 will utilize their last assigned dose level from MG0004 as their planned dose in MG0007.
- Safety Set (SS): All study participants in the FAS who received at least one dose of IMP.

9.2 General statistical considerations

Statistical evaluation will be performed by the Sponsor or designee and supervised by the Exploratory Statistics Department of UCB. For safety analyses, data will be summarized by dose levels of rozanolixizumab at the time of the event or measurement. For efficacy, data will be summarized by the dose first received in the study. Additionally, efficacy data will be summarized by dose levels of rozanolixizumab received in each treatment cycle.

All analyses will be performed using Statistical Analysis System (SAS®) version 9.3 or later (SAS Institute, Cary, NC, USA). Continuous variables will be summarized by visit (where applicable) with the statistics including the number of study participants (n), mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized by visit (where applicable) with frequency counts and percentages.

If not otherwise stated, Baseline values will be the last available predose value, or in the case of analyses done by 6-week treatment cycle, Baseline will be defined as the Baseline (Day 1) value for that cycle. This will be clearly defined in the SAP. All relevant data will be listed by treatment group and study participant.

9.2.1 Intercurrent event handling rationale and impact on the study

In MG0007, every study participant, except those coming from MG0004, will start with an initial fixed mandatory cycle. Prior to dosing in the initial fixed treatment cycle, the study participant will be assessed for MG worsening (eg, an increase of 2.0 points on the MG-ADL or 3.0 points on the QMG scale). The study participant will be initially randomized to rozanolixizumab equivalent to approximately 7mg/kg or 10mg/kg weekly (QW). After the first treatment cycle, dose adjustments may be applied at the start of each treatment cycle based on Investigator's discretion. Dose adjustments may not be applied during a treatment cycle.

For the assessment of safety and tolerability, adverse events (AEs) recorded up to 8 weeks after the last sc infusion will be utilized for main analyses, regardless of study participants receiving treatment with rescue therapy.

For the analyses of efficacy endpoints, the intercurrent events to be considered are the use of rescue therapy prior to Day 43 and permanent treatment discontinuation (or withdrawal from study) due to TEAEs. Efficacy endpoints will be summarized in line with a treatment policy approach. With this approach, rozanolixizumab results will be analyzed regardless of study participants receiving treatment with rescue therapy. Summaries will also be presented for the efficacy endpoints where participants will be censored at the time that they take rescue medication.

Missing values will not be imputed.

9.3 Planned safety analyses

9.3.1 Analysis of the primary safety endpoint

The frequency and severity of all TEAEs will be presented for each treatment group separately and overall by System Organ Class, high level term, and preferred term (Medical Dictionary for Regulatory Activities [MedDRA®]). The data will be displayed as number of participants experiencing the TEAE, percentage of participants, and number of TEAEs. All safety analyses will be based on the SS (Section 9.1).

For each cycle, a TEAE is defined as any event that was not present prior to the first administration of rozanolixizumab or any unresolved event already present before the first administration of rozanolixizumab that worsens in intensity following exposure to treatment up to and including 8 weeks after the last dose of each treatment cycle. Adverse events occurring after the 8-week TEAE period, prior to the next cycle, will be defined as intermittent period AEs. Any AEs that occurred during the study will be defined as “any AE”.

The occurrence of TEAEs and TEAEs leading to withdrawal of IMP will be summarized for the entire study by dose at AE onset. This will include all TEAEs that occurred during and between treatment cycles.

These analyses will display the TEAEs (including any TEAEs occurring up to 1 week after the last infusion) and intermittent period AEs separately. For intermittent period AEs, the summaries will be displayed as “Off-treatment”.

Further analyses will be described in the SAP.

9.3.2 Other safety analyses

The occurrence of serious TEAEs and occurrence of treatment-emergent AESM will be summarized using the same approach as for the primary endpoints.

Laboratory evaluations and vital signs as well as ECG data will be analyzed over time. All safety analyses will be listed and summarized for the SS.

9.4 Planned efficacy and other analyses

9.4.1 Efficacy analyses

The main efficacy endpoint is the "Change from Baseline (Day 1) to Day 43 in MG-ADL score," for each of the first three 6-week treatment cycles where the Baseline of the respective cycle will be used as reference.

The summaries will be provided overall and by randomized treatment in-line with a treatment policy approach. Observed results will be presented for the different cycles (1 to n) regardless of the first cycle being mandatory or not. Missing values will not be imputed. Further summaries will be presented by the treatment received in each cycle.

The other secondary efficacy endpoints, Change from Baseline (Day 1) to Day 43 in QMG score, Change from Baseline (Day 1) to Day 43 in MG-C score, Change from Baseline (Day 1) to Day 43 in MG Symptoms PRO 'Muscle Weakness Fatigability' score, Change from Baseline (Day 1) to Day 43 in MG Symptoms PRO 'Physical Fatigue' score, and Change from Baseline (Day 1) to Day 43 in MG Symptoms PRO 'Bulbar symptoms' score, will be analyzed in the same way as the main secondary endpoint based on the MG-ADL.

Time to MG-ADL response (≥2.0-point improvement from Baseline [Day 1]) for each treatment cycle will be summarized using time-to-event methodology (Kaplan Meier).

The time between consecutive treatment cycles will be summarized in order to provide information on how long the effect of rozanolixizumab lasts, ie, how long it will take to introduce a new cycle.

The number and percentage of participants achieving Minimal Symptom Expression (MG-ADL score of 0 or 1) at any time during the Treatment and Observation Periods will be summarized by cycle and by dose administration in that cycle.

Additionally, the number of treatment cycles will be summarized by treatment group.

Further summaries will be described in the SAP.

9.4.2 Other analyses

9.4.2.1 Pharmacokinetic analyses

Plasma concentration data of rozanolixizumab will be summarized by dose arm for each cycle, and time point using the number of available observations, mean, median, SD, minimum, maximum, geometric mean (and associated 95% confidence intervals), and geometric coefficient of variation (assuming log-normally distributed data) for the SS. 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 and mean concentrations of rozanolixizumab may be displayed graphically.

Plasma concentration data of rozanolixizumab may be subjected to population pharmacokinetic analysis to derive population estimates of PK parameters and test the effect of various covariates such as anti-drug antibodies, age, weight, gender. Details of the analysis will be described in a separate Data Analysis Plan (DAP). This analysis may be performed by combining the data from the current study with data from other rozanolixizumab studies if deemed appropriate. The results of the population PK analysis will not be reported in the clinical study report (CSR) but in a separate modelling report.

9.4.2.2 Pharmacodynamic analyses

For all other endpoints relating to PD endpoints, descriptive statistics for the value, change from Baseline, and percentage change from Baseline will be tabulated by dose arm, and time point for the SS for each cycle. The PD endpoints will include serum total IgG, IgG subclass levels, and anti-MuSK and -AChR autoantibodies.

For the analysis of the IgG data, in case rescue therapies are taken, only the data up to the start date of rescue therapy will be utilized for the summary tables. Listings will contain all IgG data and the measurements of study participants, which have been excluded from the summary tables. In cases where a study participant drops out, no missing value imputation will be performed for the IgG. Absolute and relative IgG reduction for a cycle will be calculated with the cycle Baseline value as reference. As for safety, the IgG reduction analyses will be compared between cycles.

Population PD or population PK/PD analyses may be conducted for the PD variables of interest. Details of such PD or PK/PD analyses will be described in a separate DAP. The results of the analyses will not be reported in the CSR but in a separate report.

9.4.2.3 Immunological analyses

For all endpoints relating to immunological assessments, descriptive statistics for the value, change from Baseline, and percentage change from Baseline will be tabulated by dose arm, and time point for the SS. The immunological assessments will include [redacted] Baseline values from MG0003 will serve as the Baseline value for MG0007.

For complement where data has been collected post adverse event, individual patient data may be correlated with infusion reaction or hypersensitivity reaction.

9.4.2.4 Anti-drug antibodies analyses

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 minimum required dilution). For ADA-positive immunodepletion samples (or subset of), further characterization for neutralizing ADA potential in vitro will be performed.

The ADA sample status will be summarized by time point for each cycle. Changes from Baseline in sample status in terms of participant ADA classification will be summarized to inform on the incidence and emergency of ADA positivity. Graphical summaries may also be presented. Associations between ADA and PK, PD, efficacy and safety endpoints may be explored if warranted. Full details will be provided in the SAP.

9.5 Handling of protocol deviations

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. 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 are made on an ongoing basis.

9.6 Handling of dropouts or missing data

All imputation of missing or partial dates for safety assessments, as well as handling missing efficacy data (where applicable), will be detailed in the SAP.

9.7 Planned interim analysis and data monitoring

No formal interim analysis is planned for this study.

An Independent Data Monitoring Committee (IDMC) will be established. The IDMC will oversee the safety of the study by reviewing safety and efficacy data at periodic data reviews to assess the benefit-risk of rozanolixizumab. The objectives and procedures for the IDMC will be detailed in the IDMC Charter.

In addition, based on data cutoffs, safety and efficacy data for submission purposes will be summarized.

9.8 Determination of sample size

No formal sample size calculation can be performed. All eligible study participants from MG0003, and MG0004 will be invited to participate in MG0007. It will be assumed that approximately 200 study participants will be enrolled into MG0007.

The number of 200 study participants is assuming a drop-out rate from the lead-in study of approximately 15% (including participants who opt not to continue in MG0007).

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 Appendix 1: Regulatory, ethical, and study oversight considerations

10.1.1 Regulatory and ethical considerations

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 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 participants or others, and any protocol deviations, to eliminate immediate hazards to 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 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 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. 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.

10.1.2 Financial disclosure

Insurance coverage will be handled according to local requirements.

Finance and insurance are addressed in the Investigator and/or CRO agreements, as applicable.

10.1.3 Informed consent process

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 participant in both oral and written form by the Investigator (or designee). Each participant will have the opportunity to discuss the study and its alternatives with the Investigator.

Prior to participation in the study, the Informed Consent form should be signed and personally dated by the participant, or his/her legal representative, and by the person who conducted the informed consent discussion (Investigator or designee). The participant or his/her legal representative must receive a copy of the signed and dated Informed Consent form. As part of the consent process, each participant must consent to direct access to his/her medical records for study-related monitoring, auditing, IRB/IEC review, and regulatory inspection. For local regulations, see Appendix 8 (Section 10.8).

If the Informed Consent form 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 Informed Consent form 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.

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

10.1.4 Data protection

UCB staff (or designee) will affirm and uphold the participant's confidentiality. Throughout this study, all data forwarded to UCB (or designee) will be identified only by the 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 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 participant's study participation, and autopsy reports for deaths occurring during the study).

The participant must be informed that his/her personal study-related data will be used by the Sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant.

The participant must be informed that his/her medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the Sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities.

10.1.5 Committees structure

An IDMC will review the safety and tolerability data in this study in order to make recommendations for the Sponsor.

An IDMC will be set up in line with the FDA regulatory requirements and EMA Guideline on IDMCs (EMEA/CHMP/EWP/5872/03 Corr, adopted 27/05/2005). The IDMC will consist of external experts who are independent from UCB and the clinical operations contract research organization, and have no conflict of interest related to the conduct or the outcomes of the study.

10.1.6 Data quality assurance

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the Sponsor or designee electronically (eg, laboratory data). The Investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

The Investigator must maintain accurate documentation (source data) that supports the information entered in the CRF.

The Investigator must permit study-related monitoring, audits, IRB/IEC review, and regulatory agency inspections and provide direct access to source data documents.

The Sponsor or designee is responsible for the data management of this study including quality checking of the data.

Study monitors will perform ongoing source data verification, encompassing remote source data verification and source data review in accordance with applicable regulatory guidance. Source data verification is performed to confirm that data entered into the CRF by authorized site personnel are accurate, legible, contemporaneous, original, and attributable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements, including national and local regulations.

All essential documents must be retained by the Investigator for the minimum retention period mandatory under the applicable local laws and regulations. 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.

Quality tolerance limits will be established for the study using parameters related to patient safety reporting and reliability of study results. The parameters will be monitored throughout the study to identify systematic issues. Parameters used, parameter values, important deviations from the quality tolerance limits, and actions taken will be summarized in the clinical study report.

10.1.6.1 Case Report form completion

The Investigator is responsible for prompt reporting of accurate, complete, and legible data in the CRFs and in all required reports.

Any change or correction to the CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry. Use of correction fluid is not permitted.

Corrections made after the Investigator's review and signature of the completed CRF will be resigned and dated by the Investigator.

The Investigator should maintain a list of personnel authorized to enter data into the CRF.

Detailed instructions will be provided in the CRF Completion Guidelines.

The Investigator is responsible for prompt reporting of accurate, complete, and legible data in the electronic CRFs and in all required reports.

Any change or correction to the CRF 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 electronic CRF.

Detailed instructions will be provided in the CRF Completion Guidelines.

10.1.7 Source documents

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 eCRFs 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, quality of life questionnaires, or video, 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 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).

10.1.8 Study and Site Closure

The Sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the Sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The Investigator may initiate study-site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the Sponsor or Investigator may include but are not limited to:

- Failure of the Investigator to comply with the protocol, the requirements of the IRB/IEC or local health authorities, the Sponsor's procedures, or GCP guidelines
- Inadequate recruitment of participants by the Investigator
- Discontinuation of further study medication development

10.1.9 Publication Policy

The results of this study may be published or presented at scientific meetings. If this is foreseen, the Investigator agrees to submit all manuscripts or abstracts to the Sponsor before submission. This allows the Sponsor to protect proprietary information and to provide comments.

The Sponsor will comply with the requirements for publication of study results. In accordance with standard editorial and ethical practice, the Sponsor will generally support publication of multicenter studies only in their entirety and not as individual site data. In this case, a coordinating Investigator will be designated by mutual agreement.

Authorship will be determined by mutual agreement and in line with International Committee of Medical Journal Editors authorship requirements.

10.2 Appendix 2: Clinical Laboratory Tests

- The tests detailed in the table below will be performed by the central laboratory.
- Local laboratory results are only required in the event that the central laboratory results are not available in time for either study treatment administration and/or response evaluation. If a local sample is required, it is important that the sample for central analysis is obtained at the same time. Additionally, if the local laboratory results are used to make either a study treatment decision or response evaluation, the results must be entered into the eCRF.
- Protocol-specific requirements for inclusion or exclusion of participants are detailed in Section 5.1 and Section 5.2 of the protocol.
- Additional tests may be performed at any time during the study as determined necessary by the Investigator or required by local regulations.

Table 10-1: Protocol-Required Safety Laboratory Assessments

<table>
<tr><th>Laboratory Assessments</th><th colspan="4">Parameters</th></tr>
<tr><td>Hematology</td><td>Platelet Count
RBC Count
Hemoglobin
Hematocrit</td><td colspan="2">RBC Indices:
MCV
MCH
%Reticulocytes</td><td>WBC Count with Differential:
Neutrophils
Lymphocytes
Monocytes
Eosinophils
Basophils</td></tr>
<tr><td rowspan="4">Clinical Chemistry[a]</td><td>Blood Urea Nitrogen (BUN)</td><td>Potassium</td><td>Aspartate Aminotransferase (AST)/ Serum Glutamic-Oxaloacetic Transaminase (SGOT)</td><td>Total and direct bilirubin</td></tr>
<tr><td>Creatinine</td><td>Sodium</td><td>Alanine Aminotransferase (ALT)/ Serum Glutamic-Pyruvic Transaminase (SGPT)</td><td>Total Protein
Albumin</td></tr>
<tr><td>Glucose (fasting state, preferred)</td><td>Calcium</td><td>Alkaline phosphatase</td><td>C-reactive protein (CRP)</td></tr>
<tr><td>Lactate dehydrogenase (LDH)</td><td>Triglycerides</td><td>Low-density lipoprotein (LDL)
High-density lipoprotein (HDL)</td><td>Total Cholesterol</td></tr>
<tr><td>Routine Urinalysis</td><td colspan="4">• Specific gravity
• pH, glucose, protein, blood, ketones, albumin, bilirubin, urobilinogen, nitrite, leukocyte esterase by dipstick, albumin/creatinine ratio, creatinine
• Microscopic examination (if blood or protein is abnormal)</td></tr>
</table>

Laboratory Assessments	Parameters
Other Screening Tests	• Follicle-stimulating hormone and estradiol (as needed in women of non-childbearing potential only) • Urine drug screen (to include at minimum: amphetamines, barbiturates, cocaine, opiates, cannabinoids and benzodiazepines) • Serum or urine human chorionic gonadotropin pregnancy test (as needed for women of childbearing potential)[b] • PTT and INR • Serology testing (for Hepatitis B, Hepatitis C, and HIV) • All study-required laboratory assessments will be performed by a central laboratory. The results of each test must be entered into the eCRF.
NOTES: For additional assessments that may be required in case of AESM, see Table 1-6. [a] Details of liver chemistry stopping criteria and required actions and follow-up assessments after liver stopping or monitoring event are given in Section 7.1.1 and Appendix 6 (Section 10.6). All events of ALT ≥3 × upper limit of normal (ULN) and bilirubin ≥2 × ULN (≥35% direct bilirubin) or ALT ≥3 × ULN and international normalized ratio (INR) >1.5, if INR measured, may indicate severe liver injury (possible Hy's Law) and must be reported as an SAE (excluding studies of hepatic impairment or cirrhosis). [b] Local urine testing will be standard for the protocol unless serum testing is required by local regulation or IRB/IEC.	

Investigators must document their review of each laboratory safety report.

10.3 Appendix 3: Adverse Events – Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

Definition of AE

AE Definition
• An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study medication, whether or not considered related to the study medication. • NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study medication.

Events Meeting the AE Definition
• Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, ECG, radiological scans, vital signs measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the Investigator (ie, not related to progression of underlying disease). • Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition. • New conditions detected or diagnosed after study medication administration even though it may have been present before the start of the study. • Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction. • Signs, symptoms, or the clinical sequelae of a suspected overdose of either study medication or a concomitant medication. Overdose per se will not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae. • "Lack of efficacy" or "failure of expected pharmacological action" per se will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfil the definition of an AE or SAE. • The signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfil the definition of an AE or SAE. Also, "lack of efficacy" or "failure of expected pharmacological action" also constitutes an AE or SAE.

Events NOT Meeting the AE Definition
• Any clinically significant abnormal laboratory findings or other abnormal safety assessments which are associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the participant's condition. • The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the study participant's condition.

- Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE.
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.

Definition of SAE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met (eg, hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

A SAE is defined as any untoward medical occurrence that, at any dose:
a. Results in death
b. Is life-threatening The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization In general, hospitalization signifies that the participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the Physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.
d. Results in persistent disability/incapacity • The term disability means a substantial disruption of a person's ability to conduct normal life functions. • This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.
e. Is a congenital anomaly/birth defect
f. Important medical events: • Medical or scientific judgment should be exercised in deciding whether SAE reporting is appropriate in other situations such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious. • Examples of such events include, but are not limited to, potential Hy's law, invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic

bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

Recording and Follow-Up of AE and/or SAE

AE and SAE Recording

- When an AE/SAE occurs, it is the responsibility of the Investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostics reports) related to the event.
- The Investigator will then record all relevant AE/SAE information in the CRF.
- It is **not** acceptable for the Investigator to send photocopies of the participant's medical records to UCB in lieu of completion of the UCB AE/SAE eCRF page.
- There may be instances when copies of medical records for certain cases are requested by UCB. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to UCB.
- The Investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE.

Assessment of Intensity

The Investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- 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 a 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).

The National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) should be used as a supportive standardization instrument to evaluate AEs and SAEs but the final intensity grading by the Investigator must be mild, moderate, or severe.

Assessment of Causality

- The Investigator is obligated to assess the relationship between study medication and each occurrence of each AE/SAE.
- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- The Investigator will use clinical judgment to determine the relationship.

- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study medication administration will be considered and investigated.
- The Investigator will also consult the Investigator's Brochure (IB) and/or Product Information, for marketed products, in his/her assessment.
- For each AE/SAE, the Investigator **must** document in the medical notes that he/she has reviewed the AE/SAE and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the Investigator has minimal information to include in the initial report to UCB. However, **it is very important that the Investigator always make an assessment of causality for every event before the initial transmission of the SAE data to UCB.**
- The Investigator may change his/her opinion of causality in light of follow-up information and send a SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.

Follow-up of AEs and SAEs

- The Investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by UCB to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.
- An AE should be followed until it has resolved, has a stable sequelae, the Investigator determines that it is no longer clinically significant, the event is otherwise explained, or the participant is lost to follow up. This follow-up requirement applies to AEs, SAEs, and AEs of special interest.
- If a participant dies during participation in the study or during a recognized follow-up period, the Investigator will provide UCB with a copy of any post-mortem findings including histopathology.
- New or updated information will be recorded in the originally completed CRF.
- The Investigator will submit any updated SAE data to the Sponsor within 24 hours of receipt of the information.

Reporting of SAEs

SAE Reporting to UCB via an Electronic Data Collection Tool

- The primary mechanism for reporting an SAE to UCB will be the electronic data collection tool.
- If the electronic system is unavailable for more than 24 hours, then the site will use the paper SAE data collection tool (see next section).
- The site will enter the SAE data into the electronic system as soon as it becomes available.
- 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 (see next section).
- Contacts for SAE reporting can be found in SERIOUS ADVERSE EVENT REPORTING.

SAE Reporting to UCB via Paper CRF

- Facsimile transmission of the SAE paper CRF is the preferred method to transmit this information to UCB.
- In rare circumstances and in the absence of facsimile equipment, notification by telephone is acceptable with a copy of the SAE data collection tool sent by overnight mail or courier service.
- Initial notification via telephone does not replace the need for the Investigator to complete and sign the SAE CRF pages within the designated reporting time frames.
- Contacts for SAE reporting can be found in SERIOUS ADVERSE EVENT REPORTING.

10.4 Appendix 4: Contraceptive Guidance and Collection of Pregnancy Information

Definitions

Woman of Childbearing Potential (WOCBP)

A woman is considered fertile following menarche and until becoming post-menopausal unless permanently sterile (see below).

Women in the following categories **are not considered WOCBP**:

1. Premenarchal
2. Premenopausal female with 1 of the following:
   - Documented hysterectomy
   - Documented bilateral salpingectomy
   - Documented bilateral oophorectomy

   Note: Documentation can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview.
3. Postmenopausal female
   - A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.
   - Females on HRT and whose menopausal status is in doubt will be required to use one of the non-estrogen hormonal highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

Contraception Guidance

Female participants

Female participants of childbearing potential are eligible to participate if they agree to use a highly effective method of contraception consistently and correctly as described in the table below.

Highly Effective Contraceptive Methods[a]

Highly Effective Contraceptive Methods That Are User Dependent[b] Failure rate of <1% per year when used consistently and correctly.
Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation[c] • Oral • Intravaginal • Transdermal

Progestogen only hormonal contraception associated with inhibition of ovulation • Oral • Injectable
Highly Effective Methods That Are User Independent[c]
Implantable progestogen only hormonal contraception associated with inhibition of ovulation • Intrauterine device (IUD) • Intrauterine hormone-releasing system (IUS) • Bilateral tubal occlusion
Vasectomized partner A vasectomy is a highly effective contraception method provided that the vasectomized partner is the sole male sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used (eg, proper use of condom in combination with spermicide)
Sexual abstinence Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study medication. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.
NOTES: a) In case of newly started contraception pills/IUDs, the investigator should consider the correct timing of starting/applying such methods in relation to the menstrual cycle and the manufacturing instruction as when these newly started methods would become effective. b) Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants participating in clinical studies. c) Hormonal contraception may be susceptible to interaction with the study medication, which may reduce the efficacy of the contraceptive method. In this case, two highly effective methods of contraception should be utilized during the treatment period and for at least 90 days after the last dose of study medication

Pregnancy testing

- WOCBP should only be included after a confirmed menstrual period and a negative highly sensitive urine pregnancy test.
- Additional pregnancy testing should be performed during the Treatment Period (Section 1.3), at the EOS visit, corresponding to protocol-defined time frame in Section 10.4 after the last dose of study medication and as required locally.
- Pregnancy testing will be performed whenever a menstrual cycle is missed or when pregnancy is otherwise suspected
- Pregnancy testing, with a sensitivity of ≥25mIU/mL will be performed. Urine pregnancy tests will be performed at all other visits.

Male participants with partners who become pregnant

- The Investigator will attempt to collect pregnancy information on any male participant's female partner who becomes pregnant while the male participant is in this study. This applies only to male participants who receive study medication. If the study participant is later found to be on placebo, then pregnancy data collection can stop.
- After obtaining the necessary signed informed consent from the pregnant female partner directly, the Investigator will record pregnancy information on the appropriate form and submit it to the Sponsor within 24 hours of learning of the partner's pregnancy. The female partner will also be followed to determine the outcome of the pregnancy. Information on the status of the mother and child will be forwarded to the Sponsor. Generally, the follow-up will be at least 12 months after the delivery date. Any termination of the pregnancy will be reported regardless of fetal status (presence or absence of anomalies) or indication for the procedure.

Female Participants who become pregnant

- Any female participant who becomes pregnant while participating in the study will be withdrawn from the study.
- The Investigator will collect pregnancy information on any female participant who becomes pregnant while participating in this study. Information will be recorded on the appropriate form and submitted to the Sponsor within 24 hours of learning of a participant's pregnancy. The participant will be followed to determine the outcome of the pregnancy. The Investigator will collect follow-up information on the participant and the neonate and the information will be forwarded to the Sponsor. Generally, the follow-up will be at least 12 months after the delivery date. Any termination of pregnancy will be reported, regardless of fetal status (presence or absence of anomalies) or indication for the procedure.
- While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy will be reported as an AE or SAE. A spontaneous abortion is always considered to be an SAE and will be reported as such. Any post-study pregnancy related SAE considered reasonably related to the study medication by the Investigator will be reported to the Sponsor as described in Section 8.3.5. While the Investigator is not obligated to actively seek this information in former study participants, he or she may learn of an SAE through spontaneous reporting.

10.5 Appendix 5: Genetics

Not applicable.

10.6 Appendix 6: Liver Safety – Suggested Actions and Follow-up Assessments

Participants with potential drug-induced liver injury must be assessed to determine if study medication must be discontinued. In addition, all concomitant medications and herbal supplements that are not medically necessary should also be discontinued.

Investigators should attempt to obtain information on study participants in the case of study medication disconintuation to complete the final evaluation.

Study participants with potential drug-induced liver injury 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 study medication discontinuation and/or participant withdrawal (if applicable), must be recorded in the source documents. The CRF must document the primary reason for discontinuation of study medication.

A specific monitoring plan must be agreed between the UCB Study Physician and the Investigator for study participants who have ALT >5 ULN. The monitoring plan should include any necessary follow-up assessments (until resolution of the abnormal lab values).

Phase 3-4 liver chemistry stopping criteria are designed to assure participant safety and to evaluate liver event etiology.

Phase 3-4 liver Chemistry Stopping Criteria and Follow-Up assessments

Liver Chemistry Stopping Criteria	
ALT-absolute	ALT ≥8xULN
ALT Increase	ALT ≥5xULN but <8xULN persists for ≥2 weeks ALT ≥3xULN but <5xULN persists for ≥4 weeks
Bilirubin[a,b]	ALT ≥3xULN **and** bilirubin ≥2xULN (>35% direct bilirubin)
INR[b]	ALT ≥3xULN **and** INR >1.5, if INR measured
Cannot Monitor	ALT ≥5xULN but <8xULN and cannot be monitored weekly for ≥2 weeks ALT ≥3xULN but <5xULN and cannot be monitored weekly for ≥4 weeks
Symptomatic[c]	ALT ≥3xULN associated with symptoms (new or worsening) believed to be related to liver injury or hypersensitivity

Suggested Actions and Follow up Assessments	
Actions	**Follow Up Assessments**
• **Immediately** discontinue study medication. • Report the event to the UCB within **24 hours.** • Complete the liver event CRF, and complete an SAE data collection tool if the event also met the criteria for an SAE.[b] • Perform liver chemistry follow-up assessments.	• Viral hepatitis serology[d] • Obtain INR and recheck with each liver chemistry assessment until the transaminases values show downward trend • Only in those with underlying chronic hepatitis B at study entry (identified by positive hepatitis B surface antigen),

Liver Chemistry Stopping Criteria	
• Monitor the participant until liver chemistry test abnormalities resolve, stabilize, or return to baseline (see **MONITORING**). • **Do not restart/rechallenge** participant with study medication unless allowed per protocol and UCB approval is granted. • If restart/rechallenge **not allowed per protocol or not granted**, permanently discontinue study medication and continue participant in the study for any protocol specified follow up assessments.Consider the need for a toxicology screening. **MONITORING:** **<u>For bilirubin or INR criteria</u>** • Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, bilirubin) and perform liver event follow-up assessments within **24 hours.** • Monitor participant twice weekly until liver chemistry test abnormalities resolve, stabilize, or return to baseline. • A specialist or hepatology consultation is recommended. **<u>For all other criteria</u>** • Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, bilirubin) and perform liver chemistry follow-up assessments within **24 to 72 hours.** • Monitor participants weekly until liver chemistry abnormalities resolve, stabilize, or return to baseline.	quantitative hepatitis B DNA and hepatitis delta antibody[e] • Obtain blood sample for pharmacokinetic (PK) analysis after the most recent dose[f] • Serum CPK and LDH • Fractionate bilirubin, if total bilirubin ≥ 2xULN • Obtain complete blood count with differential to assess eosinophilia • Record the appearance or worsening of clinical symptoms of liver injury (eg, fatigue, nausea, vomiting, right upper quadrant pain), or hypersensitivity, on the AE report form • Record use of concomitant medications (including acetaminophen, herbal remedies, and other over-the-counter medications) on the concomitant medications CRF. • Record alcohol use on the liver event alcohol intake CRF • Exclude pregnancy **<u>For bilirubin or INR criteria:</u>** • Antinuclear antibody, antismooth muscle antibody, Type 1 anti-liver kidney microsomal antibodies, and quantitative total IgG or gamma globulins. • A serum acetaminophen adduct assay for assessing the potential acetaminophen contribution to liver injury in participants with definite or likely acetaminophen use in the preceding week. • Liver imaging (ultrasound, magnetic resonance, or computerizsed tomography) andor liver biopsy to evaluate liver disease; complete Liver Imaging and/or Liver Biopsy CRFs.

AE=adverse event; ALT=alanine aminotransferase; AST=aspartate aminotransferase; CPK=creatine phosphokinase; CRF=case report form; DNA= deoxyribonucleic acid; HBcAb=hepatitis B core antibody; HBsAg= hepatitis B core antigen; Ig=immunoglobulin; INR=international normalized ratio; LDH=lactate dehydrogenase; PK=pharmacokinetic; SAE=serious adverse event; ULN=upper limit of normal

[a] Serum bilirubin fractionation should be performed if testing is available. If serum bilirubin fractionation is not immediately available, discontinue study medication if ALT ≥3xULN **and** bilirubin ≥2xULN. Additionally, if serum bilirubin fractionation testing is unavailable, **record the absence/presence of detectable urinary bilirubin on dipstick** which is indicative of direct bilirubin elevations suggesting liver injury.

[b] All events of ALT ≥3xULN and bilirubin ≥2xULN (>35% direct bilirubin) or ALT ≥3xULN and INR >1.5 may indicate severe liver injury **(possible 'Hy's Law') and must be reported as an SAE (excluding studies of**

hepatic impairment or cirrhosis). The INR measurement is not required and the stated threshold value will not apply to participants receiving anticoagulants.

[c] New or worsening symptoms believed to be related to liver injury (such as fatigue, nausea, vomiting, right upper quadrant pain or tenderness, or jaundice) or hypersensitivity (such as fever, rash, or eosinophilia).

[d] Includes: Hepatitis A [redacted] antibody; HBsAg and HBcAb; hepatitis C RNA; cytomegalovirus [redacted] antibody; Epstein-Barr viral capsid antigen [redacted] antibody (or if unavailable, heterophile antibody, or monospot testing); and hepatitis E [redacted] antibody.

[e] If hepatitis delta antibody assay cannot be performed,, it can be replaced with a PCR of hepatitis D RNA virus (where needed) (Le Gal, 2005).

[f] Pharmacokinetic sample may not be required for participants known to be receiving placebo or non-comparator interventions. Record the date/time of the PK blood sample draw and the date/time of the last dose of study medication prior to the PK blood sample draw on the CRF. If the date or time of the last dose is unclear, provide the participant's best approximation. If the date/time of the last dose cannot be approximated OR a PK sample cannot be collected in the time period indicated above, do not obtain a PK sample. Instructions for sample handling and shipping are in the Study Reference Manual.

Phase 3-4 Liver Chemistry Increased Monitoring Criteria with Continued Study medication

Liver Chemistry Increased Monitoring Criteria	
Criteria	**Actions**
ALT ≥5xULN and <8xULN **and** bilirubin <2xULN **without** symptoms believed to be related to liver injury or hypersensitivity, **and** who can be monitored weekly for 2 weeks. OR ALT ≥3xULN and <5xULN **and** bilirubin <2xULN **without** symptoms believed to be related to liver injury or hypersensitivity, **and** who can be monitored weekly for 4 weeks.	• Notify the Sponsor Medical Monitor medical monitor **within 24 hours** of learning of the abnormality to discuss participant safety. • Participant can continue study medication • Participant must return weekly for repeat liver chemistry tests (ALT, AST, alkaline phosphatase, bilirubin) until the abnormalities resolve, stabilize, or return to baseline. • If at any time, the participant meets liver chemistry stopping criteria, proceed as described in Section 7.1.1. • If ALT decreases from ALT ≥5xULN and <8xULN to ≥3xULN but <5xULN, continue to monitor liver chemistries weekly. • If, after 4 weeks of monitoring, ALT <3xULN and bilirubin <2xULN, monitor participants twice monthly until liver chemistry tests resolve, stabilize, or return to baseline.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal

10.7 Appendix 7: Rapid Alert Procedures

Not applicable.

10.8 Appendix 8: Country-specific Requirements

Japan

Specific requirements for study participants in Japan include:

- In reference to Section 5.1, for study participants <20 years of age, written informed consent will be obtained from both the participant and the legal representative.
- In reference to Section 5.3, the use of medicinal cannabidiols and medicinal marijuana are prohibited by law.
- In reference to Section 8.2.6, TB assessment by IGRA; the preferred screening test is IGRA performed at a Central Laboratory by QuantiFERON tube test, **or using a T-SPOT.TB test at each site**.
- The country-specific requirements for Japan aligned with Japan GCP will be provided separately in Protocol Exhibit.

For medical devices used, locally approved devices are to be used during the study. If a pump and infusion set are used that are regarded in Japan as investigational devices, then additional adherence to specific reporting obligations will be required. All adverse device effects (ADEs), serious adverse device effects (SADEs), and medical device deficiency (including malfunction use error, and inadequate labeling) of these investigational devices shall be documented and reported by the Investigator throughout the study and appropriately managed by the Sponsor.

This reporting requirement is not applicable for locally approved devices for the purpose of sc infusions or other purposes in the course of this study, regardless if provided by the sponsor or not.

Furthermore, specific rules for repetition of an ADE and device deficiency should be followed by all study sites in Japan; *this requirement is not applicable for locally approved devices, regardless if provided by the sponsor or not.*

For ADEs and/or device deficiencies that are not related to the natural course of the disease under study, an increase in the intensity of the original ADE, and/or device deficiency should lead to the repetition of the original ADE and/or device deficiency with the following guidelines:

- The outcome date of the original ADE and/or device deficiency must be the same as the start date of the repeated ADE and/or device deficiency.
- The outcome of the original ADE and/or device deficiency must be recorded as “worsening.”
- The verbatim term for the repeated ADE and/or device deficiency must be the same as the verbatim term for the original ADE and/or device deficiency so that the repeated ADE and/or device deficiency is obviously a worsening of the original.

As per local requirements in Japan, SAEs associated to an investigational device, and device deficiencies (eg, infusion pump product provided from Sponsor) should be reported in accordance with the following:

This reporting requirement is not applicable for locally approved devices for the purpose of sc infusions or other purposes in the course of this study, regardless if provided by the Sponsor or not.

Medical Device – AEs, adverse device effects (ADEs), serious adverse events (SAEs) and device deficiencies

Medical devices are being provided for use in this study subcutaneous infusions. In order to fulfill regulatory reporting obligations worldwide, the Investigator is responsible for the detection and documentation of events meeting the definitions of incident or malfunction that occur during the study with such devices.

Adverse events will be reported according to the ISO 14155:2011, while recognizing and following requirements including reporting timelines specified in other specific laws, regulations, directives, standards and/or guidelines as appropriate and as required by the countries in which the clinical investigation is conducted.

NOTE: Events fulfilling the definition of an AE/SAE will also follow the processes outlined in Section 8.3.3 and Appendix 3 (Section 10.3) of the protocol.

Time period for detecting medical device deficiencies

Medical device deficiency or malfunctions of the device that result a reportable event will be detected, documented, and reported during all periods of the study in which the medical device is used.

If the Investigator learns of any deficiency at any time after a participant has been discharged from the study, and such event(s) is considered reasonably related to a medical device provided for the study, the Investigator will promptly notify the Sponsor.

Follow-up of medical device deficiencies

Follow-up applies to all study participants, including those who discontinue study medication and/or the study.

The Investigator is responsible for ensuring that follow-up includes any supplemental investigations as indicated to elucidate the nature and/or causality of the deficiency.

New or updated information will be recorded on the originally completed form with all changes signed and dated by the Investigator.

Prompt reporting of medical device deficiencies to Sponsor

Device deficiencies will be reported to the Sponsor within 24 hours after the Investigator determines that the event meets the protocol definition of a medical device deficiency.

The Adverse Event and Device Deficiency Report Form will be sent to the Sponsor by email. If email is unavailable, then fax should be utilized.

The Sponsor will be the contact for the receipt of device deficiency reports.

Regulatory reporting requirements for medical device deficiencies

The Investigator will promptly report all device deficiencies occurring with any medical device provided for use in the study in order for the Sponsor to fulfill the legal responsibility to notify appropriate regulatory authorities and other entities about certain safety information relating to medical devices being used in clinical studies.

The Investigator, or responsible person according to local requirements (eg, the head of the medical institution), will comply with the applicable local regulatory requirements relating to the reporting of device deficiencies to the IRB/IEC.

Medical Device AEs (ADEs, UADEs, SAEs, SADEs, and USADEs) and device deficiencies: Definition and procedures for recording, evaluating, follow-up, and reporting

This reporting requirement is not applicable for approved devices for the purpose of sc infusions or other purposes in the course of this study, regardless if provided by the Sponsor or not.

The definitions and procedures detailed in this appendix are in accordance with ISO 14155.

Both the Investigator and the Sponsor will comply with all local medical device reporting requirements.

The detection and documentation procedures described in this protocol apply to all Sponsor medical devices provided for use in the study.

Definition of AE and ADE

AE and ADE Definition
• An AE is defined as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory finding) in study participants, users, or other persons, whether or not related to the investigational medical device. This definition includes events related to the investigational medical device or comparator and events related to the procedures involved except for events in users or other persons, which only include events related to investigational devices. • An adverse device effect (ADE) is defined as an adverse event related to the use of an investigational medical device. This definition includes any adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device as well as any event resulting from use error or from intentional misuse of the investigational medical device.

Definition of SAE, SADE and USADE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met (e.g., hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

An SAE is an AE that:
a. Led to death
b. Led to serious deterioration in the health of the participant, that either resulted in: 1. A life-threatening illness or injury. The term ‘life-threatening' in the definition of serious' refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe 2. A permanent impairment of a body structure or a body function, 3. Inpatient or prolonged hospitalization, Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered an SAE

4. Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
c. Led to fetal distress, fetal death or a congenital abnormality or birth defect
SADE definition
• A SADE is defined as an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
USADE definition
• A USADE is a serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis report (see Section 8.3.8).

Definition of Device Deficiency

Device Deficiency definition
• A device deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling.

Recording and Follow-Up of AE and/or SAE and Device Deficiencies

AE, SAE and Device Deficiency Recording
• When an AE/SAE/device deficiency occurs, it is the responsibility of the Investigator to review all documentation (e.g., hospital progress notes, laboratory reports, and diagnostics reports) related to the event. • The Investigator will then record all relevant AE/SAE/device deficiency information in the participant's medical records, in accordance with the Investigator's normal clinical practice and on the appropriate form of the CRF. • It is **not** acceptable for the Investigator to send photocopies of the participant's medical records to UCB in lieu of completion of the AE/SAE/device deficiency CRF page. • There may be instances when copies of medical records for certain cases are requested by UCB. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to UCB. • The Investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE. • For device deficiencies, it is very important that the Investigator describes any corrective or remedial actions taken to prevent recurrence of the deficiency ◦ A remedial action is any action other than routine maintenance or servicing of a medical device where such action is necessary to prevent recurrence of a device deficiency. This includes any amendment to the device design to prevent recurrence. The Investigator should complete a Product Complaint Form for all reported device deficiencies.
Assessment of Intensity
The Investigator will make an assessment of intensity for each AE/SAE/device deficiency reported during the study and assign it to one of the following categories:

- 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 a 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.

Assessment of Causality

- The Investigator is obligated to assess the relationship between study intervention and each occurrence of each AE/SAE/device deficiency
- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- The Investigator will use clinical judgment to determine the relationship.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration will be considered and investigated.
- The Investigator will also consult the IB in his/her assessment.
- For each AE/SAE/device deficiency, the Investigator **must** document in the medical notes that he/she has reviewed the AE/SAE/device deficiency and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the Investigator has minimal information to include in the initial report to UCB. However, it is very important that the Investigator always make an assessment of causality for every event before the initial transmission of the SAE data to UCB.
- The Investigator may change his/her opinion of causality in light of follow-up information and send a SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.

Follow-up of AE/SAE/device deficiency

- The Investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by UCB to elucidate the nature and/or causality of the AE/SAE/device deficiency as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.
- If a participant dies during participation in the study or during a recognized follow-up period, the Investigator will provide UCB with a copy of any post-mortem findings including histopathology.
- New or updated information will be recorded in the originally completed CRF.

- The Investigator will submit any updated SAE data to UCB within 24 hours of receipt of the information.

Reporting of SAEs

SAE Reporting to UCB via an Electronic Data Collection Tool

- The primary mechanism for reporting an SAE to UCB will be the electronic data collection tool.
- If the electronic system is unavailable, then the site will use the paper SAE data collection tool (see next section) in order to report the event within 24 hours.
- The site will enter the SAE data into the electronic system as soon as it becomes available.
- 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 (see next section) or to the Medical Monitor/SAE coordinator by telephone.
- Contacts for SAE reporting can be found in this protocol.

SAE Reporting to UCB via Paper CRF

- Facsimile transmission of the SAE paper CRF is the preferred method to transmit this information to the UCB.
- In rare circumstances and in the absence of facsimile equipment, notification by telephone is acceptable with a copy of the SAE data collection tool sent by overnight mail or courier service.
- Initial notification via telephone does not replace the need for the Investigator to complete and sign the SAE CRF pages within the designated reporting time frames.
- Contacts for SAE reporting can be found in this protocol.

Reporting of SADEs

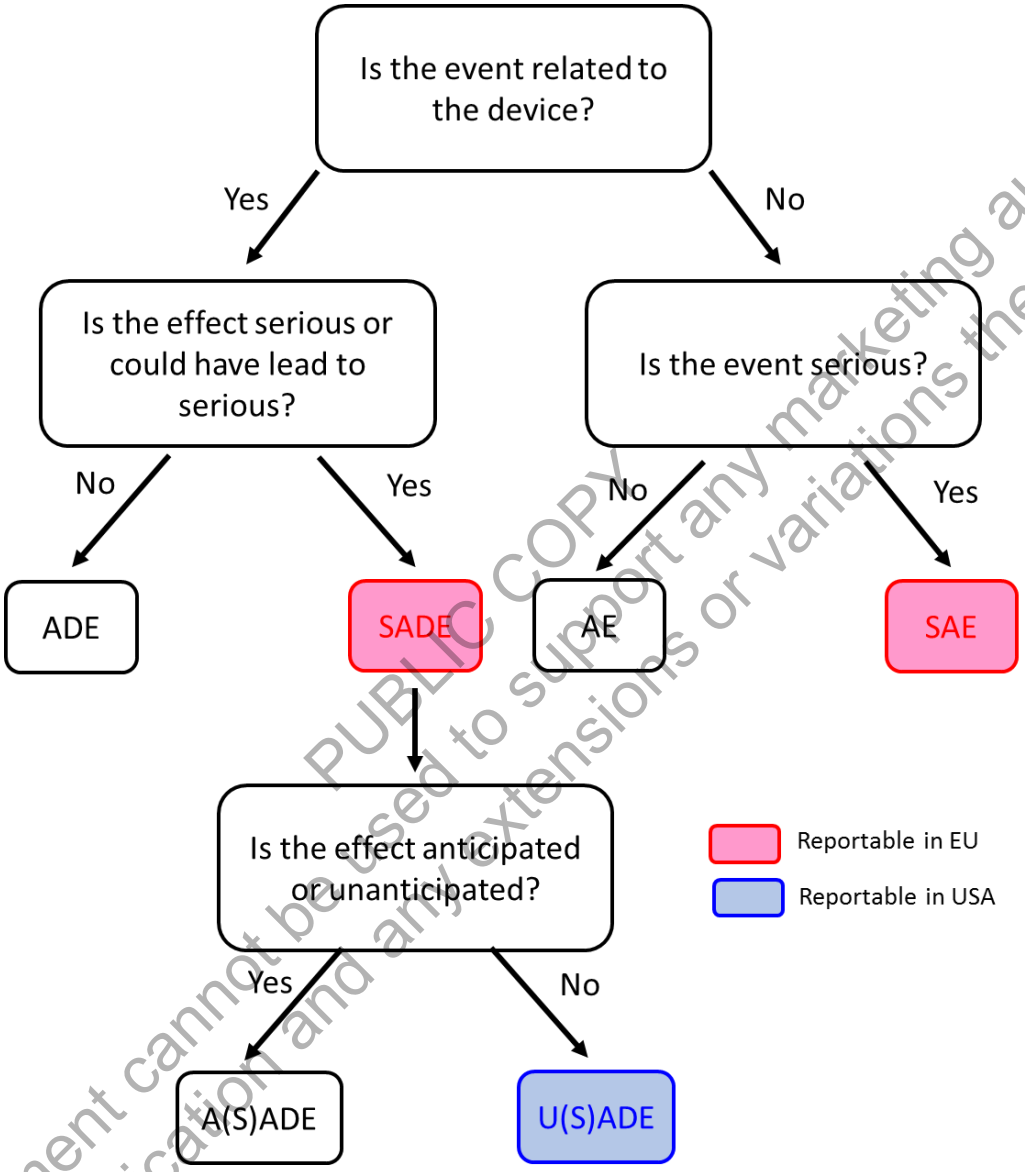
SADE Reporting to UCB

NOTE: There are additional reporting obligations for medical device deficiencies that are potentially related to SAEs that must fulfil the legal responsibility to notify appropriate regulatory authorities and other entities about certain safety information relating to medical devices being used in clinical studies.

- Any device deficiency that is associated with an SAE must be reported to the Sponsor within 24 hours after the Investigator determines that the event meets the definition of a device deficiency.
- The Sponsor shall review all device deficiencies and determine and document in writing whether they could have led to an SAE. These shall be reported to the regulatory authorities and IRBs/IECs as required by national regulations.
- Contacts for SAE reporting can be found in this protocol.

AE, ADE, SAE, SADE determination flow chart

Note: Adverse event reporting for countries other than the USA and EU must follow the regulatory and ethical requirements for that country.



Denmark

In reference to Section 1.1 and Section 4.1, the managed access program will not be applicable, and the study duration for each study participant will be 14 months.

France

Specific requirements for study participants in France include 1 additional inclusion criterion and 2 additional exclusion criterions, as listed below.

Inclusion Criteria (Section 5.1):

6. Study participant must be registered at the Sécurité Sociale (French national health system) or be beneficiary of a similar system.

Note: *this criterion will be number 3 in the gap period inclusion criteria (Section 10.12).*

Exclusion Criteria (Section 5.2):

18. Study participant is deprived of their liberty by a judicial or administrative decision, or is receiving psychiatric care under sections L3212-1 and L3213-1 who are not covered by section L1121-8, and study participant is admitted to a health or social institution (Article L1121-6 of the French Public Health Code).
19. Study participant who is subject to legal protection or is unable to express consent (Article L1121-8 of the French Public Health Code).

Note: *these criterions will be number 42 and 43, respectively, in the gap period exclusion criteria (Section 10.12).*

UK

Specific requirements for study participants in the UK include:

- In reference to Section 1.1 and Section 4.1, the managed access program will not be applicable, and the study duration for each study participant will be 14 months.
- In reference to Section 1.3, a second pregnancy test is scheduled at Day 29 during the treatment periods (Visit 6 in the initial fixed treatment cycle and Visit 5 in the subsequent treatment cycles).
- In reference to Section 5.2, exclusion criterion #14a, if any of the repeated tests (ALT, AST, or ALP) are >3.0xULN, the study participant will automatically meet the exclusion criterion #12 and will not be eligible for participation in MG0007.

10.9 Appendix 9: Abbreviations and Trademarks

AChE	acetylcholinesterase
AChR	acetylcholine receptor
ADA	anti-drug antibody
ADE	adverse device effect
ADL	activities of daily living
ADR	adverse drug reaction
AE	adverse event
AESM	adverse events of special monitoring
AESI	adverse event of special interest
ALP	alkaline phosphatase
ALT	alanine aminotransferase
ASADE	anticipated serious adverse device effect
AST	aspartate aminotransferase
BP	blood pressure
BUN	blood urea nitrogen
CI	confidence interval
CNS	central nervous system
COVID-19	Coronavirus Disease 2019
CPM	Clinical Project Manager
CPMP	Committee for Proprietary Medicinal Products
CRF	Case Report form
CRO	contract research organization
CSF	cerebrospinal fluid
C-SSRS	Columbia Suicide Severity Rating Scale
CTCAE	Common Terminology Criteria for Adverse Events
DAP	Data Analysis Plan
DCP	Data Cleaning Plan
DIAM	drug-induced aseptic meningitis
ECG	electrocardiogram
eCRF	electronic Case Report form
EMA/EMEA	European Medicines Agency

EQ VAS	EuroQol visual analogue scale
FcRn	neonatal Fc receptor
FIH	first in human
EudraCT	European Union Drug Regulating Authorities Clinical Trials
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GI	gastrointestinal
gMG	generalized myasthenia gravis
HBsAg	Hepatitis B surface antigen
HIV	human immunodeficiency virus
HRT	hormonal replacement therapy
IB	Investigator's Brochure
IBD	inflammatory bowel disease
ICF	Informed Consent form
ICH	International Council for Harmonisation
IDMC	Independent Data Monitoring Committee
IEC	Independent Ethics Committee
Ig	immunoglobulin
IGRA	interferon-gamma release assay
IMP	investigational medicinal product
IND	Investigational New Drug
INR	international normalized ratio
IRB	Institutional Review Board
IRT	interactive response technology
[redacted]	[redacted]
iv	intravenous
IVIg	intravenous immunoglobulin
LDH	lactate dehydrogenase
LLOQ	lower limit of quantification
LS	least squares
LTBI	latent tuberculosis infection
MedDRA	Medical Dictionary for Regulatory Activities

MG	myasthenia gravis
MG-ADL	Myasthenia Gravis-Activities of Daily Living
MG-C	Myasthenia Gravis Composite
MGFA	Myasthenia Gravis Foundation of America
MG-QOL15r	Myasthenia Gravis Quality of Life
MMRM	mixed model for repeated measures
MuSK	muscle-specific kinase
NMJ	neuromuscular junction
NTMBI	nontuberculous mycobacterial infection
OLE	open-label extension
PD	pharmacodynamics(s)
PDILI	potential drug-induced liver injury
PEF	peak expiratory flow
PEOT	premature end of treatment
PEX	plasma exchange
PK	pharmacokinetic(s)
PRO	patient-reported outcome
QMG	quantitative myasthenia gravis
SADE	serious adverse device effect
SAE	serious adverse event
SAP	statistical analysis plan
SOP	Standard Operating Procedure
SS	Safety Set
TB	tuberculosis
TEAE	treatment-emergent adverse event
UADE	unanticipated adverse device effect
ULN	upper limit of normal
USADE	unanticipated serious adverse device effect

10.10 Appendix 10: Protocol Amendment History

Amendment 2 (30 Jun 2022)

Overall Rationale for the Amendment

The primary reason for this protocol amendment is to incorporate new wording on the options for the route of administration, changes specific to the schedule of activities, updates to the study medication permanent discontinuation criteria, as well as providing additional information on the benefit-risk for study participants who have received a full COVID-19 vaccination.

This amendment is considered to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.

Section # and Name	Description of Change	Brief Rationale
Global	Minor administrative and formatting changes have been made.	To provide clarity and remain consistent with remainder of protocol.
1.1 Synopsis 3 Objectives and endpoints	The following other efficacy endpoint on MG-C responder rate has been amended; responder rate has changed from ≥5.0-point to ≥3.0-point.	Corrected.
1.1 Synopsis 3 Objectives and endpoints 9.4.1 Efficacy analyses	Other efficacy endpoint on minimal symptom expression has been amended to include the Treatment and Observation Periods in the time frame.	Updated to provide clarity and remain consistent with the study design.
1.1 Synopsis 3 Objectives and endpoints	Cross reference to Section 8.9 has been added to footnote b.	Updated to provide clarity on which exploratory safety biomarkers may be assessed.
1.1 Synopsis 4.1 Overall design 6.5.4 Rescue medication 7.1.4 Study medication permanent discontinuation criteria	Wording on participants who receive rescue therapy has been updated.	Taking into account the efficacy and safety results from MG0003 and MG0004, the permanent discontinuation criteria was updated to provide more flexibility to the investigators and adjust this criterion to the cyclic treatment regimen.
1.2 Schema	Updated to provide defined periods for the 22-week (6+16 weeks) cycle.	Updated to provide clarity and remain consistent with the study design.
1.3 Schedule of activities, Table 1-2	Visit 9 has been added to demographic and baseline characteristics. The following new activity has been added for Visits 1 and 9: Medical history update.	Included as demographic and baseline data are required to be reviewed. Included as part of a requirement for open-label extension studies.

Section # and Name	Description of Change	Brief Rationale
	Study withdrawal: Visit every 4 weeks during the no treatment with rozanolixizumab period has been added. Medical history has been removed.	Previously missing from protocol amendment 1. Removed as any new conditions occurring after the screening visit of the lead-in study are recorded as AEs, not as medical history.
1.3 Schedule of activities, Table 1-3	Scheduled visits have been removed from the full physical activity, and additional visits have been added to brief physical activities	Updated to match the correct procedures at sites.
1.3 Schedule of activities, Table 1-2	Footnote b: Updated to remove "minus (-)" from the visit window, and to include wording on the requirement to complete missing activities from the lead-in study. Footnote c: Updated to include “MG0003” in relation to study participants and “initial” in reference to the baseline timepoint. Footnote j: Updated to remove "until the study participants has been evaluated by a TB specialist" New footnote (l): Only applicable if study participant requires PEOT added to Visit 8. Subsequent footnotes have been reordered. New footnote (m): Required for study withdrawal or study completion visit (Section 4.4). Footnote q and s (previously o and q, respectively): timings of collecting additional samples have been updated.	Updated to provide clarity and remain consistent with the study design. Updated for additional clarity and align with updates to the participant eCRF. Not applicable. Study participant would need to be positive, and therefore treatment would be terminated. Updated to remain consistent with the study design. Updated to remain consistent with the study design. Updated to remain consistent with the study design.
1.3 Schedule of activities, Table 1-3(subsequent cycles)	General medical history has been updated to medical history update.	Updated to record conditions that were not captured during the course of the lead-in study, and not new conditions that initially occurred after the

Section # and Name	Description of Change	Brief Rationale
		screening visit of the lead-in study.
1.3 Schedule of activities, Table 1-3(subsequent cycles)	For call or enter IRT to register the visit, Visit 2 has been added and Visit 8 has been removed.	An IRT call or entry must be registered at Visit 2 but is not required at Visit 8.
1.3 Schedule of activities, Table 1-3(subsequent cycles)	Body weight and associated footnote (g) have been added to the schedule of activities. Study withdrawal: Visit every 4 weeks during the no treatment with rozanolixizumab period has been added. Study drug discontinuation criteria removed at Visit 1.	Weight-based dose adjustments are limited to a maximum of every 6 months during the study. Previously missing from protocol amendment 1
1.3 Schedule of activities, Table 1-3(subsequent cycles)	For QMG scale, visits specific to treatment with no rozanolixizumab (every 12 weeks) was updated to replace footnote "i" with "m".	Updated to correct an error in protocol amendment 1.
1.3 Schedule of activities, Table 1-3(subsequent cycles)	Footnote b: Updated to remove "minus (-)" from the visit window Footnote f: Updated to remove "until the study participants has been evaluated by a TB specialist"	To provide clarity and remain consistent with the study design. Not applicable. Study participant would need to be positive, and therefore treatment would be terminated.
1.3 Schedule of activities, Table 1-3(subsequent cycles)	New footnote (g): Weight-based dose adjustments are limited to a maximum of every 6 months has been added. Subsequent footnotes have been reordered. New footnote (h): In case of switching to manual push administration, for the first 2 infusions vital signs will be measured prior to IMP administration, at the end of the infusion (±15 minutes), and 1 hour after the end of the infusion (±15 minutes). For the subsequent infusions all assessments will be performed prior to any blood sampling and IMP administration. New footnote (i): Only applicable if study participant requires PEOT added to Visit 7.	To provide clarity and remain consistent with the study design.

Section # and Name	Description of Change	Brief Rationale
	Footnote i and j, now l and m, respectively: timings of collecting additional samples has been updated.	
1.3 Schedule of activities, Table 1-4 (initial fixed cycle - study participants who receive full COVID-19 vaccination before or during the study)	Table title was updated to include "full". Footnote a: New footnote specific to define a full COVID-19 vaccination. Footnote c: Update to the timing for collecting biomarker samples.	Updated to provide clarity. Added to provide some guidance on a full COVID-19 vaccination is defined differently per country or region To remain consistent with the study design
1.3 Schedule of activities, Table 1-5 (subsequent cycles - study participants who receive full COVID-19 vaccination before or during the study)	A new schedule of activities table has been included specific for study participants treated with subsequent cycles who receive full COVID-19 vaccination before or during the study.	Included as part of the objective on [redacted]
2.3 Benefit/Risk assessment	Additional wording specific to COVID-19 vaccine has been included.	To provide information on the benefit-risk on participant who have received the COVID-19 vaccination and remain consistent with the Phase 3 rozanolixizumab clinical program.
4.1 Overall design	Wording on withheld IMP for low IgG in MG0004 and missed doses has been removed.	Updated to remove duplicate wording.
4.4 End of study definition	Additional wording for the timing of completing an EOS visit at the time of product approval or the availability of a MAP has been added.	Updated to provide clarity and remain consistent with the study design.
6.1 Treatments administered	Table 6-1: "via syringe driver or manual push method" has been added to the route of administration row. Additional wording on the options for route of administration have been added.	To clarify the methods of IMP administration allowed in the study.
6.8 Treatment after the End of the Study	The following wording in reference to participants considered for additional treatment with prophylactic	Updated to provide clarity and remain consistent with the study design.

Section # and Name	Description of Change	Brief Rationale
	antimicrobial therapy has been removed.	
7.1.3 Temporary IMP discontinuation	An additional criterion (#3) on the decision to start a new treatment cycle after moderate to severe infection that may or may not result in hospitalization has been added.	Taking into account the safety results related to infections from the studies MG0003 and MG0004, the permanent discontinuation criteria was updated to allow more flexibility to the investigators, adjust this criterion to a cycling regimen with an observation period, and better reflect clinical practice.
7.1.4 Study medication permanent discontinuation criteria	Criteria #3 has been updated to state the following: "Study participant experiences a significant infective episode including but not limited to bacteremia/sepsis, infectious meningitis, septic arthritis, osteomyelitis, complicated pneumonia, or visceral abscess which may or may not result in hospitalization during a treatment period. However, if a significant infective episode is reported during the observation period, decision to start a new treatment cycle should be based on careful evaluation by the Principal Investigator of the Benefit-Risk for the individual study participant and provided a full recovery from infection, an acceptable level of total IgG (≥ 2 g/L) and no other discontinuation criteria were met" Criteria #9 has been updated to include wording on participants who receive rescue therapy.	Taking into account the safety results related to infections from the studies MG0003 and MG0004, the permanent discontinuation criteria was updated to allow more flexibility to the investigators, adjust this criterion to a cycling regimen with an observation period, and better reflect clinical practice.
8.2.2 Vital signs	Wording on the requirement to collect vital signs for participants switching to manual push and the option to collect additional vital signs in the case of an untoward event have been included.	Updated to provide clarity to manual push administration recommendations and provide the option to collect data in case of untoward event. Touchless forehead temperature assessment is an option for

Section # and Name	Description of Change	Brief Rationale
	Temporal (touchless forehead temperature assessment) has been added.	measuring participants' temperature to adapt to the current clinical practice.
8.2.3 Electrocardiograms	Wording was updated to remove references to triplicate.	No identification of cardiotoxicity from nonclinical data, supported by lack of signal cardiac events in the rozanolixizumab program. Updated in order to decrease burden to the sites and study participants.
8.2.6 Assessment and management of TB and TB risk factors	The text was updated to remove "appropriate rigorous" and to add that assessment and management of TB and TB risk factors should follow local or national guidelines.	Patients with known tuberculosis (TB) infection, at high risk of acquiring TB infection, or latent tuberculosis infection (LTBI), or current/history of nontuberculous mycobacterial infection (NTMBI) are already excluded from MG0003, therefore the sites are expected to follow national/local guidelines for the management of TB, in case needed. In addition, the mechanism of action of rozanolixizumab is expected to have little or no impact on the immune response against intracellular organisms which is involved in controlling the infection with mycobacterium tuberculosis.
8.2.6 Assessment and management of TB and TB risk factors	Under Latent TB, text regarding 2 indeterminate IGRA test results as suggestive of TB infection was removed	Updated for consistency with study design.
8.3.6 Adverse events of special interest	The definition of Hy's Law has been updated.	Updated for consistency with study design.
8.9.1 Immunological assessments	Updated to reference "full" COVID-19 vaccine.	Updated to provide clarity and remain consistent with the study design.
10.2, Appendix 2: Clinical Laboratory Tests	Table 10-1: Urine drug screen has been added.	The addition of urine drug screen will further aide in proper workup and diagnosis of the etiology of elevated liver enzymes.

Section # and Name	Description of Change	Brief Rationale
	For routine urinalysis, albumin/creatinine ratio, creatinine has been added.	Urine creatinine has already been measured in the urine collected for the urinalysis (for other protocol-specified assessments) but by error was not included in the wording in the protocol.
10.8, Appendix 8: Country-specific Requirements	The numbering for exclusion criterions specific to France have been corrected.	Updated to correct an error in protocol amendment 1.
10.10 Appendix 10: Protocol Amendment History	Details of the previous amendment (protocol amendment 1) have been added.	General update.
10.13.1 Management of headaches	The following wording has been added: "The questionnaire should be administered by a health care professional via an interview with the study participant"	To add further clarity.
10.13.3 Management of infections and hypogammaglobulinemia	The following wording has been added: "Study participant experiences a significant infective episode including but not limited to bacteremia/sepsis, infectious meningitis, septic arthritis, osteomyelitis, complicated pneumonia, or visceral abscess which may or may not result in hospitalization during a treatment period. If a significant infective episode is reported during observation period, decision to start a new treatment cycle should be based on careful evaluation by the Principal Investigator of the Benefit-Risk for the individual study participant and provided a full recovery from infection, an acceptable level of total IgG (≥ 2 g/L) and no other discontinuation criteria were met"	Taking into account the safety results related to infections from the studies MG0003 and MG0004, the permanent discontinuation criteria was updated to allow more flexibility to the investigators, adjust this criterion to a cycling regimen with an observation period, and better reflect clinical practice.
10.13.4 Management of infusion reactions or hypersensitivity reactions	Table 10-3: Alert crash team has been replaced with "emergency care services".	Updated to provide clarity

Amendment 1 (03 Mar 2021)

Overall Rationale for the Amendment

The primary reason for this protocol amendment is to incorporate an additional study objective and endpoint on [redacted]. Other required changes include aligning this protocol with the updates for the rozanolixizumab myasthenia gravis clinical program, and to incorporate specific local ethics committees and/or agency requirements into this global protocol.

This amendment is considered to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.

Section # and Name	Description of Change	Brief Rationale
Global	Minor administrative, formatting, and typographical changes have been made.	Updated to provide clarity and be consistent with remainder of protocol.
Global	All references to MGC003 within body text, tables and figures have been removed.	The China MGC003 study will no longer be conducted.
1.1 Synopsis 3 Objectives and Endpoints	An additional efficacy endpoint specific to symptom expression has been added.	Updated to be consistent with the SAP.
1.1 Synopsis 3 Objectives and Endpoints	Other endpoints specific to Change from Baseline (Day 1) in [redacted] and in serum cytokines have been updated to remove gastrointestinal disturbances.	Gastrointestinal disturbance in relation these endpoints will not be analyzed.
1.1 Synopsis 3 Objectives and Endpoints	An additional objective and associated endpoint specific to the effect of rozanolixizumab on COVID-19 biomarkers has been included.	New objective and endpoint is needed for the collection of information on [redacted]
1.1 Synopsis 4.1 Overall design	The following wording in reference to participants opting to receive rescue medication has been updated to remove: "after the end of rescue therapy"	Updated to provide clarity and remain consistent with the study design.
1.1 Synopsis 4.1 Overall design	Cross-reference to Appendix 8 has been included.	Updated to provide clarity and additional information for country-specific requirements.

Section # and Name	Description of Change	Brief Rationale
1.1 Synopsis 4.1.1 Study population 9.8 Determination of sample size	The approximate number of study participants has decreased from 230 to 200.	The China MGC003 study will no longer be conducted resulting in a decreased number of study participants for MG0007.
1.3 Schedule of activities, Table 1-2	A new column has been added to include the scheduled procedures required for a gap period Screening Visit.	Updated to provide clarity and be consistent with remainder of protocol.
1.3 Schedule of activities, Table 1-2 and Table 1-3	Visit windows have been added for the no treatment with rozanolixizumab period and the EOS visit.	Updated to factor in visit windows during Treatment and Observation Period.
1.3 Schedule of activities, Table 1-2	Written informed consent and Verification of inclusion/exclusion criteria have been added to Visit 9. A new footnote has been added: f: Only applicable to study participants enrolling from MG0004.	Updated to provide clarification for study participants enrolling from MG0004.
1.3 Schedule of activities, Table 1-2	Vital signs have been added to Visit 9 (Day 71).	Updated to be consistent with remainder of protocol.
1.3 Schedule of activities, Table 1-2	Visits 2, 9, 10, 11, and 12 as well as no treatment visits have been removed for Call or enter IRT to register the visit.	All visits will be tracked (electronic data capture); this update will reduce site burden and potential backlogged visit entries.
1.3 Schedule of activities, Table 1-2	PTT and INR have been added to the abbreviation list.	Updated to be consistent with remainder of protocol.
1.3 Schedule of activities, Table 1-2	The following footnotes have been added: a: Only applicable to study participants with a gap period, defined as any study participant who does not enroll in MG0007 within 4 weeks (or ≤32 days) of the screening visit from the lead-in study (see gap period screening assessments, Appendix 11, Section 10.11). g: Only applicable to study participants with a gap period (see gap period eligibility criteria, Appendix 12, Section 10.12).	Updated to provide clarity and be consistent with remainder of protocol.

Section # and Name	Description of Change	Brief Rationale
	h: For criteria pertaining to laboratory measures, the last values from MG0003 or MG0004 will be used for evaluation of study participant eligibility, as long as the measurement was taken within the last 4 weeks prior to MG0007 Baseline (Day 1). k: For UK-specific requirements on additional pregnancy test, see Appendix 8, Section 10.8. As a result, the order of footnotes has been updated.	Updated to align with the MHRA recommendations.
1.3 Schedule of activities, Table 1-2	The following footnotes have been updated: a (updated to b): Updated to amend specific for participants enrolling from MG0004, and to include the following additional text: "all activities should be completed at Visit 1 (±1 week)" and a cross reference to footnote a. f (updated to j): Updated to remove the following text: "Additional IGRA TB testing will be done at least 12 months since last test" and include the correct visit numbers applicable to MG0004. New wording on Wording on requirements positive or two indeterminate IGRA tests result has been updated. i (updated to n): Updated to include "Day 1, Visit 2" in reference to Baseline, and to remove the following text: "2 hours" in reference to collection of additional samples and "serious" in relation to severity of headaches. m (updated to r): Reduced observation time from 2 hours to 1 hour.	Updated to provide clarity and be consistent with remainder of protocol. Updated to be consistent with the study design as the IGRA TB test will be performed at the Screening Visit, not the Baseline Visit. Updated to provide clarity and be consistent with remainder of protocol. Updated to be consistent with the Phase 3 rozanolixizumab clinical program for an OLE study.

Section # and Name	Description of Change	Brief Rationale
1.3 Schedule of activities, Table 1-2 and Table 1-3	All footnotes with reference to MGC003 have been updated to remove this reference.	Updated to provide clarity and be consistent with remainder of protocol.
1.3 Schedule of activities, Table 1-3	Visits 2, 9, 10, 11, and 12 as well as no treatment visits have been removed for Call or enter IRT to register the visit.	All visits will be tracked (electronic data capture); this update will reduce site burden and potential backlogged visit entries.
1.3 Schedule of activities, Table 1-3	The following footnotes have been added: b: For any study participant enrolling from MG0004, the final visit in MG0004 (Visit 52 [PEOT] or Visit 53 [EOS]) will serve as the Baseline Visit in MG0007. All activities should be completed at Visit 1 (±1 week). For study participants with a gap period (>4 weeks), see Section 4.1. g: For UK-specific requirements on additional pregnancy test, see Appendix 8, Section 10.8. As a result, the order of footnotes has been updated.	Include to ensure consistency with the overall study design. Updated to align with the MHRA recommendations.
1.3 Schedule of activities, Table 1-3	The following footnotes have been updated: e (now f): Updated to include new wording on positive or two indeterminate IGRA tests result has been updated g (updated to i): Updated to remove wording relating to Baseline measures from MG0003 and "safety exploratory biomarkers" and "2 hours" in reference to collection of additional samples. h (updated to j): Updated to remove wording relating to Baseline measures from MG0003 and "GI disturbances." j (updated to l): Reduced observation times for first and subsequent infusions.	Updated to provide clarity and be consistent with remainder of protocol. Updated to provide clarity and be consistent with remainder of protocol. Updated to be consistent with the Phase 3 rozanolixizumab clinical program for an OLE study.

Section # and Name	Description of Change	Brief Rationale
1.3 Schedule of activities, Table 1-4	A new schedule of activities table has been included specific for study participants who receive COVID-19 vaccination before or during the study.	Included as part of the objective on [redacted]
2.2 Background	"Ongoing" has been removed from the study status for UP0060.	The study is complete.
2.3 Benefit/Risk assessment	Text on potential risks associated with administration of rozanolixizumab has been updated.	Updated to remove events that are no longer considered a potential risk across the Phase 3 rozanolixizumab clinical program.
4.1 Overall design	Wording relating to the start of follow up for study participants receiving rescue therapy has been updated. "Steroids" has been replaced with corticosteroids.	Updated to provide clarity and remain consistent with the study design. Added to correct an error from the original protocol.
4.1.1 Study population	The total number of study sites has increased from 120 to 130. China has been removed from the list of sites.	Updated due to the increased number of study sites in the lead-in study, MG0003. This study will no longer be conducted in China.
4.2 Scientific rationale for study design	Wording related to choice of doses and regimen has been removed.	Deleted to remove repetitive wording.
5.1 Inclusion criteria	Criterion #1 (now 1a) has been updated to remove MGC003.	Updated to provide clarity and be consistent with remainder of protocol.
5.1 Inclusion criteria	Criterion #3 (now 3a) has been updated to include "a negative urine pregnancy test prior to the first dose of study medication at Baseline Visit of the initial and subsequent treatment cycles"	Updated to provide clarity regarding the timings of a negative pregnancy test for each treatment cycle.
5.1 Inclusion criteria	New wording on France-specific requirements has been included.	Updated to align with French Ethics Committee query on French Social Security cover for study participants.
5.2 Exclusion criteria	Criterion #3 (now 3a) has been updated to include "or other anti-FcRn medications."	Updated to be consistent and aligned with eligibility language used in Phase 3 rozanolixizumab clinical program.

Section # and Name	Description of Change	Brief Rationale
	Criterion #4 (now 4a) has been updated with new ineligibility details relating to tuberculosis. Criterion #15 (now 15a) has been updated to include use of Fredericia's formula.	
5.2 Exclusion criteria	Criterion #5 (now 5a) has been updated to remove MGC003. Criterion #14 (now 14a) has been updated to remove "rescreening" and include a reference to UK-specific requirements.	Updated to provide be consistent with remainder of protocol. Updated to incorporate feedback received from the MHRA.
5.2 Exclusion criteria	Criterion (#17) specific to history of suicide attempt has been added.	Added to correct an error from the original protocol.
5.2 Exclusion criteria	New wording on France-specific requirements has been included.	Updated to align with French Ethics Committee query on exclusion criteria pertaining the French Public Health Code.
5.4 Screening failure	New text has been added to clarify this section is applicable to study participants with a gap period only.	Updated to provide clarity and to correct an error from the original protocol.
6.1 Treatments administered	Table 6-1: Updated to replace infusion with "injection" for the dose formulation and to remove the following details: "[redacted]" and "no less than [redacted] extractable volume of." New table (6-2) presenting dose levels and body weight tiers has been included.	Updated to reflect the foreseeable changes in vial size. Updated to provide further clarity.
6.1.1 Medical devices	This section has been deleted and all text has been moved to Section 10.8 Appendix 8: Country-Specific Requirements.	Updated to provide clarity and be consistent with remainder of protocol.
6.2 Preparation, handling, storage, and accountability requirements	The following text has been removed: The Investigator (or designee) will instruct the participant to store the study medication following the instructions on the label.	There is no requirement for the study participant to store study medication in this study.
6.2.1 Drug accountability	In relation to recording study medication dispensing, "drug	Updated to provide further clarity.

Section # and Name	Description of Change	Brief Rationale
	accountability" has replaced case report. In reference to SOPs used, "and/or site" has been included.	
6.3 Measures to minimize bias: randomization and blinding	The following text has been added: "Randomization in MG0007 is to a ratio of 1:1."	Updated to provide further clarity.
6.5.1 Permitted concomitant treatments (medications and therapies)	The following text has been removed "and dose adjustments are allowed between treatment cycles". Additionally, "steroids" has been replaced with corticosteroids. New text has been added in specific to the requirement to collect information on COVID-19 vaccinations in the eCRF.	Updated to remove conflict with the requirement for maintaining a stable dose of permitted concomitant medications. Information on COVID-19 vaccination will be required.
6.5.2 Prohibited concomitant treatments (medications and therapies)	The following prohibited concomitant treatment "vinca alkaloids (vincristine, vinblastine)" has been added. Additionally, wording specific to treatment-free periods prior to initiating a 6-week treatment cycle has been removed.	Updated to correct an error from the original protocol.
6.5.3 Treatments specific to NMJ interference	A new section on treatments that may interfere with the function of the NMJ has been added.	Updated to correct an inadvertent omission from the original protocol.
7.1.1 Liver chemistry stopping criteria	New text specific to continued treatment with increased monitoring has been added.	Updated to provide further clarity.
7.3 Lost to follow up	The following text has been removed: Investigators should contact the Medical Monitor, whenever possible, to discuss the withdrawal of a study participant in advance. Study participants who are withdrawn will not be replaced.	Updated to remove duplication in previous section.
8.2.2 Vital signs	Wording on blood pressure and pulse measurements has been removed.	Updated to remove repetitive wording.

Section # and Name	Description of Change	Brief Rationale
8.2.5 Suicidal risk monitoring	Wording on the use of C-SSRS at specific timepoints has been removed.	Updated to be consistent with the study design and schedule of activities.
8.2.6 Assessment and management of TB and TB risk factors	TB assessment by IGRA; the following updates have been made: - Baseline has been replaced with Screening. - Visit numbers in reference to MG0004 have been updated. - Added a cross reference to the schedule of activities. Wording on indeterminate IGRA tests result has been updated. Test conversion: the following has been deleted, "The IGRA result must be negative for study participants to enroll in this study"	Updated to be consistent with the study designs for MG0004, and MG0003 for the IGRA TB test to be performed at the Screening Visit, not the Baseline Visit.
8.3.3 Follow-up of AEs and SAEs	AESM and the associated cross reference have been added.	Updated to be consistent with remainder of protocol.
8.9 Biomarkers	This section has been updated to remove "2 hours" in reference to collection of additional samples and to update the severity of AESMs, as well as new examples of GI disorders.	Updated to be consistent with remainder of protocol.
8.9.1 Immunological assessments	New text has been added in specific to blood sampling for the measurement of COVID-19 antibodies.	COVID-19 antibodies will be collected in this study for all participants who have received a COVID-19 vaccine.
8.10 Medical resource utilization and health economics	This section has updated to remove "not".	Updated as medical resource utilization and health economics will be measured in this study.
8.11 Participant exit interview	This section has been removed.	The optional participant exit interview will no longer be conducted.
9.1 Definition of analysis sets	The randomization analysis set has been replaced with full analysis set and consequently amends the definition of the safety set.	Updated to be consistent with the SAP.

Section # and Name	Description of Change	Brief Rationale
9.2 General statistical considerations	The approach to summarizing data for safety and efficacy analyses have been amended.	Updated to be consistent with the SAP.
9.2.1 Intercurrent event handling rationale and impact on the study	Adverse events will be recorded up to 8 weeks after last sc infusion rather than the completion of each 6-week treatment cycle.	Updated to be consistent with remainder of protocol.
9.3.1 Analysis of the primary safety endpoint	Summarizing TEAEs and TEAEs leading to withdrawal of IMP will be summarized by dose at AE onset, and not randomized treatment. Additionally, the following wording was removed, "The primary endpoints will also be summarized by treatment cycle by the rozanolixizumab dose given during that cycle".	Updated to be consistent with the SAP.
9.4.1 Efficacy analyses	The following new wording has been added: "The number and percentage of participants achieving Minimal Symptom Expression (MG-ADL score of 0 or 1) at Day 43 will be summarized by treatment group."	Updated to be consistent with the SAP.
10.1.6 Data quality assurance	In reference to ongoing source data verification, new wording pertaining to encompassing remote source data verification and source data review, and national and local regulations have been included.	Updated to provide clarity on allowing remote data verification as per applicable regulatory guidance.
10.2 Appendix 2: Clinical Laboratory Tests, Table 10-1	The following parameter, glucose, has been updated to include "fasting state, preferred". The following have been added: "Low-density lipoprotein (LDL), High-density lipoprotein (HDL), triglycerides, total cholesterol"	Updated to clarify the specifics for fasting glucose testing. Lipid profile will be assessed in the study.
10.3 Appendix 3: Adverse Events – Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting	Additional wording for the requirements of follow-up of AEs and SAEs has been included.	Updated to be consistent with the procedures for follow-up across the Phase 3 rozanolixizumab clinical program.

Section # and Name	Description of Change	Brief Rationale
10.4 Appendix 4: Contraceptive Guidance and Collection of Pregnancy Information	Contraception guidance for male participants has been updated to include "for the duration of the study" and to remove "agree to use a male condom plus partner use of a contraceptive method with a failure rate of <1% per year as described in the table below when having penile-vaginal intercourse with a woman of childbearing potential who is not currently pregnant."	Updated to provide further clarity on the use of contraception during the study.
10.4 Appendix 4: Contraceptive Guidance and Collection of Pregnancy Information	Contraception guidance for female participants and vasectomized partner has been updated.	Updated to be consistent with the Phase 3 rozanolixizumab clinical program.
10.6 Appendix 6: Liver Safety: Suggested Actions and Follow-Up Assessments	New tables describing Phase 3-4 liver chemistry stopping criteria. and follow up assessments have been included.	Updated as information was missing from the original protocol.
10.8 Appendix 8: Country-specific Requirements	New requirements specific to Denmark, France, Japan, and UK have been included.	Updated in accordance with local requirements
10.11 Appendix 11: Gap Period Screening Assessments	PTT and INR have been added as a Screening assessment.	Updated as information was missing from the original protocol.
10.12 Gap Period Eligibility Criteria	Appendix title has been updated. Gap period inclusion criteria has been included to cover eligibility in reference to pregnancy and contraception use, as well as moving the following criterion from the exclusion criteria to inclusion criteria: 1. Study participant has MGFA Class II to IVa at Visit 1.	Updated for further clarity and to correct errors from the original protocol.
10.12 Gap Period Eligibility Criteria	The following updates for exclusion criterion relating to scheduled visits include: Criterions #2, #11, #27, and #31: Screening replaces Visit 1. Criterions #7, #9, and #10: Baseline replaces Visit 2.	Updated for further clarity and to correct errors with scheduled visits.

Section # and Name	Description of Change	Brief Rationale
	Criterion #16: Updated to replace Visit 1 and Visit 2 with Screening and Baseline, respectively. Consequently, eligibility criteria have been renumbered.	
10.12 Gap Period Eligibility Criteria, Table 10-2	The following updates for exclusion criterions include: Criterion #12 was updated to remove "history thereof in past 6 months prior to Visit 1" Criterion #32: The timeframe was amended to cover duration of study participation. Two new exclusion criterions on human immunodeficiency virus (#35) and primary immunodeficiency (#36) have been added.	Updated to be consistent with the Phase 3 rozanolixizumab clinical program.
10.12 Gap Period Eligibility Criteria, Table 10-2	Table title: Visit 2 has been replaced with Visit 1. A new biologic (inebulizumab) as well associated the treatment-free period were added.	Updated to be consistent with exclusion criterion #9. Updated to be consistent across the Phase 3 rozanolixizumab clinical program.

10.11 Appendix 11: Gap Period Screening Assessments

Gap criteria

Study participants who do not enroll in MG0007 within 4 weeks (or ≤32 days) of the EOS or PEOT visit from the lead-in study will need to complete a specific Screening visit undergoing the following assessments:

- Written informed consent
- Demographic and Baseline characteristics
- Verification of inclusion/exclusion criteria
- Prior and concomitant medications and medical procedures
- General medical history
- Body weight
- Columbia Suicide Severity Rating Scale (CSSRS)
- Psychiatric history/Query for suicidality
- IGRA TB test
- TB Signs and Symptoms questionnaire
- 12-lead ECG
- Full physical examination
- Pregnancy test (serum)
- PTT and INR
- Hematology, serum chemistry and urinalysis
- Serology testing for HIV, Hepatitis B, and Hepatitis C
- Vital signs
- Call or enter IRT to register the visit
- Recording of AEs
- Blood sampling for total IgG and IgG subclasses
- MGFA classification
- MG-ADL
- QMG scale
- MG-C scale
- MG Symptoms PRO
- Study withdrawal criteria

10.12 Appendix 12: Gap Period Eligibility Criteria

Gap Period Inclusion Criteria

Study participants eligible to be included in the study only if all of the following criteria apply:

1. Study participant has MGFA Class II to IVa at Screening.

2a. Study participants may be male or female:

   a) Removed.

   b) A female participant is eligible to participate if she is not pregnant (see Appendix 4), not breastfeeding, and at least one of the following conditions applies:

      i) Not a woman of childbearing potential (WOCBP) as defined in Appendix 4

      OR

      ii) A WOCBP who agrees to follow the contraceptive guidance in Appendix 4 during the treatment period and for at least for at least 90 days after the last dose of study treatment. The study participant must have a negative urine pregnancy test prior to the first dose of study medication at Baseline (Day 1) of the initial and subsequent treatment cycles.

For France-specific inclusion criteria, see Appendix 8 (Section 10.8).

Gap Period Exclusion Criteria

Study participants who do not enroll within the 4 weeks (or ≤32 days) prior to MG0007 Baseline (Visit 1) will be excluded from the study if any of the following criteria apply:

Medical conditions

1. Study participant has any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the study participant's ability to participate in this study.
2. 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 prior to Screening.
3. Study participant has a known hypersensitivity to any components of the study medication or other anti-FcRn medications.
4. Study participant has a known history of [redacted], since [redacted] is a constituent of the rozanolixizumab formulation.
5. Study participant has a clinically relevant active infection (eg, sepsis, pneumonia, or abscess) in the opinion of the Investigator, or had a serious infection (resulting in hospitalization or requiring parenteral antibiotic treatment) within 6 weeks prior to the first dose of IMP.
6. Study participant with a known tuberculosis (TB) infection, at high risk of acquiring TB infection, or latent tuberculosis infection (LTBI), or current/history of nontuberculous mycobacterial infection (NTMBI).

7. Study participant has received a live vaccination within 8 weeks prior to Baseline; or intends to have a live vaccination during the course of the study or within 8 weeks following the final dose of rozanolixizumab.
8. Study participant has been treated with prohibited immunosuppressants, biologics, and other therapies within timeframe shorter than no-treatment period detailed in Table 10-2.
9. Study participant has been treated with any biological agent other than those listed in Table 10-2 in the past 3 months or within 5 half-lives prior to Baseline, whichever was longer.

Table 10-2: Treatment-free Period for Exclusionary Immunosuppressants, Biologics, and Other Therapies Prior to Baseline (Visit 1)

Generic name (commercial/trade names)	Period relative to Baseline Visit (regardless of route)
Immunosuppressants	
Cyclophosphamide (Cytoxan®)	6 months
Pimecrolimus (Elidel®)	4 weeks
Vinca alkaloids (vincristine, vinblastine)	12 weeks
Biologics (Mabs and fusion proteins)	
Abatacept (CTLA 4-Ig) (Orencia®)	6 months
Eculizumab (Soliris®)	3 months
Belimumab (Benlysta®)	6 months
Golimumab (Simponi®)	6 months
Natalizumab (Tysabri®)	6 months
Ofatumumab (Arzerra)	6 months
Rituximab (Rituxan®)	6 months or 12 months if B-cells did not return to normal range
Ocrelizumab (Ocrevus®)	6 months or 12 months if B-cells did not return to normal range
TACI-Ig (Atacicept)	10 months
Veltuzumab	6 months
Other biologics	3 months, or within 5 half-lives (whichever was longer) prior to the Baseline Visit
Inebulizumab	6 months (prior to Baseline Visit) and B-cells are within normal range
Others	
Intravenous or subcutaneous immunoglobulin	4 weeks
IPP-201101 (Lupuzor™)	3 months
PEX	4 weeks
Immunoadsorption	4 weeks

Mabs=monoclonal antibodies; PEX=plasma exchange

10. Study participant has prior treatment with rituximab in the 6 months prior to Baseline or study participant has prior treatment with rituximab in the 12 months prior to Baseline and B cells monitoring have shown they did not return to normal range.

11. Study participant had a thymectomy in the past 6 months or a thymoma at any time that required chemotherapy and/or radiotherapy prior to Screening.
12. Study participant has any of the following active GI disorders: inflammatory bowel disease (IBD), GI ulceration or diverticulitis.

Prior/Concurrent clinical study experience

13. Study participant has participated in another study of an IMP (and/or an investigational device) within the previous 3 months or is currently participating in another study of an IMP and/or an investigational device.
14. Study participant has been previously randomized in this study (re-screening for screen-failed participants is allowed with prior consultation and permission of the medical monitor).
15. Study participant has experienced hypersensitivity reaction after exposure to other anti-FcRn drugs.

Diagnostic assessments

16. Study participant with severe (defined as Grade 3 on the MG-ADL scale) weakness affecting oropharyngeal or respiratory muscles, or who has myasthenic crisis or impending crisis at Screening or Baseline.
17. Study participant has a serum total IgG level ≤5.5g/L.
18. Study participant has absolute neutrophil count <1500 cells/mm^3.
19. Study participant has any laboratory abnormality that, in the opinion of the Investigator, is clinically significant, has not resolved at randomization, and could jeopardize or compromise the study participant's ability to participate in this study.
20. Study participant has 12-lead ECG with findings considered to be clinically significant upon medical review. The clinical significance of the findings needs to be assessed by the Investigator to determine eligibility, and any queries regarding continuation of the study participants will have to be addressed with the Medical Monitor.
21. Study participant has renal impairment, defined as GFR less than 45ml/min/1.73m^2 at Visit 1.
22. Alanine transaminase (ALT), aspartate aminotransferase (AST), or alkaline phosphatase (ALP) are >3x upper limit of normal (ULN), or bilirubin >1.5xULN (isolated bilirubin >1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin <35%).
23. Study participant has elevations only in total bilirubin that were >ULN and <1.5xULN, fractionate bilirubin to identify possible undiagnosed Gilbert's syndrome (ie, direct bilirubin <35%).
24. For randomized study participants with a Baseline result >ULN for ALT, AST, ALP, or total bilirubin but <1.5xULN, a Baseline diagnosis and/or the cause of any clinically meaningful elevation will have to be understood and recorded in the electronic Case Report form (eCRF).
25. If study participant has >ULN, ALT, AST, or ALP that does not meet the exclusion limit at Visit 1, the tests should be repeated, if possible, prior to dosing to ensure there was no further

ongoing clinically relevant increase. In case of a clinically relevant increase, inclusion of the study participants will have to be discussed with the Medical Monitor.

26. Tests that result in ALT, AST, or ALP up to 25% above the exclusion limit (>3xULN) will have to be repeated once for confirmation. This includes rescreening.
27. Presence of Hepatitis B surface antigen (HBsAg) at Screening.
28. Positive Hepatitis C antibody test result at Visit 1 or within 3 months prior to starting study treatment. NOTE: Study participant with a positive Hepatitis C antibody due to prior resolved disease can be enrolled, only if a confirmatory negative Hepatitis C RNA test is obtained.
29. Positive Hepatitis C RNA test result at Visit 1 or within 3 months prior to first dose of study treatment. NOTE: Test is optional and a study participant with negative Hepatitis C antibody test is not required to also undergo Hepatitis C RNA testing.
30. Current unstable liver or biliary disease per Investigator assessment defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, persistent jaundice, or cirrhosis. NOTE: with exception of stable hepatobiliary conditions (including Gilbert's syndrome, asymptomatic gallstones).
31. Study participant has active neoplastic disease or history of neoplastic disease within 5 years of study entry prior to Screening (except for basal or squamous cell carcinoma of the skin or carcinoma in situ of the uterine cervix that have been definitively treated with standard of care approaches).
32. Study participant has a planned major elective surgical procedure for the duration of their participation in the study.
33. Study participant has a history of a solid organ transplant or hematopoietic stem cell/marrow transplant.
34. Study participant has corrected QT interval (QTcF) >450 msec (for male participants) or QTc >470 msec (for female participants) or QTc >480 msec in participants with bundle branch block.
35. Study participant tests positive for HIV.
36. Study participant has a current or medical history of primary immunodeficiency.

Other exclusions

37. The study participant is not considered capable of adhering to the protocol visit schedule, or medication intake according to the judgment of the Investigator.
38. A female study participant, who tests positive for pregnancy, plans to get pregnant during the participation in the study, or who is breastfeeding.
39. Study participant has a lifetime history of suicide attempt (including an [redacted], or had suicidal ideation in the past 6 months as indicated by a positive response (Yes) to either Question 4 or Question 5 of the Columbia Suicide Severity Rating Scale (C-SSRS).
40. Participant with current or medical history of [redacted] deficiency.

41. Participant with a medical history of splenectomy.

For France-specific exclusion criteria, see Appendix 8 (Section 10.8).

10.13 Appendix 13: Management of infections and hypogammaglobulinemia and infusion reactions or hypersensitivity reactions

10.13.1 Management of infections and hypogammaglobulinemia

Study participants who have signs or symptoms of any infection should be monitored closely and managed according to local guidelines. This may include tests for specific organisms if clinically indicated.

Study participants **MUST discontinue IMP AND move** into **the SFU Period** if he/she develop a significant infective episode including but not limited to bacteremia/sepsis, infectious meningitis, or septic arthritis, osteomyelitis, complicated pneumonia, or visceral abscess which may or may not result in hospitalization during a treatment period.

If a significant infective episode is reported during observation period, the decision to start a new treatment cycle should be based on careful evaluation by the Principal Investigator of the Benefit-Risk for the individual study participant and provided a full recovery from infection, an acceptable level of total IgG (≥2g/L) and no other discontinuation criteria were met.

To maintain the study integrity, IgG level will remain blinded to the study sites and the UCB study team for the first 4 weeks of the study. To ensure patient safety, serum IgG level will be monitored by an independent Medical Monitor external to UCB including signs and symptoms of infection and associated laboratory parameters. The IMP may be temporarily discontinued as requested by the independent Medical Monitor when deemed appropriate.

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. Treatment may be temporarily discontinued for the study participant who develops a non-serious persisting or recurrent infection with a serum total IgG level between ≥1g/L and <2g/L. Upon resolution of infection and the IgGs returning to the level of ≥2g/L, the study participant may be allowed to resume treatment with the IMP. Ad hoc assessment can be performed to monitor the recovery of IgG levels.

Treatment must be temporarily discontinued for the study participant who develops an event of hypogammaglobulinemia with a serum total IgG of <1g/L irrespective of infection. When the IgG level reaches ≥2g/L, the study participant may be allowed to continue treatment with IMP.

10.13.2 Management of infusion reactions or hypersensitivity reactions

Study participants must be closely monitored for reactions during and after the study treatment administration period. Standard precautions must be taken for the study participants with regard to sc infusion complications. Suggested management guidelines for infusion-related reactions and anaphylaxis at the study site are provided in Table 10-3. Definitions of mild, moderate, and severe events will be consistent with CTCAE version 5.0 (Section 10.3).

Nurses administering the IMP at home should follow their own management guidelines, which should be reviewed and endorsed by the Investigator prior to first home administration.

Table 10-3: Suggested management guidelines for infusion reactions or anaphylaxis

Type of reaction	Suggested action
Acute – Mild Grade 1	Monitor vital signs every 10 min. If the reaction worsens to Grade 2, follow the instruction below.
Acute – Moderate Grade 2	Interrupt/hold infusion temporarily to further assess and initiate treatment if necessary. Consider the use of iv fluid and antihistamine iv/im. Consider administering paracetamol or NSAIDs. Monitor vital signs initially every 5 min. If the reaction improves and upon further assessment it is clear that the event is not an anaphylaxis, restart the infusion cautiously. Continue monitor vital signs every 5 minutes. If reaction recurs or worsens to Grade 3, discontinue infusion.
Acute – Severe Grade 3 or anaphylaxis	Discontinue IMP infusion permanently. Emergency care services. Maintain airway; ensure oxygen is available. Administer: – Antihistamine iv/im, corticosteroids iv, epinephrine im, and iv fluids as appropriate. – Monitor vital signs every 2 min. – Hospitalize, if condition not improving or worsens – Monitor patient until symptoms resolve.

CTCAE=Common Terminology Criteria for Adverse Events; im=intramuscular; IMP=investigational medicinal product; iv=intravenous(ly); NSAID=nonsteroidal anti-inflammatory drug
Note: Management criteria were adapted from the CTCAE v5.0 (National Cancer Institute, 2017).

Conditions in which anaphylaxis is likely should be diagnosed using Sampson's Criteria (Sampson et al, 2006. The infusion must be discontinued immediately, and emergency resuscitation measures implemented.

If an infusion-related reaction or anaphylaxis occurs, a blood sample will be collected from the study participant as soon as possible, while the event is ongoing, to investigate the nature of the reaction as per Schedule of Activities (Section 1.3).

Samples for [redacted] should be collected as specified in the Schedule of Activities (Section 1.3). Additional tests such as [redacted] levels, [redacted] may be performed at the discretion of the investigator, when there is a suspicion of Type I or III hypersensitivity reaction. The results of all monitoring, including laboratory testing, should be made available to the study site and Sponsor.

10.14 Appendix 14: Management of adverse event of special monitoring

Adverse events of special monitoring are defined as product-specific AEs, adverse reactions, or safety topics requiring special monitoring by one or more regulatory authorities or by UCB.

For rozanolixizumab, AESMs (defined by UCB) are:

- Severe and/or serious headache
- Suspected aseptic meningitis

Occurrence of AESM require immediate reporting (within 24 hours regardless of seriousness) to UCB. Upon reception of AESM by UCB a standard medical follow-up query (SMFQ) will be sent to the site to gather extensive medical information about the AESM. See Table 1-6 for additional assessments that may be required in case of AESM.

Aseptic meningitis (suspected)

Drug-induced aseptic meningitis is a diagnosis of exclusion after ruling out infectious causes (Jolles et al, 2000). A few cases of aseptic meningitis (drug-induced) have been reported in the rozanolixizumab program. Consequently, aseptic meningitis (suspected) is being managed as an AESM (see Section 8.3.7).

Participants should be monitored for signs and symptoms suggestive of central nervous system (CNS) involvement and evaluated immediately if meningitis is suspected. A full neurological workup should be strongly considered including, but not limited to imaging, eg, computed tomography (CT) scan, or preferably gadolinium-enhanced magnetic resonance imaging (MRI), a lumbar puncture with cerebrospinal fluid (CSF) analysis inclusive of glucose, protein, differential complete blood count (CBC), cultures, gram stain, and/or viral polymerase chain reactions (PCRs) as appropriate. Whenever possible, CSF should be stored for assessment of rozanolixizumab PK, PD, specific antibody titers, or other biomarkers. A concurrent blood sample should be collected as per local practice. The ultimate investigative procedures are at the discretion of the Investigator or the treating physician. For studies where a neurologist is not the Investigator, a neurological consultation is also recommended to aid in decision making and patient management. In addition, blood samples for exploratory safety biomarkers (see Section 8.9) should be collected for participants with a diagnosis of DIAM preferably within 72 hours after onset of symptoms. These investigations will be performed to further understand the potential mechanisms of DIAM in the participants.

All procedures related to the diagnosis, treatment, and investigation of meningitis should be recorded in the eCRF, and preliminary data should be included on the SAE form used for reporting the event as an AESM within 24 hours (ie, preliminary data reported on the first reporting may not have CSF results yet, but the reporting should occur as soon as there is a suspected diagnosis. Full results should be communicated in subsequent exchanges with the sponsor).

Treatment must be temporarily held if a participant has a diagnosis of suspected meningitis of any cause until the diagnostic workup is complete. Based on CSF findings, negative cultures, absence of other disease causes, and relationship with IMP, a diagnosis of DIAM can be made. If deemed appropriate by the Investigator and agreed upon by the participant and the Sponsor, the

study treatment can resume upon the complete resolution of symptoms. The benefit and risk of the treatment should be carefully considered prior to reinitiating the IMP. If a participant experiences a second episode of similar symptoms suggestive of DIAM, then the participant must permanently discontinue the IMP.

Participants experiencing an event of DIAM should be strongly encouraged to remain in the study regardless of IMP discontinuation. This will allow for monitoring and follow-up of the participant including a complete neurological exam on subsequent physical examinations. Longer term follow-up on any AEs related to DIAM that are ongoing may be warranted until resolution.

Associated symptoms with aseptic meningitis should be managed at the Investigator's discretion.

Severe and/or serious headache

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

Determination of the severity of headache will be consistent with National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Severe headache is defined as severe pain limiting self-care activities of daily living (ADL). Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, and taking medications.

In the event of a headache, the Investigators should take the medical history of previous headaches, concomitant medication, and co-morbidities (eg, asthma) in consideration.

If the severe and/or serious headache is initially reported at a home visit or during a telephone call, the study participant should be evaluated by a healthcare professional as soon as possible for further investigations. Study participants should be monitored for signs and symptoms suggestive of CNS involvement and evaluated immediately if other causes (eg, meningitis, intracranial bleeding) are suspected (please see Section 1.3.1 [Table 1-6]). In addition, samples for exploratory safety biomarkers should be collected for study participants experiencing severe or serious headache when possible. These investigations will be performed to further understand the mechanism of headaches in the study participants.

If deemed appropriate by the Investigator and agreed upon by the study participant and the Sponsor, the study treatment can resume upon the resolution of the severe and/or serious headache event. The benefit and risk of the treatment should be carefully considered prior to reinitiating the IMP.

Headaches will be treated as clinically indicated according to national guidelines. It is recommended that the study participants have an analgesic available in case of headache with the instruction for frequency and dosage provided by a healthcare professional. The analgesic can be started at the early onset of headache. Study participants experiencing any treatment-related headache will be followed until resolution of the event.

Prophylactic treatment of headaches may be permitted for study participants who have experienced previous episodes of treatment-related headache after discussion with the Medical Monitor. The benefit risk of continuing treatment with IMP and chronic prophylactic with analgesics must be carefully evaluated by the Investigator.

10.15 Appendix 15: Sampson Criteria Questionnaire

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 GI symptoms (eg, crampy abdominal pain, vomiting)

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

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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.

Approval Signatures

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