STATISTICAL ANALYSIS PLAN

A Phase 2 Trial to Investigate the Efficacy, Safety, and Tolerability of Efgartigimod PH20 SC in Adult Patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Protocol:	ARGX-113-1802
SGS Internal Reference:	BE-80-1902615
Development phase:	Phase 2
Sponsor:	argenx
Analysis purpose:	Final analysis
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SIGNATURE PAGE

Name and function	Signature and date (ddMMMyyyy)
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Sponsor's approval: The approver agrees the statistical analysis will be performed according to this statistical analysis plan.	
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PROTOCOL HISTORY

Protocol:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the changes on the statistical analysis**
Final 1.0	30OCT2019	NAP
Final 2.0	10JAN2020	Stage A: no impact on the statistical analysis. Stage B: • The time window for confirmation of INCAT deterioration has been shortened to reduce the time of clinical deterioration, and offer follow-up treatment as soon as possible. The minimal interval is shorted to the shortest interval of IMP injection allowed in the protocol, ie, 3 days. The confirmation of clinical deterioration during Stage B for those participants with an adjusted INCAT increase of 2 points or more compared to Stage B baseline has been deleted to prevent further deterioration. • Addition of a secondary efficacy endpoint to learn how participants improve over longer time period (longer than the 4–12 weeks in Stage A) when treated with efgartigimod PH20 SC.
Final 3.0	04MAY2020	No impact on the statistical analysis.
Final 4.0	30NOV2020	General amendment 3. No impact on the statistical analysis.
Final 5.0	12OCT2022	General amendment 4 • Measurements of IgG subtypes were removed. • EQ-5D-5L has been moved from the exploratory endpoints to the secondary endpoints

Country specific amendments:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the amendment on the statistical analysis**
Amendment 2.1	24JAN2020	Japan specific amendment. Two additional PK samples will be taken; i.e., one sample 48 to 96 hours after the 1st IMP injection and one sample 48 to 96 hours after the 4th IMP injection in approximately 10 Japanese participants in Stage A. Note that no additional PD samples will be taken at these timepoints.
Amendment 2.1	15APR2020	UK specific amendment. No impact on the statistical analysis.
Amendment 3.1	06MAY2020	Japan specific amendment. Two additional PK samples will be taken; i.e., one sample 48 to 96 hours after the 1st IMP injection and one sample 48 to 96 hours after the 4th IMP injection in approximately 10 Japanese participants in Stage A. Note that no additional PD samples will be taken at these timepoints.
Amendment 3.1	13MAY2020	German specific amendment. Extension of safety follow-up period from 28 days to 42 days.
Amendment 3.1	29MAY2020	UK specific amendment. No impact on the statistical analysis.
Amendment 3.2	14JUL2020	Japan specific amendment. Additional samples for blood & urine clinical laboratory safety tests at the 9th visit of Stage A, i.e., visit A-V9 (Day 57).
Amendment 3.1	07SEP2020	Denmark specific amendment. No impact on the statistical analysis.
Amendment 4.1	17DEC2020	Japan specific amendment. No impact on the statistical analysis.
Amendment 4.1	29JAN2021	Denmark specific amendment. No impact on the statistical analysis.
Amendment 4.1	27JAN2021	German specific amendment.

		No impact on the statistical analysis.
Amendment 4.1	31JAN2021	UK specific amendment. No impact on the statistical analysis.
Amendment 4.1	01APR2021	China specific amendment. IgG subtypes will not be measured in China. Cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), total cholesterol/HDL ratio, triglycerides may be monitored throughout the study instead of at screening visit only. Some study site laboratories in China only report one of the coagulation parameters "activated partial thromboplastin time" and "Prothrombin time".
Amendment 4.2	15APR2021	China specific amendment. No impact on the statistical analysis.
Amendment 4.2	03FEB2022	Germany specific amendment. No impact on the statistical analysis.
Amendment 4.2	07MAR2022	Japan specific amendment. No impact on the statistical analysis.
Amendment 4.2	28MAR2022	UK specific amendment. No impact on the statistical analysis.

Amendment 4.3	25AUG2021	China specific amendment. No impact on the statistical analysis.
Amendment 4.4	31MAR2022	China specific amendment. No impact on the statistical analysis.
Amendment 5.1	12OCT2022	China specific amendment • Cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), total cholesterol/HDL ratio, triglycerides should be monitored at screening visit only. • EQ-5D-5L has been moved from the exploratory endpoints to the secondary endpoints

This statistical analysis plan (SAP) only considers the last version of the protocol, and of the protocol amendments, as listed above.

LIST OF ABBREVIATIONS

Ab	Antibody
Ag	Antigen
ADA	anti-drug antibodies
ADaM	analysis data model
AE	adverse event
AESI	adverse events of special interest
ALQ	above the limit of quantification
ASTDY	relative days in the study
ATC	anatomical therapeutic chemical
AWSTDY	relative days for windowing
BLQ	below the limit of quantification
BMI	body mass index
[redacted]	[redacted] – [redacted]
bpm	beats per minute
CCC	CIDP confirmation committee
CD4	cluster of differentiation 4
CDAS	CIDP disease activity status
CI	confidence interval
CIDP	chronic inflammatory demyelinating polyneuropathy
CRF	case report form
C-SSRS	Columbia-suicide severity rating scale
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
D1A	baseline of Stage A
D1B	baseline of Stage B
DBP	diastolic blood pressure
DY	relative day
ECG	Electrocardiogram
ECI	evidence of clinical improvement
ECMD	evidence of clinically meaningful deterioration
ED	early discontinuation

efgartigimod PH20 SC	efgartigimod co-formulated with rHuPH20 for SC administration
EOSA	end of Stage A
EQ-5D-5L	EuroQoL 5 Dimensions 5 Levels
FU	follow-up
[redacted]	[redacted]
HBc Ab	anti-hepatitis B core antibody
HBsAb	anti-hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HCV Ab	anti-hepatitis C virus antibody
HDL	high-density lipoprotein cholesterol
HIV	human immunodeficiency virus
HR	hazard ratio
ICE	intercurrent event
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IgG	immunoglobin G
IMM-A	Stage A immunogenicity analysis set
IMM-B	Stage B immunogenicity analysis set
IMP	investigational medicinal product
INCAT	Inflammatory Neuropathy Cause and Treatment
I-RODS	Inflammatory-Rasch-built Overall Disability Scale
IRR	Injection-related reaction
ISR	Injection site reaction
ITT	intention-to-treat; all randomized participants
IVD	*in vitro* diagnostics
IVIg	intravenous immunoglobulin
MedDRA	Medical Dictionary for Regulatory Activities
MGS	mean grip strength
mITT	modified intent-to-treat analysis set
MRC	Medical Research Council
NAb	neutralizing antibody

NCI	National Cancer Institute
OLE	open-label extension
PD	Pharmacodynamics
[redacted]	[redacted]
PHQ-9	Patient Health Questionnaire-9
PK	Pharmacokinetics
PK-A	Stage A PK analysis set
PK-B	Stage B PK analysis set
PP	per protocol analysis set
PRO	patient-reported outcome
PYFU	participant-year of follow-up
QTc	corrected QT interval
QTcB	Bazett's corrected QT interval
QTcF	Fridericia's corrected QT interval
rHuPH20	recombinant human hyaluronidase PH20
RI	run-in analysis set
RI-V1	run-in period visit 1
[redacted]	[redacted]
SAE	serious adverse event
SAF-A	Stage A safety analysis set
SAF-B	Stage B safety analysis set
SAF-AB	Stage A+B safety analysis set
SAP	statistical analysis plan
SBP	systolic blood pressure
SC	subcutaneous(ly)
SCIg	subcutaneous immunoglobulin
SCR	all screened participants analysis set
SD	standard deviation
SE	standard error
SGS CR	SGS Clinical Research
SoA	schedule of activities
SOP	standard operating procedure
STAT	Statistics

TEAE	treatment-emergent adverse event
[redacted]	[redacted]
TUG	Timed Up-and-Go
UK	United Kingdom
VS	vital signs
WHO	World Health Organization
WI	work instructions

DEFINITION OF TERMS

case report form (CRF)	A printed, optical, or electronic document in which protocol required information is recorded for each study participant.
[redacted]	[redacted]'s
display	Analysis table, figure or listing.
estimand	A precise description of the treatment effect reflecting the clinical question posed by the study objective. It summarizes at a population-level what the outcomes would be in the same participants under different treatment conditions being compared.
estimate	A numerical value computed by an estimator.
estimator	A method of analysis to compute an estimate of the estimand using clinical study data.
intercurrent event	Events occurring after treatment initiation that affect either the interpretation or the existence of the measurements associated with the clinical question of interest.
IMP	Investigational medicinal product. In Stage A this is efgartigimod PH20 SC. In Stage B this is efgartigimod PH20 SC and placebo.
phase	Interval of time in the planned conduct of a study that is associated with a specific purpose: for example, screening, treatment, follow-up.
sensitivity analysis	A series of analyses conducted with the intent to explore the robustness of inferences from the main estimator to

	deviations from its underlying modeling assumptions and limitations in the data.
study drug	Pharmaceutical form of an active ingredient or placebo, being tested or used as a reference in a clinical study.
supplementary analysis	A general description for analyses that are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.
treatment-emergent abnormality/toxicity	Any post-baseline abnormality/toxicity that was not present at baseline (e.g. hemoglobin normal at baseline and grade 1 post-baseline; glucose low at baseline and high post-baseline; QTcF]450; 480] ms at baseline and >500 ms post-baseline).
treatment policy strategy	Strategy for handling intercurrent events: the occurrence of the intercurrent event is considered irrelevant in defining the treatment effect of interest; the values for the variable of interest are used regardless of whether the intercurrent event occurs.
while-on-treatment strategy	Strategy for handling intercurrent events: values up to the time of the intercurrent event are used.

TABLE OF CONTENTS

1. INTRODUCTION

This SAP describes the final statistical analysis to be performed for the ARGX-113-1802 (BE-80-1902615) study.

This SAP covers the efficacy, pharmacokinetic (PK), pharmacodynamic (PD), immunogenicity, safety, and general characteristics parts of the statistical analysis. It specifies the analysis displays to be presented and describes the methods and procedures in a more elaborate way than in the statistical methods section of the protocol. PK and PK/PD modelling analyses will be described in a separate SAP.

The statistical analysis will process and present the results following the International Council for Harmonisation (ICH) standards, in particular the ICH-E3, ICH-E6, and ICH-E9 guidelines.

1.1 STUDY OBJECTIVES

Stage A:

According to the protocol, the primary objective of Stage A is to assess the activity of efgartigimod PH20 SC based on the percentage of participants classified as treatment responders.

According to the protocol, the secondary objectives of Stage A are:

- To assess the time to clinical improvement.
- To determine the treatment effect of efgartigimod PH20 SC based on clinical functional assessments of motor function and muscle strength.
- To assess the short-term safety and tolerability of efgartigimod PH20 SC.
- To assess the PK of efgartigimod PH20 SC.
- To assess the PD effect of efgartigimod PH20 SC.
- To assess the immunogenicity of efgartigimod and rHuPH20.
- To assess the EuroQol 5 dimensions and 5 levels health-related quality-of-life questionnaire (EQ-5D-5L)

According to the protocol, the exploratory objectives of Stage A are:

- [redacted]
- [redacted]
- [redacted]
- [redacted]

Stage B:

According to the protocol, the primary objective of Stage B is to determine the efficacy of efgartigimod PH20 SC compared to placebo based on the time needed for the occurrence of the first evidence of clinical deterioration.

According to the protocol, the secondary objectives of Stage B are:

- To determine the efficacy of efgartigimod PH20 SC compared to placebo based on clinical functional assessments of disease disability and motor function and muscle strength
- To assess the safety and tolerability of efgartigimod PH20 SC
- To assess the PK of efgartigimod PH20 SC
- To assess the PD effect of efgartigimod PH20 SC
- To assess the immunogenicity of efgartigimod and rHuPH20
- To assess the EQ-5D-5L

According to the protocol, the exploratory objectives of Stage B are:

- [redacted]
- [redacted]
- [redacted]
- [redacted]

1.2 STUDY DESIGN

This is a Phase 2, prospective, multicenter study on the efficacy, safety, tolerability, immunogenicity, PK, and PD of efgartigimod PH20 SC in patients aged 18 years and older with CIDP.

This study will be conducted in 2 stages: an open-label Stage A and a randomized-withdrawal Stage B.

During the screening period of a maximum of 28 days, diagnosis of CIDP will be confirmed by a CIDP confirmation committee (CCC), and overall eligibility will be confirmed by the medical monitor.

Eligible patients receiving treatment for CIDP at screening will discontinue that treatment and enter the run-in period for up to 12 weeks until evidence of clinically meaningful deterioration (ECMD) is confirmed (i.e., observed during a study visit), at which time eligible patients will enter Stage A at baseline (D1A). Evidence of ECMD is defined as fulfilling of any of the following criteria during the run-in period only:

1) Adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) score increase by ≥1 point from the first visit of the run-in period (RI-V1), and/or

2) Inflammatory Rasch-built Overall Disability Scale (I-RODS) decrease by ≥4 points (using the centile metric) from RI-V1, and/or

3) Mean grip strength decrease by ≥8 kiloPascal (kPa) in one hand using the handheld vigorimeter from RI-V1.

Eligible patients who are treatment-naïve or discontinued treatment with corticosteroids and/or intravenous immunoglobulin (IVIg) or subcutaneous immunoglobulin (SCIg) at least 6 months prior to screening (who are considered equal to treatment-naïve patients) will enter Stage A directly, if during screening documented evidence for worsening on the adjusted INCAT disability score within 3

months prior to screening is available compared to previous adjusted INCAT score within 6 months prior to screening.

Patients eligible for Stage A will receive open-label IMP as weekly SC administrations of efgartigimod PH20 SC for up to 12 weeks (with optional one additional week for confirmation of evidence of clinical improvement [ECI] defined in section 4.1.2.3.3, if needed), with a minimum of 4 administrations. During Stage A, patients will be monitored for ECI.

Patients who fulfilled the criteria for ECI at 2 consecutive visits (confirmed ECI status), will roll over to the randomized-withdrawal, placebo-controlled Stage B. Patients who do not have confirmed ECI are not eligible for Stage B and will end the study after performing the safety follow-up visit 28 days after the last administration of the IMP.

Patients for whom ECI in Stage A has been confirmed, will enter the double-blind, randomized-withdrawal Stage B and will be randomized at Stage B baseline (D1B) in a 1:1 ratio to receive weekly IMP consisting of efgartigimod PH20 SC or placebo. The randomized-withdrawal Stage B will last for up to 48 weeks.

All patients randomized to the double-blind, randomized-withdrawal Stage B will be dosed with IMP weekly but will return to the clinic in 4-week intervals (every 4 weeks). Administration of randomized IMP treatment can only occur after completion of all indicated assessments. Patients will be discharged from the center if there are no safety concerns in the opinion of the investigator.

In between the study visits in Stage B, patients will be given the option to come to the study center weekly for drug administration or will be provided with home nurse service for IMP injecting. Upon agreement with the investigator, site personnel, and the patient, the most suitable solution will be provided. Administration of IMP will occur always within a time window of ± 2 days with respect to the pre-planned date of administration.

Patients completing Week 48 and in the opinion of the investigator benefit from study treatment at Week 48 or patients having an event of worsening on the adjusted INCAT score of 1 point or a worsening on the adjusted INCAT score of ≥2 points compared to Stage B baseline (for the latter, no confirmation is needed) will be allowed to roll over to the open-label extension (OLE) study ARGX-113-1902 when they are receiving IMP.

Patients completing Week 48 who will not roll over to the OLE study as well as patients with an early discontinuation, will have a safety follow-up visit 28 days after the last IMP administration, will stop the study, and will be treated as considered appropriate by the investigator.

After a total of 30 patients had reached the EOSA visit, an interim analysis was conducted and "Go" decision was announced. The interim analysis only included Stage A data. More details are presented in the interim analysis SAP.

When eighty-eight (88) events have been observed for the primary endpoint analysis of Stage B, then the study will stop. In that case, patients in Stage A and Stage B will perform an early discontinuation visit and patients who are receiving IMP will be

given the opportunity to continue efgartigimod PH20 SC treatment in the OLE study. Patients who will not roll over to the OLE study, will attend a follow-up visit 28 days after the last IMP dose.

From Stage A onwards, patients will receive training for self-administration of IMP, which is foreseen in the OLE study (not in the ARGX-113-1802 study).

The schedule of assessments is in appendix 10.3.

1.3 EXPECTED SAMPLE SIZE

Approximately 360 participants aged 18 years and older are planned to be enrolled in Stage A.

Sample Size Considerations for Stage B: if it is hypothesized that the event rate of efgartigimod PH20 SC to placebo is 0.50 (ie, hazard ratio of 0.50), then 88 events are required to provide 90% power at a 1-sided alpha level of 0.025 using a log rank test. An event is defined as an adjusted INCAT increase during Stage B (an increase [worsening] of 1 point will need to be confirmed at a consecutive visit 3-7 days after the first adjusted INCAT score increase of 1 point. For participants with an increase of 2 or more points on the adjusted INCAT score compared to Stage B baseline, no confirmation is required). The events will be monitored in a blinded way to ensure the study is sufficiently powered. The table below shows the expected sample size for different scenarios for median time to event for the placebo arm, assuming a 48 weeks maximum follow-up period for each participant, an accrual rate of 4 participants per month during the first 6 months and an accrual rate of 7.8 participants per month thereafter. To obtain a sufficient number of patients randomized into Stage B, up to 360 patients would be required to be enrolled into Stage A. Patients will continue to be randomized into Stage B until 88 events are observed as per the sample size calculation, the trial will end when the 88th event is observed.

Median Time To Event[a] for Placebo	Expected Sample Size for Stage B
1 month	96 participants
2 months	107 participants
3 months	119 participants
4 months	132 participants
5 months	146 participants
6 months	159 participants
7 months	173 participants
8 months	186 participants

[a] Event = increase in adjusted INCAT score relative to Stage B baseline in the adjusted INCAT score.

1.4 RANDOMIZATION AND BLINDING

Stage A will be open-label with administration of efgartigimod PH20 SC.

In Stage B, participants will be randomized to double-blind efgartigimod PH20 SC or placebo in a 1:1 ratio. Participants will be stratified according to their prior CIDP medication and the decrease of adjusted INCAT score during Stage A:

- Prior CIDP medication:
  - Treatment-naïve;
  - Pulsed corticosteroid treatment or oral corticosteroids equivalent to prednisolone/prednisone ≤10 mg/day;
  - IVIg or SCIg treatment.
- Adjusted INCAT score:
  - No change in adjusted INCAT score during Stage A;
  - Adjusted INCAT score decrease of ≥1 point during Stage A.

1.5 SOFTWARE

SAS version 9.4M5 or later will be used for programming.

1.6 VALIDATION MODEL

SGS Statistics (STAT) standard operating procedures (SOPs) and work instructions (WIs) as effective at the project start will be followed throughout the project, provided the applicable regulatory requirements are still met.

Subject-level Analysis Dataset (ADSL), the Stage A primary endpoint (percentage of participants with confirmed ECI) related ADaM and TLFs and the Stage B primary endpoint (time to first adjusted INCAT score deterioration compared to Stage B baseline) related ADaM and TLFs will be validated according to model C. The rest of the analysis will follow validation model B (see SOP.STAT.020):

- Model B: review by an independent person
- Model C: review by an independent person and independent programming of the parameters indicated in this SAP

2. GENERAL METHODOLOGY

2.1 STAGES

Stage A and Stage B will be analyzed separately and tables will be presented in separate outputs. Unless otherwise specified, the following applies:

- Stage A: only including screening, run-in and Stage A data
- Stage B: only including Stage B data

Listings will show Stage A and Stage B data together.

A selection of outputs will be created for Stage A and B combined (A+B), only including participants who were randomized to efgartigimod PH20 SC. Stage A+B analysis will include screening, run-in, Stage A and Stage B data.

2.2 ANALYSIS SETS

2.2.1 Analysis sets

The following analysis sets will be considered in the statistical analysis:

All screened participants set (SCR):	participants who *signed an informed consent* to participate in this study
<u>*Stage A*</u>	
Run-in analysis set (RI):	participants from the screened participants set who have a run-in phase
Stage A safety analysis set (SAF-A):	participants from the screened participants set who received at least one dose or part of a dose of IMP in Stage A
Stage A PK analysis set (PK-A):	participants from the Stage A safety analysis set for whom at least one serum PK concentration during Stage A is available
Stage A PD analysis set (PD-A):	participants from the Stage A safety analysis set for whom at least one serum PD concentration during Stage A is available
Stage A Immunogenicity analysis set (IMM-A):	participants from the Stage A safety analysis set for whom at least one ADA sample during Stage A is available
<u>*Stage B*</u>	
All randomized participants (ITT):	participants from the screened participants set who were randomized in Stage B
Stage B safety analysis set (SAF-B):	participants from the screened participants set who received at least one dose or part of a dose of IMP in Stage B

modified intent-to-treat (mITT):	participant who were randomized in Stage B and who received at least one dose or part of a dose of IMP in Stage B
per protocol (PP):	participants from the mITT analysis set without major protocol deviations
Stage B PK analysis set (PK-B):	participants from the Stage B safety analysis set for whom at least one serum PK concentration during Stage B is available
Stage B PD analysis set (PD-B):	participants from the Stage B safety analysis set for whom at least one serum PD concentration during Stage B is available
Stage B immunogenicity analysis set (IMM-B):	participants from the Stage B safety analysis set for whom at least one ADA sample during Stage B is available
Stage A+B	
Stage A+B safety analysis set (SAF-AB):	participants from the screened participants set who received at least one dose or part of a dose of efgartigimod PH20 SC in Stage B
Stage A+B immunogenicity analysis set (IMM-AB):	participants from the Stage A+B safety analysis set for whom at least one ADA sample during Stage A or B is available

Notes:

- Having signed an informed consent is defined as having a complete informed consent signature date in the database.
- Randomized is defined as having a complete randomisation date in the database or any information to confirm randomisation.

Unless stated otherwise, the general characteristics analysis for Stage A will be done on the all screened participants set (disposition only) or SAF-A and for Stage B on the all screened participants set (disposition only), ITT or SAF-B. Part of the general characteristics analysis will be repeated for the mITT (see section 3). The safety analysis for Stage A, B and A+B will be done on the SAF-A, SAF-B and SAF-AB respectively. The efficacy analysis for Stage A will be done on SAF-A, for Stage B on the mITT and for Stage A+B on the SAF-AB. A sensitivity analysis for the Stage B primary efficacy endpoint will be done on PP. PK/PD/immunogenicity analysis for Stage A will be done on PK-A, PD-A, IMM-A and for Stage B on PK-B, PD-B and IMM-B respectively. Part of the immunogenicity analysis will be repeated for Stage A+B on IMM-AB.

2.2.2 As planned versus as actual analysis

Not applicable to Stage A (planned equals actual treatment).

Analyses on ITT, mITT and PP will use the planned treatment, all other analyses will use the actual treatment.

Analyses using the stratification factors will use the values as randomized. For the Stage B primary endpoint a sensitivity analysis using the actual values of the stratification factors will be included.

2.3 PHASES, PERIODS AND TIME POINTS

2.3.1 Phases and periods

All events and assessments will be allocated to phases and periods.

Table 1: Analysis Phases

Phase	Period	Start	End
Screening		Date of signing the informed consent form (ICF), with 00:00 added as time part	For participants with run-in phase: date of first available run-in visit[a] – 1 day, with 23:59 added as time part
			For participants without run-in phase who receive Stage A IMP: first study drug administration date/time in Stage A – 1 minute
			For participants without run-in phase who do not receive Stage A IMP: date of last contact, with 23:59 added as time part
Run-in[b]		Date of first available run-in visit[a], with 00:00 added as time part	For participants who receive Stage A IMP: first study drug administration date/time in Stage A – 1 minute
			For participants who do not receive Stage A IMP: date of last contact, with 23:59 added as time part
Treatment	Stage A	First study drug administration date/time in Stage A	For participants treated in Stage B: first study drug administration date/time in Stage B – 1 minute
			For participants not treated into Stage B who do not roll-over to study 1902: date of EOSA visit or early discontinuation [ED] visit, with 23:59 added as time part
			For participants not treated into Stage B who roll-over to study 1902: date of study termination (of study 1802), with 23:59 added as time part

	Stage B	First study drug administration date/time in Stage B	For participants who roll-over to study 1902: date of study termination (of study 1802), with 23:59 added as time part For participants who do not roll-over to study 1902: date of Week 48 visit or ED visit, with 23:59 added as time part
Following phase is only applicable for participants in the treatment phase who do not continue from Stage A into Stage B or do not roll-over to study 1902.			
Follow-up		End of treatment phase + 1 minute	Date of last contact (of study 1802), with 23:59 added as time part

[a] Including unscheduled run-in visits
[b] Only for non-naïve participants or for naïve participants with no documented evidence of worsening on the adjusted INCAT score within 3 months prior to screening

Adverse events and concomitant medications will be allocated to phases and periods as described in sections 6.1.2 and 3.5.2 respectively. All other assessments will be allocated to phases and periods based on the assessment date/time.

In case of (partially) missing date/time fields disabling allocation or date(time) equal to dosing date(time), information from visit label and protocol SoA will be used to allocate to the correct phase and period. If this is not possible, assessments will be handled as follows:

- Run-in vs. screening: assessments will be allocated to the run-in unless the available parts of the assessments start or stop date/time provide evidence for allocating to the screening.
- Treatment vs. screening/run-in/follow-up: assessments will be allocated to the treatment unless the available parts of the assessments start or stop date/time provide evidence for allocating to the screening/run-in/follow-up.
- Stage A vs. Stage B: assessments will be allocated to Stage B unless the available parts of the assessments start or stop date/time provide evidence for allocating to Stage A.

A set of 3-monthly periods will be derived for the analyses of injection site reactions (ISRs) over time within Stage B and within stage A + B .

Table 2: Phase definition by 3-monthly period

Phase	Period	Start	End
Stage B or Stage A+B	0-3 Months	First IMP administration[a] date/time	Start date/time of Period 0-3 months + 90 days, with 23:59 added as time part or end date/time of phase, whichever comes first

4-6 Months	End date/time of Period 0-3 months + 1 minute	Start date/time of Period 4-6 months + 90 days, with 23:59 added as time part or end date/time of phase, whichever comes first
n*3-2 - n*3 Months[b]	End date/time of previous period + 1 minute	Start date/time of current period + 90 days, with 23:59 added as time part or end date/time of phase, whichever comes first

[a] first IMP administration is the first IMP dose in stage B or Stage A for per period analysis in stage B or stage A+B, respectively.
[b] Where n is 3 for the third 3-monthly period, 4 for the fourth, etc.

In case of (partially) missing date/time fields, adverse events (AEs) will be handled as follows:

- 0-3 Months vs. stage A (in case of 3-period analysis within stage B) or vs screening/run-in (in case of 3-period analysis within stage A+B): AEs will be allocated to 0-3 Months unless the available parts of the AE start and stop date/time provide evidence for allocating to the screening phase.
- Multiple 3-monthly periods: assessments will be allocated to the first 3-monthly period that is possible based on the available parts of the AE start and stop date/time.

2.3.2 Baseline and change from baseline

The baseline value for the run-in phase is the first available and non-missing value in the run-in phase.

The baseline value for Stage A is the last available and non-missing value before (or exactly equal to) the first administration of open-label study medication in Stage A. Unless otherwise specified, Stage A baseline will be used in the Stage A analysis, Stage B PD analysis and Stage A+B analysis.

The baseline value for Stage B is the last available and non-missing value before (or exactly equal to) the first administration of randomized study medication in Stage B (and after Stage A baseline). For immunogenicity analysis, evaluable results have priority in the Stage B baseline selection over unevaluable results. Unless otherwise specified, Stage B baseline will be used in the Stage B general characteristics, efficacy, immunogenicity, PRO and safety analysis.

The following assessments on Stage A day 1 and Stage B day 1 are considered pre-dose independent of the assessment time:

- Efficacy assessments
- Patient-reported outcomes
- Suicidality assessments
- Vital signs (no assessment time collected, pre-dose per protocol)

Change from baseline is defined as:

Change from baseline at time point t = value at time point t – baseline value.

Percentage change from baseline at time point t is defined as:

100*((value at time point t – baseline value) / baseline value)

2.3.3 Relative day

Relative days in the study (ASTDY) and relative days for windowing (AWSTDY) will be calculated according to the following rule:

- Concerned date < reference date: DY = concerned date – reference date
- Concerned date ≥ reference date: DY = concerned date – reference date + 1

The reference date for ASTDY is the date of first administration of study drug in the study.

Unless stated otherwise, the reference date for AWSTDY is as follows:

- For assessments in screening phase: the start date of the run-in phase for participants with a run-in phase; the date of first administration of study drug in Stage A for participants without a run-in phase.
- For assessments in run-in phase: the start date of the run-in phase.
- For assessments in Stage A period: the date of first administration of study drug in Stage A.
- For assessments in Stage B period (Stage B analysis): the date of first administration of study drug in Stage B.
- For assessments in Stage B period (Stage A+B analysis): the date of first administration of study drug in Stage A.
- For assessments in the follow-up phase: the start date of the follow-up phase.

2.3.4 Analysis visits

All assessments, including unscheduled assessments, will be allocated to analysis windows. The analysis windows are derived from the scheduled study days (see appendix 10.4). Tables will present the analysis windows as defined below, not the case report form (CRF) visits. Listings will present both the analysis windows as defined below and the CRF visits. Allocation of assessments will be done using their relative day in the period (see section 2.3.3).

Table 3: Analysis Windows

Analysis window	Target AWSTDY	Lower limit AWSTDY	Upper limit AWSTDY
Analysis phase = Screening			
Screening[a]	-28	-INF	For participants with run-in phase: -1 For participants without run-in phase: 1
Analysis phase = Run-in			
RI-baseline[a]	1	1	Relative day of the end date of the run-in phase
RI-V1[a]	1	1	14
RI-V2[a]	29	15	42
RI-V3[a]	57	43	70
RI-V4[a]	85	71	Relative day of the end date of the run-in phase
Analysis phase = Treatment Analysis period = Stage A			
Stage A Baseline[a]	1	-INF	1[b]
Week 1	8	1[b]	11
Week 2	15	12	18
Week (2 + w)	15 + (w * 7 days)	12 + (w * 7 days)	18 + (w * 7 days)
...	...	...	...
Week 11	78	75	81
Week 12	85	82	88
Week 13[c]	92	89	Relative day of the end of the Stage A period
Analysis period = Stage B (except for study drug administration) [d]			
Stage B Baseline[a]	1	-INF	1[b]
Week 4	29	1[b]	43
Week 8	57	44	71
Week (8 + x)	57 + (x * 7 days)	44 + (x * 7 days)	71 + (x * 7 days)
...	...	...	...
Week 44	309	296	323

Week 48	337	324	Relative day of the end of the Stage B period
Analysis period = Stage B (for study drug administration)			
Stage B Baseline	1	1	1
Week 1	8	2	11
Week 2	15	12	18
Week (2 + y)	15 + (y * 7 days)	12 + (y * 7 days)	18 + (y * 7 days)
...	...	...	...
Week 46	337	334	340
Week 47	344	341	Relative day of the end of the Stage B period
Analysis period = Stage A and Stage B (for Stage A+B analysis)			
Stage A Baseline[a]	1	-INF	1[b]
Week 1	8	1[b]	11
Week 2	15	12	18
Week 3	22	19	25
Week 4	29	26	32
Week 8	57	33	71
Week (8 + z)	57 + (z * 7 days)	44 + (z * 7 days)	71 + (z * 7 days)
...	...	...	...
Week 56	393	380	407
Week 60	421	408	Relative day of the end of the stage B period
Analysis phase = Follow-up			
Safety FU after Stage A[e]	28	1	Relative day of last contact
Safety FU after Stage B[e]	28	1	Relative day of last contact

w, x, y, z: w=1 to 8 by 1 week; x=4 to 36 by 4 weeks; y=1 to 43 by 1 week, z=4 to 52 by 4 weeks.

[a] Baseline is defined in section 2.3.2. As the interval between screening/last run-in analysis visit and Stage A Baseline are overlapping, it may be that the same assessment will be attributed to both timepoints. Similar for the interval between the last Stage A assessment and the Stage B baseline.

[b] An assessment on day 1 can be attributed to Baseline or to Week 1, depending on whether the assessment was done before or after first IMP intake (time) for parameters where time of first IMP intake is taken into account for baseline determination, see section 2.3.2 for more details.

[c] In theory, only for participants who show ECI after the 12th IMP administration and extend Stage A with an additional visit.

[d] For Stage B EQ-5D-5L, [redacted], ECG and clinical laboratory evaluations, scheduled assessments are only expected at Stage B Baseline, Week 12, Week 24, Week 36 and Week 48 / ED visit.

[e] Safety FU after Stage A for participants not randomized in Stage B, safety FU after Stage B for participants randomized in Stage B who do not roll-over to study 1902.

Per parameter and analysis window except RI-baseline, the latest value will be used in analysis tables for the efficacy parameters: INCAT score, IRODs, mean grip strength, MRC and TUG. For all other parameters, the value closest to the target AWSTDY will be used in analysis tables. Other values will only be listed. If more than one value is located at the same distance from the target, then the latest in time will be selected. The value latest in time will be identified using, in order of preference, the assessment time, the visit label or the group identifier (if applicable). Missing values are removed before the selection is made. For questionnaires, the date of the total score will be used to select the latest value and the according items of the same assessments will be used for the analysis. For immunogenicity data, the selection of which value to use within an analysis window, will be handled at sample level and not at parameter level. Missing values resulting in an unavailable ADA/NAb status are given the lowest priority when the selection is made.

Partially missing assessment dates disabling allocation to analysis windows will not be imputed for allocation to analysis windows and thus assessments with a (partially) missing date will not be considered in the per-timepoint analysis. Note that these assessments are included in analyses on worst-case. For vital signs, no time part is collected. Day 1 vital sign assessments will be assumed to be done pre-dose, as per protocol.

2.3.5 Worst-case

A worst-case analysis visit will be created per Stage and overall for parameters for which abnormalities and/or toxicity grades are defined to summarize values considered as the worst-case. For abnormalities it is derived per parameter and in case both the lowest and the highest values are considered abnormal, a participant can have two worst-case analysis visits for a same parameter. For toxicity grades the worst-case is the value associated to the highest toxicity grade and is derived per parameter and toxicity direction (hypo / hyper).

All non-missing post-baseline values, including unscheduled assessments and assessments in the FU will be considered when deriving the worst-case analysis visit.

2.3.6 Best-improvement

A best-improvement analysis visit will be created for Stage B adjusted INCAT disability score (i.e. analysis visit with the largest decrease in change from Stage A baseline for adjusted INCAT disability score). All non-missing post-Stage B baseline values, including unscheduled assessments, will be considered when deriving the best-improvement analysis visit.

2.3.7 Last assessment

A last assessment analysis visit will be created for Stage A and Stage B for efficacy, PRO and safety parameters. It will be derived per Stage and per parameter for adjusted INCAT disability score, I-RODS, MGS, MRC, TUG, PRO, safety laboratory, vital signs and ECG assessments. It is defined as the last non-missing post-baseline value in the phase/period, including unscheduled assessment.

2.4 IMPUTATION AND ROUNDING RULES

2.4.1 Missing values

Unless explicitly mentioned otherwise, no imputation will be done for missing values (i.e. observed cases analyses).

2.4.2 Handling partially or completely missing dates in calculations

Partially missing date of CIDP diagnosis will be imputed as follows:

- Missing day of diagnosis will be imputed with first day of the month
- Missing day and month of diagnosis will be imputed with 1JAN

2.4.3 Values below or above a threshold

Anti-drug antibodies (ADA) against efgartigimod: titer of positive ADA samples reported as 'negative titer' will be imputed by 1.

Antibodies (Ab) against rHuPH20: titer of positive rHuPH20 Ab samples reported as 'negative titer' will be imputed by 5.

Neutralizing antibodies (NAb) against rHuPH20: titer of positive rHuPH20 NAb samples reported as 'negative titer' will be imputed by 100.

Listings will always present 'negative titer'.

Safety values expressed as below (or above) the detection limit will be imputed by the value of the detection limit itself. Listings will always show the non-imputed values.

PD values (total IgG) expressed as below (or above) the detection limit will not be imputed.

PK concentrations below/above the detection limit will be flagged as Below/Above the Limit of Quantification (BLQ/ALQ) in the listings. For descriptive statistical analysis, all BLQ values will be set to zero. For Above the Limit of Quantification (ALQ) values, all ALQ values will be set to the upper limit of quantification for descriptive analysis. Listings will always present the original value.

2.4.4 Rounding of derived variables

Derived variables will be rounded to the appropriate number of decimals at display level:

- Phase/period duration, BMI, treatment duration, time to parameters, mean grip strength and mean of ECG triplicates will be rounded to 1 decimal.
- Estimated glomerular filtration rate (eGRF) will be rounded to 2 decimals.
- Safety laboratory results will be rounded to a maximum of 3 decimals.
- Efgartigimod serum concentrations will be rounded to a maximum of 3 decimal places

2.5 PRESENTATION OF RESULTS

Region/country specific outputs will be created to support region/country specific submissions. Specifically, all descriptive outputs described in this SAP will be repeated by region (Japanese / Non-Japanese as defined in the study protocol) to support the J-MAA submission. The definition of a Japanese participant in the protocol is a participant whose parents and 4 grandparents are Japanese, who has the Japanese nationality, was born in Japan, has not lived outside of Japan for a total of >10 years, and currently lives in Japan.

To support the Chinese submission, all outputs described in this SAP will be repeated for the following two subpopulations: Mainland Chinese and East Asian. Mainland Chinese is defined as any participant enrolled by an investigational site located in mainland China and with a race “Chinese”. East Asian is defined as any participant enrolled by an investigational site located in East Asia (mainland China, Taiwan, Japan), and with a race “Asian”. In addition, the Pharmacokinetic analysis described in section 4.2 (except the Japanese-specific analysis) will be repeated for the compliment of the Mainland Chinese and East Asian subgroups (i.e. Non-Mainland Chinese and Non-East Asian).

To support the EU submission, all outputs described in this SAP will be repeated for the following subgroup: [redacted]

Note that these additional outputs will not be included in the US submission.

2.5.1 Calculation of descriptive statistics and percentages

For continuous variables, full descriptive statistics will only be presented if there are at least 2 non-missing observations. Alternatively, only the number of non-missing data points and mean are shown.

Descriptive statistics will include the number of non-missing data points, the arithmetic mean, the standard deviation (SD), the median, Q1, Q3, minimum and maximum. For efficacy,PD and PRO the standard error (SE) may be provided in addition (see mocks for details). For PK concentrations the coefficient of variation (CV%) will be provided in addition. For immunogenicity the geometric mean and geometric SD will be provided in addition.

Mean, geometric mean, median, Q1 and Q3 will be presented with one more decimal place than the measured values. SE, SD and geometric SD will be presented with two more decimal places than the measured values. Minimum and maximum will be presented with the same number of decimal places as the measured values.

For PK serum concentrations, results will be presented with 3 significant digits. If more than half of values are BLQ, mean will be reported as BLQ, SD and CV% will not be calculated.

For event-type safety data, the number and percentage of participants with an event will be shown. The denominator will be all participants in the analysis set per treatment and phase or period. All periods will be shown, even if no events are present.

For frequency tabulations and cross-tabulations, when computing percentages the denominator will be all participants in the analysis set per treatment (and if applicable, per time point), excluding missing values. For cross-tabulations of post-baseline results versus baseline results, a 'missing' category will be shown for baseline results if applicable.

Summary tables presenting descriptive statistics or frequency tabulations by analysis visit will only show time points with observed data for at least 10 participants (overall).

2.5.2 Presentation of treatments

The following treatment labels will be used in the tables:

- EFG PH20 SC;
- PBO PH20 SC

In the general characteristics analyses for Stage B tables, an 'all participants' group will be added to summarize the total over treatments.

The following treatment labels (or abbreviated labels) will be used in the listings:

- EFG PH20 SC (EFG SC);
- EFG PH20 SC – EFG PH20 SC (EFG SC – EFG SC);
- EFG PH20 SC – PBO PH20 SC (EFG SC – PBO SC).

2.5.3 Ordering in tables and listings

All listings will be ordered by treatment, participant, analysis visit and time point, unless specified otherwise. Stage A and Stage B data will be shown together in listings, with treatment sorted in order: EFG SC, EFG SC – EFG SC and EFG SC – Placebo.

Tables will be sorted by time point. If present, last assessment, best improvement and worst-case will be shown last.

In tables showing several parameters, each parameter will begin on a new page and parameters will be sorted alphabetically, within the parameter category if applicable.

3. GENERAL CHARACTERISTICS ANALYSES

3.1 PARTICIPANT DISPOSITION

The following participant data will be tabulated:

- The number of participants in each analysis set
- The number of participants by country
- The number of participants for each period / analysis visit
- Summary participant disposition, including the number of participants:
  - Screened: failed screening (with reason for failure), passed screening,continued to run-in period or immediately continued to Stage A.
  - Started the run-in phase: entry status in run-in phase (treatment-naïve (with or without documented evidence for worsening on the adjusted INCAT score within 3 months prior to screening) and not treatment naïve), participants who discontinued the study in the run-in phase as documented on the study termination page with each study discontinuation reason, participants who entered Stage A and ECMD status at the end of the run-in phase (with or without ECMD).
  - Stage A treated participants: participants who discontinued the treatment in Stage A as documented on the end of treatment page with each treatment discontinuation reason, and who discontinued the study in Stage A as documented on the study termination page with each study discontinuation reason.
  - Randomized: randomized into Stage B (with or without treatment in Stage B)
  - Stage B treated participants: participants who received at least one dose or part of a dose of IMP in Stage B, who completed Stage B, who discontinued the treatment in Stage B as documented on the end of treatment page with each treatment discontinuation reason, and who discontinued the study in Stage B as documented on the study termination page with each study discontinuation reason.
  - Rolled-over to ARGX-113-1902
- Dates of first signed informed consent, last visit and last contact
- Descriptive statistics of the phase and period duration (see section 2.3.1) in weeks, calculated as (phase/period end date – phase/period start date + 1)/7.
- The number of participants by 3-monthly periods, within Stage B and within stage A + B

All information collected in the CRF concerning treatment discontinuation, study discontinuation and information on analysis sets and phases and periods will be listed.

3.2 PROTOCOL DEVIATIONS AND ELIGIBILITY

Frequency tabulations will be presented for minor and major protocol deviations for SAF-A (Stage A) and ITT (Stage B). All available information concerning minor and major protocol deviations, violations on eligibility criteria and participants not treated will be listed.

The following information from the CIDP Confirmation Committee (CCC) will be listed: adjudicator, confirmed eligibility (i.e. participants meets CIDP diagnostic criteria) and clinical subtype.

3.3 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

3.3.1 Available data

The following parameters will be available:

- Demographics: sex at birth, age at informed consent, race, ethnicity, childbearing potential, height, weight at screening, date of birth, date of signing informed consent form (ICF)
- CIDP disease history at screening: date of CIDP diagnosis, CIDP type and subtype of atypical CIDP (as evaluated by CCC), CIDP disease evolution, CIDP Disease Activity Status (CDAS) score, prior CIDP medication
- Screening tests: serology testing for infections: HIV (Ag/Ab test) (CD4 count to be analyzed in case of positive HIV), Viral Hepatitis (HBsAg, anti-HBc Ab, Anti-HBs, Anti-HCV Ab [HCV RNA if reactive]), Tuberculosis (Quantiferon and other tests if available, e.g. IGRA or T-SPOT); pregnancy tests: serum pregnancy test at screening, urine pregnancy test during the study
- Suicidality assessment: Columbia-suicide severity rating scale (C-SSRS) at screening (lifetime suicidal risk), consisting of two parts: suicidal behavior and suicidal ideation
- Total Inflammatory Neuropathy Cause and Treatment (INCAT) score, I-RODs and mean grip strength at Stage A baseline

The following parameters will be available for Stage B:

- Total Inflammatory Neuropathy Cause and Treatment (INCAT) score, I-RODs and mean grip strength at Stage B baseline.
- Stratification factors, as randomized (based on CRF form 'Randomization (IRT)'):
  - Decrease of adjusted INCAT score during Stage A (No change in adjusted INCAT score during Stage A, Adjusted INCAT score decrease of >= 1 point during Stage A);
  - Prior CIDP medication (treatment-naïve, corticosteroids, IVIg or SCIg).

3.3.2 Derivation rules

The following parameters will be derived:

- Age group at informed consent: 18 - < 65 years, ≥ 65 years.
- Body weight at screening: <50, 50-<75, 75-<100, 00-<125, ≥ 125
- Body mass index (BMI) at screening (kg/m²) = (body weight at screening (kg)) / (height (m))²

Note: The BMI will be rounded as detailed in section 2.4.4.

- BMI at screening: Underweight: < 18.5 kg/m^2; Normal weight: 18.5 -< 25 kg/m^2; Overweight: 25 -< 30 kg/m^2; Obese: >= 30 kg/m^2
- Region: North-America (USA, Canada), Asia (China, Japan, Taiwan), Europe (EU, UK, EEA, EFTA countries), ROW (rest of world; incl. Ukraine, Russian Federation, Georgia, Israel, Serbia, Turkey).
- Race: White, Black or African American, Asian, other.
- Japanese (based on CRF question 'Does the patient fulfill the criteria to be considered a Japanese participant at screening?'): Japanese, non-Japanese
- Mainland Chinese: any participant enrolled by an investigational site located in mainland China and with a race "Chinese": Mainland Chinese, non- Mainland Chinese
- East-Asian: any participant enrolled by an investigational site located in East Asia (mainland China, Taiwan, Japan), and with a race "Asian": East-Asian, non-East-Asian
- Time since CIDP diagnosis (years): (date of ICF – date of CIDP diagnosis)/365.25

Notes:

- Partially missing dates will be imputed as detailed in section 2.4.2.
- Result will be rounded as detailed in section 2.4.4.

- CDAS score at screening: 1, 2 – 4, 5.
- Prior CIDP medication (based on CRF form 'CIPD disease history'):
  - Treatment-naïve;
  - Corticosteroids: Pulsed corticosteroid treatment or oral corticosteroids equivalent to prednisolone/prednisone <10 mg/day within 6 months prior to screening;
  - IVIg or SCIg: IVIg or SCIg treatment within 6 months prior to screening.
- Adjusted INCAT score: see efficacy section 4.1.2.3.1.

The following parameters will be derived for Stage B:

- Stratification factors, actual values:
  - Decrease of adjusted INCAT score during Stage A (as derived for the primary endpoint) :
    - No change in adjusted INCAT score during Stage A: change in adjusted INCAT score of 0 or an increase (worsening) of ≥1 point;
    - Confirmed adjusted INCAT score decrease of ≥1 point during Stage A.
  - Prior CIDP medication (based on CRF form 'CIPD disease history'): see above.
- Change in adjusted INCAT score during Stage A (based on Stage A last assessment (see section 2.3.7) compared to Stage A baseline):
  - Worsening: adjusted INCAT score increase of ≥1 point;
  - No change: adjusted INCAT score change of 0 points;
  - Improvement: adjusted INCAT score decrease of ≥1 point.

3.3.3 Presentation of results

Demographics will be presented using descriptive statistics for age, height, weight and BMI and frequency tabulations for age group, sex, categorized weight, race, categorized race, ethnicity, region, Japanese vs non-Japanese, Mainland Chinese vs non-Mainland Chinese and East-Asian vs non-East Asian. The table will be shown for SAF-A, SAF-B and mITT.

Baseline disease characteristics will be presented using descriptive statistics for time since diagnosis and frequency tabulations for CIDP type and subtype, CIDP disease evolution, CDAS score, categorized CDAS score and prior CIDP medication at screening and descriptive statistics for total INCAT disability score, I-RODS and mean grip strength in dominant/non-dominant hand at baseline.

In addition, the Stage A table will include a frequency tabulation for participants who entered Stage A from screening (treatment-naïve (with or without documented evidence for worsening on the adjusted INCAT score within 3 months prior to screening) and not treatment naïve) and for participants who entered Stage A from run-in (with or without evidence for ECMD).

In addition, the Stage B table will include a frequency tabulation of the entry status in stage B (participants who entered stage B with versus without evidence of ECI in stage A).

In addition, the Stage B table will include a frequency tabulation for the stratification factors (as randomized and actual values) and change in adjusted INCAT score during Stage A category (worsening/no change/improvement).

Baseline disease characteristics will be shown for SAF-A (Stage A; including values at screening and Stage A baseline), SAF-B and mITT (Stage B; including values at screening and Stage B baseline).

All demographic data and baseline disease characteristics will be listed. Listings will also be created for screening tests, pregnancy tests and suicidality (only for participants with any positive answer).

3.4 MEDICAL HISTORY AND CONCOMITANT DISEASES

3.4.1 Available data

Medical history findings are coded using the medical dictionary for regulatory activities (MedDRA) into system organ classes and preferred terms. For each finding, a start and stop date or ongoing flag is collected.

3.4.2 Derivation rules

All findings will be allocated into one of the following categories:

- Medical history: finding ended before informed consent date (not ongoing at screening)
- Concomitant disease: finding ended after informed consent date (still ongoing at screening)

3.4.3 Presentation of results

Summary tables for medical history and concomitant diseases will be created (separately) showing the number and percentage of participants by MedDRA system organ class and preferred term for SAF-A and SAF-B.

All medical history and concomitant disease data will be listed.

3.5 PRIOR AND CONCOMITANT THERAPIES AND PROCEDURES

3.5.1 Available data

All therapies are coded using WHO-DRUG. ATC selection is performed. ATC coding up to level 4 is available in the clinical database. For each therapy, a start date or prior flag and stop date or ongoing flag are collected.

Procedures are coded using the medical dictionary for regulatory activities (MedDRA) into preferred terms. For each finding, the indication and a start and stop date are collected.

3.5.2 Derivation rules

Based on their start and stop date, therapies and procedures will be allocated to each phase and period during which they were administered. A therapy/procedure can therefore be reported in more than one phase and period.

Phases and periods are defined in section 2.3.1. Therapies/procedures with (partially) missing dates will be allocated to each phase and period unless the available parts of the therapy/procedure start or stop date or prior and ongoing flags provide evidence the therapy/procedure was not taken during that phase and period.

All therapies will be allocated into one or both of the following categories:

- Prior: the therapy strictly started before the first dose date in Stage A;
- Concomitant: the therapy was taken on or after the first dose date in Stage A.

A medication that started before the first dose date in Stage A and continued during the study will be classified as both prior and concomitant.

The number of types of prior CIDP therapies will be derived for each participant as the number of distinct ATC class level 4 prior therapies with indication CIDP, and categorized into 1, 2, 3, ≥4 types of medication.

3.5.3 Presentation of results

Summary tables for prior and concomitant therapies will be created (separately) showing the number and percentage of participants by ATC class (level 1 and level 3) and generic term for SAF-A and SAF-B. Tables for concomitant therapy will only include concomitant therapy allocated to Stage A for SAF-A and concomitant therapy allocated to Stage B for SAF-B.

A frequency table will be created showing the categorized number of types of prior CIDP therapies by prior CIDP medication at screening (treatment-naïve, corticosteroid or IVIg or SCIg) for SAF-A and SAF-B.

All prior and concomitant therapies data will be listed. All prior and concomitant procedures data will be listed.

3.6 STUDY DRUG ADMINISTRATION

3.6.1 Available data

For each study drug administration, the mode of administration, the start and end date/times and the volumes will be recorded.

Participants may follow a self-administration training. Visits at which training took place, reasons for not following a training and training format are recorded.

3.6.2 Derivation rules

The following parameters will be derived separately for Stage A efgartigimod PH20 SC administration and Stage B IMP administration:

- Treatment duration (weeks) = (last study drug administration date in stage - first study drug administration date in stage + 1) / 7.
- Treatment duration in Stage A, categories:
  - 0 – 4 weeks
  - >4 – 8 weeks
  - >8 weeks
- Treatment duration in Stage B, categories:
  - 0 – 8 weeks
  - >8 – 26 weeks
  - >26 weeks
- Number of administrations: sum of all administrations of IMP.
- The IMP dose in mg will be derived from the volume administered and concentration: Dose administered (mg) = actual volume administered (mL) x concentration (mg/mL).

  The target dose is 1000 mg. The dose administered will be classified in the following categories:
  - Underdose: < -10% of the target dose, i.e. < 900 mg;
  - [-10%, 10%] of target dose, i.e. [900 mg, 1100 mg];
  - Overdose: > 10% of the target dose, i.e. > 1100 mg.
- Treatment compliance = (number of doses actually received / number of expected doses)*100. The number of expected doses (one dose per week) = = uprounded value of treatment duration (weeks).

The following parameter will be derived only for Stage B IMP administration:

- Temporary treatment interruption (yes/no): yes if the participant has a protocol deviation indicating temporary treatment interruption during Stage B, no otherwise. Per protocol a treatment interruption is considered a deviation if the participant missed more than 2 consecutive doses or more than 10% of the total planned doses.

The following parameters will be derived for IMP self-administration training for Stage A and Stage B combined:

- Total number of training visits conducted, total number of training visits conducted where staff demonstrated self-administration to participant and total number of trainings visits conducted where participant practiced self-administration under supervision.
- Number of training visits conducted before being considered capable to self-administer, categorized into 1, 2-4, 5-10, >10 training visits.
- Training compliance (before becoming capable to self-administer) = number of on-site study visits where training for self-administration was completed / total number of on-site study visits * 100. Note: assume training is mandatory until participant is considered capable of self-administration.

3.6.3 Presentation of results

Study drug administration will be summarized separately for Stage A efgartigimod PH20 SC administration (SAF-A) and Stage B IMP administration (SAF-B and mITT).

Study drug administration will be presented using descriptive statistics for the treatment duration, the total number of administrations and treatment compliance. A frequency tabulation will be presented for the treatment duration categories, for the number of participants with treatment administered by analysis visit and for the number of doses with target dose, overdose or underdose.

For Stage B IMP administration two additional summaries will be created:

- the number of participants with a temporary interruption from IMP will be tabulated;
- the number of participants per mode of administration (at the site during a study visit, by home nurse or qualified person, or at site by concierge service) will be tabulated by analysis visit.

IMP self-administration training will be presented for SAF-AB. A frequency tabulation will be created for the number of participants receiving training (at least once) and (of those trained) the number of participants considered capable to perform self-administration (at least once). Descriptive statistics will be presented for the total number of trainings conducted (overall and by training format), the number of training visits before being considered capable to self-administer and a frequency tabulation of its categorized value and descriptive statistics for training compliance.

All data on study drug administration data and self-training administration will be listed.

4. EFFICACY, PHARMACOKINETIC, PHARMACODYNAMIC AND IMMUNOGENICITY ANALYSES

4.1 EFFICACY

4.1.1 Available data

Efficacy will be assessed using total INCAT disability score, Medical Research Council (MRC) sum score, Inflammatory Rasch-built Overall Disability Scale (I-RODS), mean grip strength (MGS) and Timed Up and Go (TUG) test.

Mean grip strength collected in a different unit than kPa will not be used for analysis or listings. Mean grip strength results will be evaluated separately for left hand and right hand and will be presented by dominant hand versus non-dominant hand. The dominant hand is determined based on the first assessment in the study.

4.1.2 Stage A

4.1.2.1 PRIMARY ENDPOINT

The primary endpoint of Stage A is the percentage of participants with confirmed ECI during Stage A (ECI responders) (see section 4.1.2.3.3).

4.1.2.2 STATISTICAL HYPOTHESIS

The percentage of ECI responders on efgartigimod PH20 SC will be summarized using an exact Clopper-Pearson 2-sided 95% CI. This 95% two-sided Clopper-Pearson CI will be used to compare the results of this study with results obtained in historical controls (see Appendix 10.5)

4.1.2.3 SECONDARY ENDPOINTS

The secondary endpoints of Stage A are:

- Time to initial confirmed ECI during Stage A
- Change from Stage A baseline over time during Stage A in:
  - Adjusted INCAT score
  - MRC Sum score
  - 24-item I-RODS disability scores
  - TUG score
  - Mean grip strength assessed by Martin vigorimeter

Total MRC sum score (range: 0 - 60), I-RODS centile metric score (range: 0 – 100), TUG test score (seconds) and mean grip strength (kPa) of each hand will be used as collected, unless mentioned otherwise.

4.1.2.4 DERIVATION RULES

Stage A efficacy derivations will only use assessments in the Stage A analysis period and derivations using baseline will use R1-baseline (run-in phase) or Stage A baseline.

Adjusted INCAT disability score, ECMD and ECI will be programmatically rederived based on the methods described in this SAP.

Except for the time to first improvement and time to initial confirmed ECI during Stage A, analysis visits are considered as described in section 2.3.4.

4.1.2.4.1 Adjusted INCAT disability score

Adjusted INCAT disability score will be derived as equal to the total INCAT raw score (range: 0 – 10) except: INCAT upper extremity score that changed from 0 to 1 or from 1 to 0 with respect to RI-baseline (run-in phase) or baseline (Stage A period) will not be incorporated into the adjusted INCAT score:

- If the arm grade = 0 at baseline changes to arm grade = 1 at a post-baseline visit, this change in arm grade is ignored and thus the adjusted INCAT score at this visit is 1 less than the total INCAT score;
- If the arm grade = 1 at baseline changes to arm grade = 0 at a post-baseline visit, this change in arm grade is ignored and thus the adjusted INCAT score at this visit is 1 more than the total INCAT score.

The INCAT score at baseline (RI-baseline or Stage A baseline) is always the total INCAT score. In addition, the adjusted INCAT score change from baseline is to be calculated as: adjusted INCAT at the visit - total INCAT at the corresponding baseline.

4.1.2.4.2 ECMD

ECMD during the run-in phase will be derived from the adjusted INCAT disability score, I-RODS centile metric score and mean grip strength of either right or left hand.

The ECMD derivation will be based on the worst assessment of the run-in phase (in theory it should be the last assessment in the run-in phase), including unscheduled assessments. The participant self-assessments which are not performed on site (denoted by a missing CRF visit) will not be used. For the table of ECI by way of deterioration, the participants will be classified as follows:

Naïve participants with documented evidence for worsening on the adjusted INCAT score within 3 months prior to screening: participants who skip the run-in phase

Non-naïve participants or naïve participants without documented evidence for worsening on the adjusted INCAT score within 3 months prior to screening: participants who enter the run-in phase:

- Worsening on adjusted INCAT: participants with the worst case in run-in phase adjusted INCAT score increase of ≥1 point from the first run-in visit.
- No change on adjusted INCAT: participants with the worst case in run-in phase adjusted INCAT score increase <1 point from the first run-in visit:
  - Worsening on I-RODS only: participants with the worst case in run-in phase I-RODS decrease of ≥4 points (using the centile metric) and the worst case in run-in phase mean grip strength decrease of < 8 kPa in both hands from the first run-in visit;
  - Worsening on grip strength only: participants with the worst case in run-in phase I-RODS decrease of < 4 points and the worst case in run-in phase mean grip strength decrease of ≥8 kPa in at least one hand from the first run-in visit;
  - Worsening on I-RODS and grip strength: participants with the worst case in run-in phase I-RODS decrease of ≥4 points (using the centile metric) and the worst case in run-in phase mean grip strength decrease of ≥8 kPa in at least one hand from the first run-in visit.

4.1.2.4.3 ECI, confirmed ECI and first improvement

ECI

ECI will be derived from the adjusted INCAT disability score, I-RODS centile metric score and mean grip strength of either right or left hand, using all scheduled and unscheduled visits.

ECI is determined during Stage A and is defined as follows:

<u>For participants with run-in phase:</u>

Participants who deteriorate in adjusted INCAT score during the run-in phase (increase ≥1 point versus the first visit of the run-in phase [RI-baseline]) that show improvement in adjusted INCAT score during Stage A (decrease ≥1 point versus Stage A baseline).

For participants who have no change in adjusted INCAT score during the run-in phase and deteriorated on I-RODs and/or grip strength:

- When improvement on the adjusted INCAT score (decrease ≥1 point) versus Stage A baseline is observed.
- When no change in adjusted INCAT score is observed during Stage A and:
  - When improvement during Stage A on I-RODS (increase ≥4 points versus Stage A baseline) is observed in case deterioration on only I-RODS (decrease ≥4 points) was observed during run-in;
  - When improvement during Stage A on grip strength (increase ≥8 kPa versus Stage A baseline in at least one hand) is observed in case deterioration on only grip strength (decrease ≥8 kPa) was observed during run-in;

- When improvement during Stage A on either I-RODS (increase ≥4 points versus Stage A baseline) and/or grip strength (increase ≥8 kPa versus Stage A baseline in at least one hand) is observed in case deterioration was observed on both I-RODS (decrease ≥4 points) and grip strength (decrease ≥8 kPa) during run-in.

  In the analysis, distinction will be made between whether improvement was on "I-RODS only", "MGS only" or on "I-RODS and MGS", based on what is observed in stage A.

For participants without run-in phase:

Naïve participants, who did not enter the run-in phase and who show improvement during Stage A of at least 1 grade on the adjusted INCAT score (i.e., decrease by ≥1 point) compared to Stage A baseline.

CONFIRMED ECI

Confirmed ECI is defined as fulfilling the criteria for improvement (ECI) at 2 consecutive visits on the same efficacy parameter (with no missed CRF visit(s) in between). Additionally, the participant must have received at least 4 doses. Confirmed ECI will be derived based on the scheduled and unscheduled visits as collected per CRF.

In case, an improvement is observed on different parameters at different points in time, first the first improvement in time, regardless of which parameter the participant improves on, will be considered for assessment of confirmed improvement, and only if confirmed improvement can not be concluded on the first timepoint, the improvement at the next timepoint will be considered for assessment of confirmed improvement.

For mean grip strength, an improvement in one hand, followed at the next visit by an improvement in the other hand, is also considered as a confirmed improvement.

A participant is considered an ECI responder if they show confirmed ECI at least once during Stage A. Participants without a baseline assessment will be considered as ECI non-responders.

FIRST IMPROVEMENT

Improvement can occur on any of the following efficacy parameters, regardless of the participant's way of ECMD deterioration: adjusted INCAT score (decrease ≥1 point versus Stage A baseline), I-RODS (increase ≥4 points versus Stage A baseline), or grip strength (increase ≥8 kPa versus Stage A baseline in at least one hand).

First improvement is defined as having improvement on the same efficacy parameter at 2 consecutive visits (with no missed CRF visit(s) in between), regardless of the number of doses the participant received.

First improvement and (confirmed) ECI can be on different efficacy parameters.

4.1.2.4.4 Time to initial confirmed ECI

Time to initial confirmed ECI during Stage A (days) = date of first confirmed ECI – date of first administration + 1

Notes:

- Date of first confirmed ECI is the date of first ECI, given that it is followed by a confirmation on the next assessment and the participant has received at least 4 doses.
- If multiple parameters (INCAT, I-RODS and grip strength) fit the ECI criteria on different days, the earliest date at which ECI occurs should be considered.
- Participants who complete Stage A or discontinue the study during Stage A for any reason before experiencing confirmed ECI will be censored at the time of the last observed INCAT, I-RODS or grip strength assessment.

An additional sensitivity analysis will be performed with the following method of censoring:

- Participants who complete Stage A, or, discontinue the study during Stage A due to the occurrence of the 88th event in Stage B before experiencing confirmed ECI, will be censored at the time of the last observed INCAT, I-RODS or grip strength assessment.
- Participants who discontinue the study during Stage A before experiencing confirmed ECI, for any reason other than the occurrence of the 88th event in Stage B, will be censored at Week 12 (day 88, upper limit of the Week 12 analysis visit).

4.1.2.4.5 Time to first improvement

Time to initial first improvement during Stage A (days) = date of first improvement – date of first administration + 1. Note: for this endpoint there is no requirement that the participant received a minimum of 4 doses before ECI can be confirmed.

Notes:

- Date of first improvement is the date of first improvement, given that it is followed by a confirmation on the next assessment.
- If multiple parameters (INCAT, I-RODS and grip strength) fit the improvement criteria on different days, the earliest date at which improvement occurs should be considered.
- Censoring and the censoring date will be derived as described for time to initial confirmed ECI (section 4.1.2.3.4).

4.1.2.4.6 Subgroups

The following subgroups are defined for the Stage A efficacy analysis:

- Confirmed ECI response: ECI responders (response ≤ 4 weeks) / ECI responders (4 weeks < response ≤ 8 weeks) / ECI responders (8 weeks < response < before EOSA) / ECI responders (total) / ECI non-responders.
- Stage A Treatment duration: ≤ 4 weeks / 4 weeks - ≤ 8 weeks) / > 8weeks
- Prior CIDP medication at screening: treatment-naïve / corticosteroids / IVIg or SCIg (see section 3.3.2).
- ECMD worsening on adjusted INCAT: yes/no.
- ECMD worsening on I-RODS (only for I-RODS table): yes/no.
- ECMD worsening on MGS (only for MGS table): yes/no.

Treatment-naïve participants for whom no ECMD is determined will be classified as 'no'.

4.1.2.5 PRESENTATION OF RESULTS AND STATISTICAL ANALYSIS

All Stage A efficacy endpoints are analyzed on the SAF-A population.

A frequency tabulation will be provided for the number and percentage of confirmed ECI responders including an exact two-sided Clopper-Pearson 95% CI. The number and percentage of confirmed ECI responders will also be tabulated by prior CIDP medication at screening (add also exact two-sided Clopper-Pearson 95% CI) and by way of deterioration during the run-in phase. Note the denominator should be the number of all participants in the SAF-A analysis set (within each category for subgroup tables).

As a sensitivity analysis on the primary Stage A endpoint, a frequency tabulation will also be provided for the number and percentage of confirmed ECI responders (and exact two-sided Clopper-Pearson 95% CI), only including participants that were not ongoing in stage A at the time the 88th event in Stage B occurred. This table will be repeated by prior CIDP medication at screening.

As a second sensitivity analysis on the primary Stage A endpoint, a frequency tabulation will be provided for the number and percentage of confirmed ECI responders as assessed by the investigator (with exact two-sided Clopper-Pearson 95% CI).

A frequency tabulation will be provided for the cumulative number and percentage of participants who had confirmed ECI at the current or at an earlier analysis visit by analysis visit. The denominator for the cumulative percentage calculation is the number of participants in the SAF-A analysis set.

The time to initial confirmed ECI will be analyzed using Kaplan-Meier time to event analysis. Separate tables will be prepared for all participants and by prior CIDP medication at screening. The following will be presented:

- Number and percentage of events;
- Number and percentage of censored observations: overall and by censoring reason;
- 25th percentile, median and 75th percentile with 95% CI.
- Estimated percentage of participants with confirmed ECI at Week 12, with 95% confidence interval.

As a sensitivity analysis, these tables will be repeated only including participants that were not ongoing in stage A at the time of the 88th occurred.

Another sensitivity analysis will be performed, applying the alternative way of censoring (participants who discontinue before occurrence of confirmed ECI, for other reasons than the occurrence of the 88 th event in Stage B, will be censored at Week 12 - for details see section 4.1.2.4.4)

The Kaplan-Meier time to event analysis for all participants and by prior CIDP medication at screening will be repeated for time to first improvement.

A cross-tabulation will be prepared for way of ECMD deterioration during the run-in phase versus way of initial confirmed ECI during Stage A. The denominator for the percentage is the total number of participants per way of ECMD deterioration during the run-in phase and in the SAF-A analysis set.

Adjusted INCAT disability score, MRC total scores, I-RODS centile metric score, TUG test score and mean grip strength (dominant hand and non-dominant hand) will be summarized by means of descriptive statistics at each analysis visit and at the last assessment (see section 2.3.7). Actual values and changes from baseline will be tabulated. Changes from baseline will be calculated with reference to Stage A Baseline for the Stage A assessments. Run-in assessments will not be shown in the efficacy tables.

Descriptive statistics for secondary endpoints, except MRC and TUG, will be repeated by subgroups (see section 4.1.2.3.6).

All ECI related data will be listed, including the way of ECMD during the run-in phase and the time to first improvement and the time to initial confirmed ECI. Improvement (decrease INCAT>=1; increase IRODS>=4; increase mean grip strength>=8 kPa on either hand) versus Stage A baseline will also be flagged in the listings. The ECI overall assessment by the investigator will be listed as well.

Separate listings will be prepared for the other efficacy endpoints.

4.1.3 Stage B

4.1.3.1 PRIMARY ENDPOINT

The primary endpoint of Stage B is time to first adjusted INCAT deterioration (clinical deterioration) compared to Stage B baseline.

4.1.3.2 PRIMARY ESTIMAND AND STATISTICAL HYPOTHESIS

The primary objective of Stage B is to determine the efficacy of efgartigimod PH20 SC compared to placebo based on the time needed for the occurrence of the first evidence of clinical deterioration. To accomplish this objective the following primary estimand is constructed in accordance with the ICH E9 (R1) addendum:

- Treatment: efgartigimod PH20 SC versus placebo;
- Population: mITT population, as described in section 2.2.1;
- Endpoint: time to first adjusted INCAT deterioration compared to Stage B baseline (clinical deterioration).

The main intercurrent events (ICEs) are:

- Early withdrawal from study for efficacy related reason, due to COVID-19 infection or for other reason;
- Temporary treatment interruption or treatment discontinuation;
- Use of prohibited medication;
- Death;
- COVID-19 infection.

Details on the endpoint derivation can be found in section 4.1.3.4.2. Details on handling strategies for the ICEs can be found in the Appendix in section 10.2.

- Summary measure: hazard ratio for efgartigimod PH20 SC versus placebo model with Wald-type 95% CI. Details on the estimator and statistical inference can be found in section 4.1.3.5.

The primary hypothesis for stage B evaluates this estimand:

- Null hypothesis: The event rate of efgartigimod PH20 SC compared to placebo is 1 (ie, hazard ratio = 1)

- Alternative hypothesis: The event rate of efgartigimod PH20 SC compared to placebo is $\neq 1$ (ie, hazard ratio $\neq 1$)

4.1.3.3 SECONDARY ENDPOINTS

The secondary endpoints of Stage B are:

- Time to CIDP disease progression (defined by the time from first dose of double-blind IMP to the first I-RODS score decrease ≥ 4 points compared to Stage B baseline using the centile metric).
- Percentage of participants with improved functional level (compared to Stage B baseline) as measured by an increase in the 24-item I-RODS score up to week 48.
- Changes from Stage B baseline over time in:
  - Adjusted INCAT score;
  - MRC Sum score;

- 24-item I-RODS disability scores;
- TUG score;
- Mean grip strength assessed by Martin vigorimeter.

- Changes from Stage A baseline over time for participants randomized to efgartigimod PH20 SC in:
  - Adjusted INCAT score;
  - MRC Sum score;
  - 24-item I-RODS disability scores;
  - TUG score;
  - Mean grip strength assessed by Martin vigorimeter.
- Time to 10% decrease in I-RODS in Stage B.

4.1.3.4 DERIVATION RULES

Stage B efficacy derivations will only use assessments in the Stage B analysis period and derivations using baseline will use Stage B baseline, unless otherwise specified.

Adjusted INCAT disability score and adjusted INCAT deterioration will be programmatically rederived based on the methods described in this SAP.

Except for the time to parameters, analysis visits are considered as described in section 2.3.4.

4.1.3.4.1 Adjusted INCAT disability score

Adjusted INCAT disability score will be derived similar as described in section 4.1.2.3.1. The score will be derived twice:

- Adjusted using Stage A baseline. Changes from baseline will be calculated using Stage A baseline.
- Adjusted using Stage B baseline. Changes from baseline will be calculated using Stage B baseline.

The adjusted INCAT disability score using Stage B baseline will be used for the Stage B efficacy derived parameters. The adjusted INCAT disability score using Stage A baseline will only be shown in descriptive summaries and listings.

4.1.3.4.2 Time to first adjusted INCAT deterioration

Primary Analysis:

The primary endpoint of Stage B is the time to first adjusted INCAT deterioration compared to Stage B baseline (clinical deterioration). The time is defined as number of days from first dose of double-blind (Stage B) IMP to the first occurrence of either

- an increase (i.e. worsening) of the adjusted INCAT score of 1 point, if the deterioration is confirmed at the next visit;
- an increase of the adjusted INCAT score of at least 2 points, with no confirmation required at the next visit.

Time to deterioration: Date (first visit with adjusted INCAT deterioration) – Date (first dose of Stage B IMP) + 1.

All observed data will be considered, not only assessments closest to the target date.

Clinical deterioration will only consider adjusted INCAT score. Participants who complete the study or withdraw for any reason before experiencing adjusted INCAT deterioration will be censored at the time of last observed INCAT assessment. Participants who withdraw without any post-baseline INCAT assessments will be censored at time of first dose. Censoring is considered non-informative.

For the primary estimand of time to first adjusted INCAT deterioration all data will be used as stipulated above. The main ICEs and their analysis strategy for sensitivity analysis are defined below. The following sensitivity analyses will be conducted to investigate the effect of different ways of handling ICEs.

Extreme Case Analysis:

Following ICEs will be considered as an event in addition to the primary analysis:

- death or withdrawal from the study for any reason (except participants withdrawn from study because of the occurrence of the 88 th event in Stage B).
- Participants who have to discontinue the study early when the study is stopped (when all 88 events for the primary analysis are achieved) and who have an increase of the adjusted INCAT score of 1 point at their final INCAT assessment without a followed confirmation will also be considered as having an event of clinical deterioration.

Mixed-case analysis:

Following ICEs will be considered as an event in addition to the primary analysis:

- death or withdrawal from study for efficacy related reason (participant lost to follow-up, consent withdrawn, physician's decision, prohibited medication, lack of treatment efficacy).
- Participants who have to discontinue the study early when the study is stopped (when all 88 events for the primary analysis are achieved) and who have an increase of the adjusted INCAT score of 1 point at their final INCAT assessment without a followed confirmation will also be considered as having an event of clinical deterioration.

[redacted]

Note: as the considered ICEs occur at the end of the study, the time-to variable will be kept as in the primary analysis (at last INCAT assessment), only the event status will be changed from censored to event.

Additional sensitivity analysis - Investigator's assessment

The primary analysis will be repeated by using the investigator's assessment of clinical deterioration as recorded in the CRF (i.e. not programmatically derived).

Based on investigator's assessment: clinical deterioration will be based on the investigator's assessment of Stage B deterioration. Time to deterioration will be

calculated based on the first visit where the investigator indicated clinical deterioration, if the deterioration is confirmed at the next visit. If no clinical deterioration is indicated by the investigator, the time to deterioration will be censored at the date of the last available investigator's assessment. Participants who withdraw without any post-baseline investigator assessments will be censored at time of first dose.

4.1.3.4.3 Time to CIDP disease progression

Time to CIDP disease progression is defined as number of days from first dose of double-blind (Stage B) IMP to the first visit with I-RODS score decrease of ≥4 points (i.e. worsening) compared to Stage B baseline (using the centile metric).

Time to CIPD disease progression: Date (first visit with I-RODS score decrease of ≥4 points) – Date (first dose of Stage B IMP) + 1.

All observed data will be considered, not only assessments closest to the target date.

Participants who complete the study or withdraw for any reason without experiencing CIDP disease progression will be censored at the time of last observed I-RODS assessment.

4.1.3.4.4 Improved functional level

Participants are considered as having improved functional level if they have at least one Stage B assessment with an increase (i.e. improvement) in I-RODS score of ≥4 points compared to Stage B baseline (using the centile metric). All Stage B I-RODS assessments up to analysis visit week 48 will be considered.

4.1.3.4.5 Time to 10% decrease in I-RODS

Time to 10% decrease in I-RODS is defined as number of days from first dose of double-blind (Stage B) IMP to the first visit with I-RODS score decrease of 10% (i.e. worsening) compared to Stage B baseline (using the centile metric).

Time to 10% decrease in I-RODS: Date (first visit with I-RODS score decrease of 10%) – Date (first dose of Stage B IMP) + 1.

All observed data will be considered, not only assessments closest to the target date.

Participants who complete the study or withdraw for any reason without experiencing a 10% decrease in I-RODS will be censored at the time of last observed I-RODS assessment.

4.1.3.4.6 Subgroups

The following subgroups are defined for the Stage B efficacy analysis (see section 3.3.2 for derivation rules):

- Sex at birth: Male / Female.
- Region: North-America / Asia / Europe / ROW (rest of world).
- Race: White / Black or African American / Asian / Other.
- Age group: 18 - < 65 years / ≥ 65 years.
- Body weight: <50, 50-<75, 75-<100, 00-<125, ≥ 125
- BMI at screening: Underweight: < 18.5 kg/m^2; Normal weight: 18.5 -< 25 kg/m^2; Overweight: 25 -< 30 kg/m^2; Obese: >= 30 kg/m^2
- CDAS score at screening: 1 / 2 – 4 / 5.
- Stage B Treatment duration: ≤ 8 weeks / 8 weeks - ≤ 26 weeks / > 26 weeks (descriptive statistics over time only)

Subgoups with less than 10 participants in total will not be shown for subgroup analyses.

4.1.3.5 PRESENTATION OF RESULTS AND STATISTICAL ANALYSIS

All Stage B efficacy endpoints are analyzed on the mITT population, with exception of the sensitivity analyses on the PP as specified below.

Statistical comparisons will be made using 2-sided tests at the 0.05 significance level.

Time to first adjusted INCAT deterioration compared to Stage B baseline will be analyzed using a Cox proportional hazard model (main estimator for the primary estimand) with a fixed categorical effect for treatment (with placebo as reference). The model will be stratified by prior CIPD medication and decrease of adjusted INCAT score during Stage A. The hazard ratio for efgartigimod PH20 SC versus placebo model will be provided along with the corresponding Wald-type 95% CI and 2-sided p-value at the 0.05 significance level. The primary endpoint will be tested using this p-value for the hazard ratio (testing H0: HR = 1, as described in section 4.1.3.2)

The proportional hazard (PH) assumption will be assessed within each stratum using a log-log plot of the survival function and by plotting the Schoenfeld residuals over time. In case of substantial deviation of the PH assumption, additional analysis may be considered to assess the robustness of the analysis. If a treatment by time interaction is apparent, a piecewise survival analysis may be implemented to describe the treatment effect (HR) over time. If deemed applicable, the HR over time may be evaluated based on the ratio of the smoothed instantaneous hazard in the treatment and the placebo arm. More specifically, graphs will be created with [(1 minus ratio (EFG/placebo) of smoothed instantaneous hazard by time t) ×100%] and accompanying pointwise and simultaneous $(1 - \alpha\alpha) \times 100\%$ CIs over time since start of stage B (Gilbert et al., 2002).

A Kaplan-Meier time to event analysis for time to adjusted INCAT deterioration will also be provided. The number and percentage of events and censored observations (overall and by censoring reason), median and percentiles with 95% CI and the log-rank test (stratified for prior CIPD medication and decrease of adjusted INCAT score during Stage A) will be provided. In addition, the estimated percentage of participants with adjusted INCAT deterioration at Week 24 and Week 48, with 95% confidence interval will be provided.

The primary endpoint Kaplan-Meier analysis for time to adjusted INCAT deterioration will be repeated by quartile of each Exposure and Total IgG parameter derived from the population PK/PD model, as described in section in sections 4.2 and 4.3. The analysis will be presented separately for the efgartigimod PH20 SC and placebo treatment groups.

The Cox proportional hazard model and Kaplan-Meier analysis for time to adjusted INCAT deterioration will be repeated (sensitivity analyses):

- Analysis will be repeated on the PP population;
- Analysis will be repeated on the mITT population, but excluding participants who did not have confirmed ECI in Stage A;
- Analysis will be repeated using the sensitivity endpoints for time to deterioration (extreme-case analysis, mixed-case analysis, based on investigator's assessment) as described in section 4.1.3.4.2;
- Analysis will be repeated using actual stratification values.
- Analysis will be repeated by stratification factors:
  - Prior CIPD medication at screening: treatment-naïve / corticosteroids / IVIg or SCIg;
  - Decrease of adjusted INCAT score in Stage A: no change / decrease of ≥ 1 point;

  Note: the stratification by which the analysis is repeated will not be included in the Cox proportional hazard model.
- Analysis will be repeated by subgroups (section 4.1.3.4.6):

The proportion of participants with adjusted INCAT deterioration will be compared between treatment groups via the risk difference with an exact 95% confidence interval and a Fisher Exact test.

Time to CIDP disease progression will be analyzed using a Cox proportional hazard model as described for the main estimand for the primary endpoint, including the assessment and testing of the PH assumption. This analysis will be done overall and by stratification factors, but p-values will only be reported for the overall analysis.

In addition, the time to CIDP disease progression will be analyzed using Kaplan-Meier time to event analysis. The number and percentage of events and censored observations (overall and by censoring reason), median and percentiles with 95% CI will be provided. In addition, the estimated percentage of participants with CIDP disease progression at Week 24 and Week 48, with 95% confidence interval will be provided.

This analysis will be done overall and by stratification factors.

Improved functional level will be analyzed using an exact logistic regression model with fixed categorical effect for treatment and stratified by stratification factors. The odds ratio for efgartigimod PH20 SC versus placebo will be reported together with its 95% CI and 2-sided p-value (exact clopper-pearson test). This analysis will be done overall and by stratification factors.

The time to 10% decrease in I-RODS will be analyzed using Kaplan-Meier time to event analysis. The number and percentage of events and censored observations (overall and by censoring reason), median and percentiles with 95% CI will be provided.

Adjusted INCAT disability score, MRC total scores, I-RODS centile metric score, TUG test score and mean grip strength (dominant hand and non-dominant hand) will be summarized by means of descriptive statistics at each analysis visit. Actual values, changes from Stage A baseline and changes from Stage B baseline will be tabulated.

For all secondary endpoints, a similar table will be prepared but showing the actual values, changes from Stage A baseline and changes from Stage B baseline limited to the timepoints Stage A baseline, Stage B baseline and last assessment (see section 2.3.7).

For adjusted INCAT disability score, a similar table will be prepared but showing the actual values and changes from Stage A baseline at Stage A baseline and at best-improvement (see section 2.3.6).

Descriptive statistics for adjusted INCAT score will be repeated by stratification factors.

If COVID-19 infection occurs in >10% of mITT participants, summaries might be added to explore the impact of COVID-19 on the efficacy analysis.

All efficacy data will be listed, including derived endpoints.

4.1.4 Stage A+B

4.1.4.1 PRESENTATION OF RESULTS

Adjusted INCAT disability score, MRC total scores, I-RODS centile metric score, TUG test score and mean grip strength (dominant hand and non-dominant hand) will be summarized by means of descriptive statistics at each analysis visit. Actual values and changes from Stage A baseline will be tabulated.

4.2 PHARMACOKINETICS

PK and PK/PD modelling analyses will be described in a separate SAP.

A population PK/PD model will be generated, from which the following PK parameters will be derived on a participant level:

Exposure (PK):

- Ctrough at steady-state (CtroughSS)
- Area Under the Curve (AUC) at steady-state (SS)

Additional parameters arising from the population PK/PD model may also be explored.

Subgroup analyses will be performed for selected efficacy endpoints (time to adjusted INCAT deterioration compared to Stage B baseline) and safety endpoints (adverse event overview) by quartiles of the PK parameters.

4.2.1 Available data

Blood samples for determination of serum concentrations of efgartigimod will be collected at the time points indicated in the schedule of assessment (see appendix 10.3).

Two additional PK samples will be taken; i.e., one sample 48 to 96 hours after the 1st IMP injection and one sample 48 to 96 hours after the 4th IMP injection in approximately 10 Japanese participants in Stage A (see appendix 10.3.2).

PK samples will be allocated to the analysis visit windows defined in section 2.3.4. Additionally, time windows for PK samples are specified as follows:

- A Stage A baseline PK sample is taken pre-dose.
- A post-baseline PK sample is taken within 1 week (± 2 days) after the most recent EFG PH20 SC administration. This rule also applies to stage B baseline as it follows after EFG PH20 SC administration in Stage A.
- A Safety FU PK sample is taken within 4 weeks (± 1 week) after the most recent EFG PH20 SC administration.
- 48 to 96 hours PK sample in Japanese participants is taken within 32 and 112 hours after the most recent EFG PH20 SC administration.

All concentration data-points with deviations outside these permitted ranges will be excluded from the descriptive statistics on concentrations, explained by a footnote in the appropriate tables.

4.2.2 Derivation rules

Efgartigimod serum concentrations will be reported in ng/mL by the lab and will be converted to µg/mL for presentation in the analysis (1 ng/mL = 0.001 µg/mL). PK samples with ALQ or BLQ results will be handled as specified in section 2.4.3. Listings will always show the non-imputed original values in ng/mL.

4.2.3 Presentation of results

PK will be shown separately for Stage A (PK-A) and Stage B (PK-B).

Efgartigimod concentration actual values will be summarized by means of descriptive statistics at each analysis visit, except for the 48 to 96 hours time points.

A similar output will be created for Stage A including only Japanese participants and showing all analysis visits, including the 48 to 96 hours time points.

Individual concentration data and actual blood sampling times for PK assessments will be listed.

4.3 PHARMACODYNAMICS

PK and PK/PD modelling analyses will be described in a separate SAP.

A population PK/PD model will be generated, from which the following PD parameter will be derived on a participant level:

Total IgG (PD):

- Area Under the Effect Curve of total IgG percent change from baseline at steady-state (AUECss)

Additional parameters arising from the population PK/PD model may also be explored.

Subgroup analyses will be performed for selected efficacy endpoints (time to adjusted INCAT deterioration compared to Stage B baseline) and safety endpoints (adverse event overview) by quartiles of the PD parameter.

4.3.1 Available data

Pharmacodynamics will be assessed using total IgG.

Available IgG subtype (IgG1, IgG2, IgG3, IgG4) sample results will not be tabulated, and also not shown in listings, since the IgG subtype analysis was removed from the clinical protocol per protocol version 5.0 (amendment 4.0). For Chinese participants only total IgG will be available.

Only total IgG sample results as analyzed by PPD according the IVD method (immunoturbidimetry) will be used in the statistical analysis. Other IgG results will not be included in the analysis and will not be shown in tables or listings.

4.3.2 Derivation rules

PD samples with ALQ or BLQ results will be handled as specified in section 2.4.3. Listings will always show the non-imputed values.

4.3.3 Presentation of results

PD will be shown separately for Stage A (PD-A) and Stage B (PD-B).

Total IgG levels will be summarized by means of descriptive statistics at each analysis visit. Actual values, changes from baseline and percent changes from baseline will be tabulated.

All PD (including IgG subtype) data will be listed.

4.4 IMMUNOGENICITY

4.4.1 Available data

Presence of anti-drug antibodies (ADA) against efgartigimod and presence of antibodies (Abs) against rHuPH20 will be measured.

Immunogenicity samples are analyzed in a 3-tiered approach:

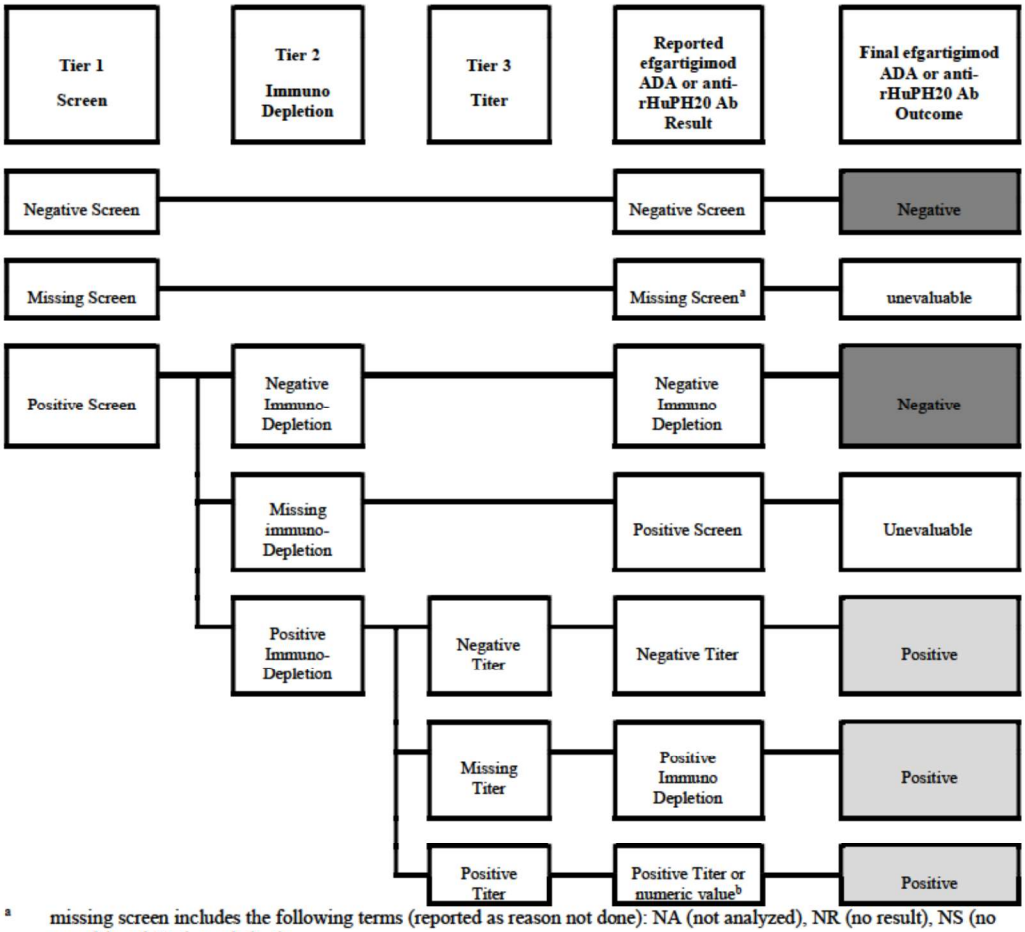
- All samples are evaluated in the efgartigimod ADA or anti-rHuPH20 Ab screening assay and are scored screening positive or negative
- If a sample scored screening positive, it is further evaluated in the confirmatory assay and is scored confirmed positive (positive immunodepletion) or confirmed negative (negative immunodepletion).
- If a sample is scored as confirmed positive, the samples are further characterized in the titration assay (to determine titer) and are also further analyzed in the NAb (neutralizing antibodies) assay to confirm neutralizing activity. For NAb against efgartigimod, a screening assay is performed and results will be reported as negative or positive. For NAb against rHuPH20, the screening NAb assay is followed by a titer NAb assay in case the sample screened positive.

A study-specific cut point may be used in the final analysis, if found needed upon statistical evaluation of the CIDP participant baseline samples, which may change the scoring and titer values of these samples in the final reported dataset (as compared to the results of the interim analysis).

If available, a titer result will be reported for the confirmed positive samples. However, a titer result is not always available:

- In case the confirmed positive sample could not be run in the titration assay (e.g. due to insufficient sample volume/quality to perform the titer analysis), the result will be described as ‘positive immuno-depletion’ and the sample should be considered as positive.
- If a sample is negative in the titration assay, it will be reported as ‘negative titer’ but it should be considered as positive since it was confirmed positive in the second tier.
- If a sample could not be analyzed or reported as ‘positive screen’, the sample status is unevaluable.

An overview of this 3-tiered approach and all possible sample results that will be reported by the laboratory is given below. From these reported efgartigimod ADA or anti-rHuPH20 Ab sample results, a final sample status needs to be derived during the statistical analysis, as presented in the final column ('Final Outcome'):



[a] missing screen includes the following terms (reported as reason not done): NA (not analyzed), NR (no result), NS (no sample) and SL (sample lost).

[b] positive titer' is reported in case it was not possible to retrieve a numeric value.

4.4.2 Derivation rules

4.4.2.1 PARTICIPANT CLASSIFICATION FOR ADA AGAINST EFGARTIGIMOD

The participant classification for ADA against efgartigimod will be determined by evaluating the highest post-baseline ADA sample status versus the baseline ADA sample status, as detailed in Table 4. For Stage A and Stage A+B, the stage A baseline sample status will be used. For Stage B, the Stage B baseline sample status will be used. Stage A and Stage B baseline are defined in section 2.3.2.

Table 4: Participant ADA classification

Participant ADA classification	Highest[c] post baseline sample status				
	ADA negative	**ADA positive (missing titer[a])**	**ADA positive (negative titer[b] or numeric titer)**		**ADA not evaluable**
Baseline ADA sample status					
ADA negative	ADA negative	Treatment Induced ADA	Treatment Induced ADA		*ADA unevaluable*
ADA positive (missing titer[a])	Treatment Unaffected ADA	*ADA unevaluable*	*ADA unevaluable*		*ADA unevaluable*
ADA positive (negative titer[b] or numeric titer)	Treatment Unaffected ADA	*ADA unevaluable*	**titer < 4 x baseline titer:** Treatment Unaffected ADA	**titer ≥ 4x baseline titer:** Treatment Boosted ADA	*ADA unevaluable*
ADA not evaluable	*ADA unevaluable*	*ADA unevaluable*	*ADA unevaluable*		*ADA unevaluable*

[a] Samples with missing titer have as reported ADA result 'positive immunodepletion' or 'positive titer';
[b] Results reported as 'negative titer', i.e. titer value <1 will be set to value of 1;
[c] Highest sample status, with order: (from low to high): ADA unevaluable, ADA negative, ADA positive (missing titer/positive immunodepletion), ADA positive with titer < 1 ('negative titer' as reported ADA result, titer value set to 1), ADA positive with titer ≥ 1 (i.e. numeric titer and selecting the sample with highest titer)

ADA evaluable participant = participant classified as any of following categories according to Table 4: ADA negative, treatment unaffected ADA, treatment induced ADA, treatment boosted ADA.

ADA unevaluable participant = participant classified as ADA unevaluable according to Table 4 or with missing baseline ADA sample or without post-baseline ADA samples

Note: Fourfold difference in titer values is considered significant in case a twofold serial dilution is applied (= two times the dilution factor) (reference to Shankar et al., 2014).

ADA incidence = percentage of participants with treatment-induced or treatment-boosted ADAs (denominator: number of evaluable participants).

ADA prevalence = percentage of participants with treatment-unaffected ADA, treatment-induced ADA or treatment-boosted ADA (denominator: number of evaluable participants).

4.4.2.2 PARTICIPANT CLASSIFICATION FOR ANTIBODIES AGAINST RHUPH20

The participant classification for anti rHuPH20 antibodies (rHuPH20 Ab) will be determined by evaluating the highest post-baseline rHuPH20 Ab sample status versus the baseline rHuPH20 Ab sample status, as detailed in Table 5. For Stage A and Stage A+B, the stage A baseline sample status will be used. For Stage B, the Stage B

baseline sample status will be used. Stage A and Stage B baseline are defined in section 2.3.2.

Table 5: Participant anti-rHuPH20 Ab classification

Participant anti-rHuPH20 Ab classification	**Highest[c] post baseline sample status**				
	rHuPH20 Ab negative	**rHuPH20 Ab positive (missing titer[a])**	**rHuPH20 Ab positive (negative titer[b] or numeric titer)**		**rHuPH20 Ab not evaluable**
Baseline rHuPH20 Ab sample status					
rHuPH20 Ab negative	rHuPH20 Ab negative	Treatment Induced rHuPH20 Ab	Treatment Induced rHuPH20 Ab		rHuPH20 Ab *unevaluable*
rHuPH20 Ab positive (missing titer[a])	Treatment Unaffected rHuPH20 Ab	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*		rHuPH20 Ab *unevaluable*
rHuPH20 Ab positive (negative titer[b] or numeric titer)	Treatment Unaffected rHuPH20 Ab	rHuPH20 Ab *unevaluable*	**titer < 2 x baseline titer:** Treatment Unaffected rHuPH20 Ab	**titer ≥ 2x baseline titer:** Treatment Boosted rHuPH20 Ab	rHuPH20 Ab *unevaluable*
rHuPH20 Ab not evaluable	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*		rHuPH20 Ab *unevaluable*

[a] Samples with missing titer have as reported rHuPH20 Ab result 'positive immunodepletion' or 'positive titer';
[b] Results reported as 'negative titer', i.e. titer value <5 will be set to value of 5;
[c] Highest sample status, with order: (from low to high): rHuPH20 Ab unevaluable, rHuPH20 Ab negative, rHuPH20 Ab positive (missing titer/positive immunodepletion), rHuPH20 Ab positive with titer < 5 ('negative titer' as reported rHuPH20 Ab result, titer value set to 5), rHuPH20 Ab positive with titer ≥ 5 (i.e. numeric titer and selecting the sample with highest titer)

rHuPH20 Ab evaluable participant = participant classified as any of following categories according to Table 5: ADA negative, treatment unaffected rHuPH20 Ab, treatment induced rHuPH20 Ab, treatment boosted rHuPH20 Ab.

rHuPH20 Ab unevaluable participant = participant classified as rHuPH20 Ab unevaluable according to Table 5 or with missing baseline rHuPH20 Ab sample or without post-baseline rHuPH20 Ab samples

Note: Twofold difference in titer values is considered significant in case a twofold serial dilution is applied (reference to Shankar et al., 2014).

Anti-rHuPH20 Ab incidence = percentage of participants with treatment-induced or treatment-boosted rHuPH20 Ab (denominator: number of evaluable participants).

Anti-rHuPH20 Ab prevalence = percentage of participants with treatment-unaffected rHuPH20 Ab, treatment-induced rHuPH20 Ab or treatment-boosted rHuPH20 Ab (denominator: number of evaluable participants).

4.4.2.3 PARTICIPANT CLASSIFICATION FOR NAB AGAINST EFGARTIGIMOD

All ADA confirmed positive samples will also be evaluated in the NAb assay. All samples that were not analyzed in the NAb assay (i.e. the ADA negatives) are per default NAb negative. Also, if a NAb sample is not reported, the NAb sample status is NAb unevaluable.

For NAb against efgartigimod, all samples evaluated in this NAb assay will be scored as NAb positive or NAb negative by the laboratory. Based on these results, the participants will be categorized based on their baseline and post-baseline sample status as detailed in Table 6. For Stage A and Stage A+B, the stage A baseline sample status will be used. For Stage B, the Stage B baseline sample status will be used. Stage A and Stage B baseline are defined in section 2.3.2.

Table 6: Participant NAb classification against efgartigimod

Participant NAb classification	**Highest[a] post baseline NAb sample status**		
	NAb negative	**NAb positive**	**NAb not evaluable**
Baseline NAb sample status			
NAb negative	baseline neg – post-baseline neg	baseline neg – post-baseline pos	*NAb unevaluable*
NAb positive	baseline pos - post-baseline neg	baseline pos – post-baseline pos	*NAb unevaluable*
NAb not evaluable	*NAb unevaluable*	*NAb unevaluable*	*NAb unevaluable*

[a] Highest sample status in order: (from low to high): NAb unevaluable, NAb negative, NAb positive.

NAb unevaluable participant = participant classified as NAb unevaluable according to Table 6 or with missing baseline NAb sample or without post-baseline NAb samples

NAb incidence = percentage of participants with participant classification 'baseline neg – post-baseline pos' and 'baseline pos – post-baseline pos' (denominator: number of evaluable participants).

NAb prevalence = percentage of participants with participant classification 'baseline neg – post-baseline pos', 'baseline pos – post-baseline pos' or 'baseline pos – post-baseline neg'. (denominator: number of evaluable participants).

4.4.2.4 PARTICIPANT CLASSIFICATION FOR NAB AGAINST RHUPH20

All rHuPH20 Ab confirmed positive samples will also be evaluated in the NAb assay. All samples that were not analyzed in the NAb assay (i.e. the rHuPH20 Ab negatives) are per default NAb negative. Also, if a NAb sample is not reported, the NAb sample status is NAb unevaluable.

For NAb against rHuPH20, all samples evaluated in this NAb assay will be scored as NAb negative or NAb positive by the laboratory. In case the sample is NAb positive, a titration assay will occur and the sample will be reported as 'negative titer', 'positive titer' or by an actual titer value. Based on these results, participants will be categorized based on their baseline and post-baseline sample status as detailed in Table 7. For Stage A and Stage A+B, the stage A baseline sample status will be used. For Stage B, the Stage B baseline sample status will be used. Stage A and Stage B baseline are defined in section 2.3.2.

Table 7: Participant classification for NAb against rHuPH20

Participant rHuPH20 NAb classification	**Highest[b] post baseline sample status**				
	rHuPH20 NAb negative	**rHuPH20 NAb positive (missing titer)**	**rHuPH20 NAb positive (negative titer[a] or numeric titer)**		**rHuPH20 NAb not evaluable**
Baseline rHuPH20 NAb sample status					
rHuPH20 NAb negative	rHuPH20 NAb negative	Treatment Induced rHuPH20 NAb	Treatment Induced rHuPH20 NAb		*rHuPH20 NAb unevaluable*
rHuPH20 NAb positive (missing titer)	Treatment Unaffected rHuPH20 NAb	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*		*rHuPH20 NAb unevaluable*
rHuPH20 NAb positive (negative titer[a] or numeric titer)	Treatment Unaffected rHuPH20 NAb	*rHuPH20 NAb unevaluable*	**titer < 2 x baseline titer:** Treatment Unaffected rHuPH20 NAb	**titer ≥ 2x baseline titer:** Treatment Boosted rHuPH20 NAb	*rHuPH20 NAb unevaluable*
rHuPH20 NAb not evaluable	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*		*rHuPH20 NAb unevaluable*

[a] Results reported as 'negative titer', i.e. titer value <100 will be set to value of 100;
[b] Highest sample status, with order: (from low to high): NAb unevaluable, NAb negative, NAb positive with titer <100 ('negative titer' as reported NAb result, titer value set to 100), NAb positive (i.e. numeric tite and selecting the sample with highest titer) .

4.4.3 Presentation of results

Immunogenicity will be shown separately for Stage A (IMM-A), Stage B (IMM-B) and Stage A+B (IMM-AB).

Frequency tabulations (number and percentages) will be provided with ADA or rHuPH20 Ab negative/positive/unevaluable samples per analysis visit. The results will be grouped (columns) by ADA or rHuPH20 Ab participant classification.

Frequency tabulations (number and percentages) will be provided by treatment on:

- participants per ADA or rHuPH20 Ab participant classification
- prevalence and incidence of ADA or rHuPH20 Ab
- ADA or rHuPH20 Ab unevaluable participants
- ADA or rHuPH20 Ab baseline positive/negative/unevaluable samples

For details on the definitions, see the above section 4.4.2.1 and 4.4.2.2.

For Stage A only, the above frequency tabulations will be repeated by prior CIDP medication at screening.

The above frequency tabulations will be repeated for NAb assay using the definitions as defined in section 4.4.2.3 and 4.4.2.4 (no tabulation by prior CIDP medication).

Titer values for ADA and rHuPH20 Ab will be summarized by means of descriptive statistics by ADA or rHuPH20 Ab participant classification respectively.

A frequency tabulation (number and percentages) will be provided for NAb against efgartigimod positive participants within the ADA participant classification (ADA negative, treatment-unaffected ADA, treatment-induced ADA, treatment-boosted ADA, ADA unevaluable).

In addition, for rHuPH20 Ab positive participants, a frequency tabulation (number and percentages) within the ADA against efgartigimod participant classification (treatment-unaffected ADA, treatment-induced ADA, treatment-boosted ADA and ADA unevaluable) will be created.

Correlation tables by ADA participant classification, by NAb against efgartigimod participant classification and by Ab against rHuPH20 participant classification will be provided for the following parameters:

- Stage A efficacy: number and percentage of confirmed ECI responders
- Stage B efficacy: Kaplan-Meier analysis of time to first adjusted INCAT deterioration
- pharmacokinetics: mean drug concentration over time
- pharmacodynamics: mean percent change from baseline in total IgG (also show 95% CI)
- safety: treatment-emergent adverse events by MedDRA system organ class and preferred term
- safety: serious treatment-emergent adverse events by MedDRA system organ class and preferred term
- safety: treatment-emergent IRRs by MedDRA system organ class and preferred term
- safety: treatment-emergent ISRs by MedDRA system organ class and preferred term

Correlation tables for Stage B efficacy, pharmacokinetics and pharmacodynamics will include both treatment groups.

Correlation tables by NAb against efgartigimod participant classification will only be produced if at least 5 positive NAb against efgartigimod participants are observed in any treatment group (positive participant = treatment-induced or treatment-boosted NAb against efgartigimod).

All immunogenicity data will be listed.

5. PATIENT-REPORTED OUTCOMES

5.1 AVAILABLE DATA

The following patient-reported outcomes (PRO) are expected: health-related quality-of-life questionnaire (EQ-5D-5L), [redacted]

5.2 DERIVATION RULES

5.2.1 [redacted]

[redacted]

5.2.2 [redacted]

[redacted]

5.3 PRESENTATION OF RESULTS

Continuous PRO parameters will be summarized by means of descriptive statistics of the actual values and changes from baseline at each analysis visit.

Continuous parameters:

- EQ-5D-5L VAS score
- [redacted]

For [redacted] two tables will be provided: a summary at run-in baseline by prior CIDP medication ([redacted]), and a summary at each post-baseline analysis visits ([redacted]).

For [redacted] actual values are shown (changes from baseline are not applicable to these outcomes).

Categorical PRO parameterswill be summarized in a tabulation of the outcome at each analysis visit. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the analysis set.

Categorical parameters:

- EQ-5D-5L (not VAS)
- [redacted]

- [redacted]
- [redacted]
- [redacted]

In Stage A tables only the baseline and last assessment will be presented (for [redacted] also the assessment on analysis visit Week 1). In Stage B tables, the baseline and all scheduled analysis visits and the last assessment will be presented.

For [redacted], additionally, the number (and %) of participants with [redacted] at each analysis visit will be tabulated.

All PRO data will be listed.

6. SAFETY ANALYSES

6.1 ADVERSE EVENTS

6.1.1 Available data

Adverse events (AEs) are coded into system organ classes and preferred terms using the medical dictionary for regulatory activities (MedDRA). AEs are graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. For each AE, start and stop date/times are collected as well as severity, a seriousness flag, treatment relatedness, relatedness to protocol-required procedures, action taken towards the study drug and outcome.

The occurrence of an infection is an adverse event of special interest (AESI). For AESI the relatedness to the participant's underlying condition, relatedness to the participant's concomitant therapies, recurrence of a previous infection, relatedness to medical history, confirmation by procedure/culture, need for urgent medical intervention and location of infection are also collected.

6.1.2 Derivation rules

Treatment-emergent adverse events (TEAE) are defined as AEs starting on or after first administration of any study drug.

Based on their start date/time, AEs will be allocated to the phase and period during which they started. Each AE will therefore be reported in only one phase and period. Phases and periods are defined in section 2.3.1. In case the AE start date/time is incomplete or missing and the AE could consequently be allocated to more than one phase or period, a worst-case allocation will be done as detailed below:

- Run-in vs. screening phase: the AE will be allocated to the run-in phase unless the available parts of the AE start or stop date/time provide evidence for allocating to the screening phase.
- Treatment phase vs. screening/run-in/follow-up phase: the AE will be allocated to the treatment phase unless the available parts of the AE start or stop date/time provide evidence for allocating to the screening/run-in/follow-up phase.
- Stage A vs. Stage B: the AE will be allocated to Stage B unless the available parts of the AE start or stop date/time provide evidence for allocating to Stage A.
- Multiple 3-monthly periods: the AE will be allocated to the first 3-monthly period that is possible based on the available parts of the AE start and stop date/time.

A fatal AE is defined as an AE with outcome 'fatal' or an AE graded as NCI CTCAE grade 5.

An AE for which the study drug was discontinued is defined as an AE with action taken 'drug withdrawn'.

Treatment relatedness will be dichotomized as follows in tables:

- Treatment-related: related, probably related, possibly related or missing
- Not treatment-related: not related, unlikely related

AESI will be defined using MedDRA system organ class 'Infections and infestations'.

Injection-related reactions (IRRs) will be defined as all AEs with MedDRA preferred terms that are listed in either of the below standardized MedDRA queries (SMQ) :

- Hypersensitivity (SMQ) (broad selection)
- Anaphylactic reaction (SMQ) (broad selection)
- Extravasation events (injections, infusions and implants) (SMQ) (broad selection), excluding preferred terms that refer to implants

AND occurring within 48 hours of an injection, or within 2 days in case no AE start time is available. In case of (partially) missing AE start date, the AE will be considered as an IRR, unless the available parts of the AE start date provide evidence it did not occur within 48 hours of an injection.

Injection site reactions (ISRs) will be defined as all AEs with MedDRA high level term ‘Injection site reactions’ regardless of the time of AE onset relative to an injection.

AE onset and duration will be calculated as follows when start and stop dates are fully known:

- AE onset day vs. first administration in Stage A (ASTDY)
  - AE start date ≥ date of first administration: AE start date – date of first administration + 1 day
  - AE start date < date of first administration: AE start date – date of first administration
- AE onset day vs. start of analysis phase (run-in) or period (Stage A and Stage B) (ASTDYP) = AE start date – analysis phase / period start date + 1 day
- AE duration (days) =
  - AE end date – AE start date + 1 day
  - Study completion date or study discontinuation date – AE start date + 1 day (when the AE start date is fully known but the AE is not resolved at the end of the study)

    In this case the duration will be presented as “>x days”.

Event rates per 100 participant-year of follow-up (PYFU) will be derived separately for Stage A and Stage B, with PYFU defined as:

- For Stage A: (duration of Stage A period + follow-up phase)/365.25 summed over all participants
- For Stage B: (duration of Stage B period + follow-up phase)/365.25 summed over all participants

Note: the duration of the follow-up phase will only be considered once per participant and will be counted with the last applicable Stage for that participant.

Event rate per 100 PYFU = number of events*100 / PYFU.

6.1.3 Presentation of results

Tables will present TEAEs only. Pre-treatment AEs will only be listed.

AEs will be summarized separately for Stage A and Stage B:

- Stage A (SAF-A): only including AEs with onset day in analysis period Stage A or follow-up phase (if follow-up phase follows immediately after Stage A)
- Stage B (SAF-B): only including AEs with onset day in analysis period Stage B or follow-up phase (if follow-up phase follows after Stage B)

An overview table will show the number and percentage of participants with at least one event, the number of events and the event rate per 100 participant years of follow-up for the following:

- TEAEs
- Serious TEAEs
- Grade ≥ 3 TEAEs
- Fatal TEAEs
- Treatment related TEAEs
- Serious treatment related TEAEs
- Procedure related TEAEs
- TEAEs for which the study drug was discontinued
- TEAEs for which the study drug was interrupted
- TEAEs of special interest
- Treatment-emergent IRRs
- Serious treatment-emergent IRRs
- Treatment-emergent ISRs
- Serious treatment-emergent ISRs

The above overview table will be repeated specifically for ISRs overall, and by 3-monthly periods within stage B and within stage A + B . The lines summarizing IRRs will be omitted.

In addition, the above overview table will be repeated for COVID-19 cases (AE high level term = 'Coronavirus infections')

Summary tables by MedDRA system organ class and preferred term will show the number and percentage of participants with at least one event, the number of events and will include the rate per 100 participant-years of follow-up.

Separate tables will be prepared for the following:

- TEAEs
- Serious TEAEs
- Non-serious TEAEs
- Grade ≥ 3 TEAEs
- Treatment-related TEAEs
- Procedure related TEAEs
- TEAEs for which the study drug was discontinued
- TEAEs for which the study drug was interrupted
- TEAEs of special interest
- Treatment-emergent IRRs
- Serious treatment-emergent IRRs
- Treatment-emergent ISRs
- Serious treatent-emergent ISRs

The table on treatment-emergent ISRs will be repeated overall, and by 3-monthly periods within stage B and within stage A + B. Tables by 3-monthly periods will not include the number of events and AE rate per 100 participant-years of follow-up.

In addition, the number and percentage of participants with TEAEs of special interest by MedDRA system organ class, preferred term and worst grade will be summarized. Note that in this table, the worst-case severity is always applied within each period. For example, when a participant is reporting both a mild and a moderate headache during the same period, the participant is counted once, under the moderate headache. The same rule is applied for tabulations at system organ class and participant level. For example, when a participant reports mild vomiting and moderate nausea during the same period, the participant is counted only once, under moderate gastrointestinal disorders.

Time to first onset and duration of TEAEs of special interest will be tabulated. For the duration, all AESI will be considered, not only the first one in onset time.

The overview table and summary table for TEAEs by MedDRA system organ class and preferred term will be repeated for SAF-AB, including all TEAEs with onset day in analysis period Stage A or Stage B.

The overview table for TEAEs will be repeated by quartile of AUCss and AUECss parameters, derived from a population PK/PD model as described in sections 4.2 and

4.3, for Stage A and B separately, for the efgartigimod PH20 SC treatment group only.

All AEs, including pre-treatment events will be listed. Separate listings will be prepared for AEs which occurred in the run-in phase, serious AEs, fatal AEs, AEs for which the study drug was discontinued, AEs of special interest and COVID-19 cases. A listing showing all coding information will be prepared as well.

6.2 CLINICAL LABORATORY EVALUATION

6.2.1 Available data

Per protocol, the following safety laboratory parameters are expected:

- Biochemistry: glucose, creatinine, total protein, albumin, bilirubin, alkaline phosphatase, aspartate transferase, alanine transferase, gamma glutamyl transferase, cholesterol (at screening only), high-density lipoprotein (HDL) cholesterol (at screening only), low-density lipoprotein (LDL) cholesterol (at screening only), total cholesterol/HDL ratio (at screening only), triglycerides (at screening only), estimated glomerular filtration rate (creatinine clearance adjusted for BSA), high-sensitive C reactive protein, blood urea nitrogen, hemoglobin A1c, lactate dehydrogenase, uric acid, potassium, sodium, calcium (total)

  Total cholesterol, HDL and LDL cholesterol and tryglyceridesare only expected at screening for participants enrolled by an investigational site not located in mainland China.
- Coagulation: international normalized ratio, activated partial thromboplastin time, prothrombin time
- Hematology: red blood cell count, hemoglobin, hematocrit, mean cell volume, mean cell hemoglobin, mean cell hemoglobin concentration, red cell distribution width, platelets, white blood cell count, lymphocytes count, monocytes, eosinophils, basophils, neutrophils count
- Serology (screening tests): human immunodeficiency virus antigen/antibody (HIV Ag/Ab), viral hepatitis (hepatitis B surface antigen [HbsAg], anti-hepatitis B core antibody [HBc Ab], anti-hepatitis B surface antibody [HbsAb], anti-hepatitis C virus antibody [HCV Ab], tuberculosis
- Urinalysis: pH, protein, glucose, ketone, bilirubin, urobilinogen, blood, nitrite, leucocytes, and specific gravity; in case of abnormal dipstick results, light microscopy: erythrocytes, leucocytes, casts, and epithelial cells

Normal ranges are available as provided by the laboratories.

6.2.2 *Derivation rules*

If not provided by the lab, estimated glomerular filtration rate (eGFR) (Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)) will be derived:

$$\text{eGFR (mL/min/1.73m}^2) = 141 * \min\left(\frac{\text{creatinine (mg/dL)}}{K}\ ;\ 1\right)^{\alpha} * \max\left(\frac{\text{creatinine (mg/dL)}}{K}\ ;\ 1\right)^{-1.209} * 0.993^{\text{age (years)}} * 1.018\ \text{[if female]} * 1.159\ \text{[if black]}$$

where K = 0.7 if female and K = 0.9 if male;

α = -0.329 if female and α = -0.411 if male.

Note: in case results in mg/dL are not available, results in µmol/L will be used after conversion in mg/dL: 1 mg/dL = 88.4 µmol/L.

Toxicity grades will be computed according to the National Cancer Institute (NCI) common toxicity criteria for adverse events (CTCAE) toxicity grading list (version 5.0). The implementation of these toxicity grades for analysis is presented in appendix 10.2. Only the parameters described in appendix 10.2 will be computed, according to the declared limits for each grade.

The following abnormality categories will be defined for parameters with no toxicity grade available:

- Low: value < lower limit of normal range
- Normal: lower limit of normal range ≤ value ≤ upper limit of normal range
- High: value > upper limit of normal range

Notes:

- Classification will be done in standardized units, using non imputed values and limits.
- For the worst-case analysis visits, as defined in section 2.3.5, an additional category low + high is defined in case there are both low and high post-baseline values.
- All results will be used, both from fasted and non-fasted samples.
- If not straightforward how to categorize urinalysis results, a worst-case approach will be used. A value of '4 to 6' with normal range '0 to 5' will thus be classified as normal for predose assessments but as high for post-dose assessments.

6.2.3 *Presentation of results*

The statistical analysis will present results in standardized units, except for eGFR, which will be reported in mL/min/1.73m^2.

Laboratory results will be summarized separately for Stage A (SAF-A, using Stage A baseline) and Stage B (SAF-B, using Stage B baseline).

Continuous laboratory parameters will be summarized by means of descriptive statistics at each analysis visit and at the last assessment (see section 2.3.7). Categorical parameters will be listed only.

Laboratory abnormalities will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit, at the last assessment (see section 2.3.7) and at the worst-case analysis visit versus the baseline abnormality. Number of participants with treatment-emergent abnormalities (see Definition of terms) will also be shown. Parameters for which toxicity grades are defined will not be included in the abnormalities tables. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the analysis set.

Laboratory toxicity grades will be presented as cross-tabulations of the toxicity at each post-baseline analysis visit, at the last assessment (see section 2.3.7). and at the worst-case analysis visit versus the baseline toxicity. Numbers and cumulative numbers over decreasing toxicity grading of participants with treatment-emergent toxicities will also be shown. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the analysis set. Parameters having toxicity grades defined in both directions (hypo and hyper) will be shown by direction.

All laboratory data will be listed, but only for participants with any post-baseline abnormality or toxicity grade ≥1.

6.3 VITAL SIGNS

6.3.1 Available data

The following vital signs parameters are collected: systolic (SBP) and diastolic blood pressure (DBP) in semi-supine position, heart rate, body temperature and weight.

6.3.2 Derivation rules

Abnormalities are defined in below table.

	SBP (mmHg)	DBP (mmHg)	Temperature (°C)
Low	<90	<45	<35.8
Normal	90-150	45-90	35.8-37.5
High	>150	>90	>37.5

Note: For the worst-case analysis visits, as defined in section 2.3.5, an additional category low + high is defined in case there are both low and high post-baseline values.

6.3.3 Presentation of results

Heart rate and weight will not be displayed.

Vital signs results will be summarized separately for Stage A (SAF-A, using Stage A baseline) and Stage B (SAF-B, using Stage B baseline).

Vital signs parameters will be summarized by means of descriptive statistics at each analysis visit and at the last assessment (see section 2.3.7).

Abnormalities will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit, at the last assessment (see section 2.3.7) and at the worst-case analysis visit versus the baseline abnormality. Number of participants with treatment-emergent abnormalities (see Definition of terms) will also be shown. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the analysis set.

All vital signs data will be listed, but only for participants with any post-baseline abnormality or clinically significant values (as assessed by the investigator).

6.4 ELECTROCARDIOGRAMS

6.4.1 Available data

The following electrocardiogram (ECG) parameters will be collected: heart rate, QRS interval, RR interval, PR interval, QT interval, QTcF and QTcB.

6.4.2 Derivation rules

Mean values of the triplicates (screening and part A baseline only) will be calculated per time point and rounded as detailed in section 2.4.4. Throughout the analysis, including the derivation of baseline and abnormalities, the mean values will be used in case the assessment was done in triplicates. Individual triplicate values will only be listed. Nevertheless, mean triplicate results will not be prioritized over single 12-lead ECG results in any derivation (baseline, worst-case, windowing, …).

Abnormalities for heart rate, QRS and PR interval are defined in below table.

	Heart Rate (bpm)	PR (ms)	QRS (ms)
Low	<40	<120	-
Normal	40-100	120-220	0-120
High	>100	>220	>120

Note: For the worst-case analysis visit, as defined in section 2.3.5, an additional category low + high is defined in case there are both low and high post-baseline values.

For QTcB and QTcF interval (ms), the following categories are defined:

- Actual values:
  - ≤ 450 (normal)
  -]450; 480]
  -]480; 500]
  - > 500

- Changes:
  - ≤ 30 (normal)
  -]30; 60]
  - > 60

Note: The worst-case, as defined in section 2.3.5, is the highest post-baseline value and associated change.

6.4.3 Presentation of results

Uncorrected QT interval will only be listed, RR interval will not be displayed.

ECG results will be summarized separately for Stage A (SAF-A, using Stage A baseline) and Stage B (SAF-B, using Stage B baseline).

ECG parameters will be summarized by means of descriptive statistics at each analysis visit and at the last assessment (see section 2.3.7).

Abnormalities of the actual values will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit, at the last assessment (see section 2.3.7) and at the worst-case analysis visit versus the baseline abnormality. Numbers and cumulative numbers (QTc only) of participants with treatment-emergent abnormalities will also be shown. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the analysis set.

Abnormalities of the QTc changes will be presented as tabulations of the change abnormality at each post-baseline analysis visit and at the worst-case analysis visit. Cumulative numbers of participants with change abnormalities will also be shown. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the analysis set.

All ECG data will be listed, but only for participants with any post-baseline abnormality or clinically significant value or change (as assessed by investigator).

6.5 PHYSICAL EXAMINATIONS

6.5.1 Available data

Physical examination results per body system will be available.

6.5.2 Presentation of results

Abnormal physical examination results will be listed.

6.6 SUICIDALITY ASSESSMENT

6.6.1 Available data

The following suicidality assessments are expected: Columbia-suicide severity rating scale (C-SSRS) at screening and patient health questionnaire-9 (PHQ-9; ‘Over the last 2 weeks, how often have you been bothered by thoughts that you would be better off dead or of hurting yourself in some way?’) at post-screening visits.

6.6.2 Presentation of results

PHQ-9 will be summarized separately for Stage A (SAF-A, using Stage A baseline) and Stage B (SAF-B, using Stage B baseline).

PHQ-9 will be summarized in a cross-tabulation of the outcome at each analysis visit and at the worst-case analysis visit versus the baseline outcome. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the analysis set.

All suicidality data will be listed, but only for participants with a post-baseline PHQ-9 answer not equal to 'Not at all'.

7. CHANGES TO THE PLANNED ANALYSIS

7.1 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS BEFORE DATABASE LOCK

1. Per protocol adjusted INCAT deterioration is defined as number of days from first dose of double-blind (Stage B) IMP to the first occurrence of either

- an increase (i.e. worsening) of the adjusted INCAT score of 1 point, if the deterioration is confirmed at the next visit within a 3-7 day time window;
- an increase of the adjusted INCAT score of at least 2 points, with no confirmation required at the next visit.

For the purpose of this analysis, the 3-7 day time window can be ignored as long as adjusted INCAT deterioration is confirmed at the next visit.

The 3-7 days window restriction in the protocol was added mainly for safety reasons, in order to avoid that a participant that starts deteriorating, would stay too long untreated. But for the assessment of clinical deterioration for efficacy purposes, the time between first deterioration and confirmation of deterioration is less critical, as long as the deterioration gets confirmed.

2. The protocol defines the Stage A/B safety (SAF-A/B) and Stage B mITT populations as follows:

- The Stage A safety population (SAF-A) will include all patients who received at least 1 dose of IMP in Stage A.

- The Stage B safety population (SAF-B) will include all patients who received at least 1 dose of IMP in Stage B.

- The mITT population will include all randomized patients who received at least 1 dose of IMP in Stage B.

In order make sure that all participants, who received any amount (not necessarily the full dose of an injection) of IMP in a Stage, are included in the in the Stage A/B safety and mITT analysis sets, the definitions of the Stage A/B safety and mITT analysis sets have been updated by specifying that besides at least 1 dose of IMP, also participants who received part of a dose of IMP should be included in these analysis sets.

3. Section 10.1.3 of the protocol specifies that the safety data analysis will be presented as follows:

• Stage A will be done on the Stage A safety population (SAF-A).

• Stage B will be done on the Stage B safety population (SAF-B).
• Stages A and B combined on the Stage A safety population (SAF-A).

• Stages A and B combined on the Stage B safety population (SAF-B)

Since the exposure time for patients who do not progress from Stage A to B is limited, it was decided not to perform Stages A and B combined analyses on Stage A safety analysis. A pooled analysis of data across studies 1802 and 1902 will be performed in the integrated summary of safety.

7.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

Not applicable.

7.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

Not applicable.

8. REFERENCES

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9. LIST OF TABLES AND LISTINGS

Topline results tables are flagged as 'TLR'.

9.1 TABLES

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EFFICACY

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14.2.10.6	I-RODS: Descriptive Statistics of Actual Values and Changes from Stage A Baseline – Stage A+B	SAF-AB	
14.2.11.1	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline – Stage A	SAF-A	TLR
14.2.11.2.1	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline by Confirmed ECI Response – Stage A	SAF-A	TLR
14.2.11.2.2	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline by Prior CIDP Medication – Stage A	SAF-A	
14.2.11.2.3	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline by ECMD Worsening on Adjusted INCAT – Stage A	SAF-A	
14.2.11.2.4	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline by ECMD Worsening on Mean Grip Strength – Stage A	SAF-A	
14.2.11.2.5	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline at Stage A Baseline and Last Assessment by Prior CIDP Medication and by ECMD Worsening on Mean Grip Strength – Stage A	SAF-A	
14.2.11.2.6	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline by Treatment Duration Group in Stage A – Stage A	SAF-A	TLR
14.2.11.3	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values, Changes from Stage A Baseline and Changes from Stage B Baseline – Stage B	mITT	TLR
14.2.11.4	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values, Changes from Stage A Baseline and Changes from Stage B Baseline at Last Assessment – Stage B	mITT	
14.2.11.5	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values, Changes from Stage A Baseline and Changes from Stage B Baseline by Treatment Duration Group in Stage B – Stage B	mITT	TLR
14.2.11.6	Mean Grip Strength (kPa): Descriptive Statistics of Actual Values and Changes from Stage A Baseline – Stage A+B	SAF-AB	
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14.2.12.2	Total MRC Sum Score: Descriptive Statistics of Actual Values, Changes from Stage A Baseline and Changes from Stage B Baseline – Stage B	mITT	

14.2.12.3	Total MRC Sum Score: Descriptive Statistics of Actual Values, Changes from Stage A Baseline and Changes from Stage B Baseline at Last Assessment – Stage B	mITT
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14.2.13.1	Time to Complete TUG Test (Sec): Descriptive Statistics of Actual Values and Changes from Stage A Baseline – Stage A	SAF-A
14.2.13.2	Time to Complete TUG Test (Sec): Descriptive Statistics of Actual Values, Changes from Stage A Baseline and Changes from Stage B Baseline – Stage B	mITT
14.2.13.3	Time to Complete TUG Test (Sec): Descriptive Statistics of Actual Values, Changes from Stage A Baseline and Changes from Stage B Baseline at Last Assessment – Stage B	mITT
14.2.13.4	Time to Complete TUG Test (Sec): Descriptive Statistics of Actual Values and Changes from Stage A Baseline – Stage A+B	SAF-AB
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14.2.18.23	AE Correlation: Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by rHuPH20 Ab Participant Classification – Stage A	SAF-A
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14.2.18.26	AE Correlation: Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Anti-Drug Antibodies Against Efgartigimod Participant Classification – Stage B	SAF-B
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14.2.18.28	AE Correlation: Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by NAb Against Efgartigimod Participant Classification – Stage B	SAF-B
14.2.18.29	AE Correlation: Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by rHuPH20 Ab Participant Classification – Stage A	SAF-A
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14.2.18.34	AE Correlation: Treatment-Emergent Injection-Related Reactions by NAb Against Efgartigimod Participant Classification – Stage B	SAF-B
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14.2.18.38	AE Correlation: Treatment-Emergent Injection Site Reactions by Anti-Drug Antibodies Against Efgartigimod Participant Classification – Stage B	SAF-B
14.2.18.39	AE Correlation Treatment-Emergent Injection Site Reactions by NAb Against Efgartigimod Participant Classification – Stage A	SAF-A
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9.1.3 Patient-reported outcomes

PATIENT REPORTED OUTCOMES

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14.2.20.1	EQ-5D-5L: Descriptive Statistics of Actual Values and Changes from Stage A Baseline in VAS Score over Time – Stage A	SAF-A
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14.2.21.2	[redacted]	SAF-B
14.2.22.1	[redacted]	SAF-A
14.2.22.2	[redacted]	SAF-B
14.2.23.1	[redacted]	SAF-A
14.2.23.2	[redacted]	SAF-B
14.2.23.3	[redacted]	SAF-A
14.2.23.4	[redacted]	SAF-B
14.2.24.1	[redacted]	SAF-A
14.2.24.2	[redacted]	SAF-B
14.2.25.1	[redacted]	SAF-A
14.2.25.2	[redacted]	SAF-B
14.2.26.1	[redacted]	SAF-A
14.2.26.2	[redacted]	SAF-B
14.2.27.1	[redacted]	SAF-A
14.2.27.2	[redacted]	SAF-B
14.2.28.1	[redacted]	SAF-A
14.2.28.2	[redacted]	SAF-B
14.2.29.1	[redacted]	SAF-A
14.2.29.2	[redacted]	SAF-B

9.1.4 Safety analyses

SAFETY

ADVERSE EVENTS

14.3.1.1	Adverse Events Overview – Stage A	SAF-A	TLR
14.3.1.2	Adverse Events Overview – Stage B	SAF-B	TLR
14.3.1.3	Adverse Events Overview – Stage A + B	SAF-AB	
14.3.1.4	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.5	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.6	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage A + B	SAF-AB	
14.3.1.7	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.8	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.9	Non-serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	
14.3.1.10	Non-serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	
14.3.1.11	Grade 3 or More Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.12	Grade 3 or More Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.13	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.14	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.15	Procedure-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.16	Procedure-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.17	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.18	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.19	Treatment-Emergent Adverse Events Leading to Interruption of Study Drug by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.20	Treatment-Emergent Adverse Events Leading to Interruption of Study Drug by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR

14.3.1.21	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.22	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.23	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class, Preferred Term and Worst Severity – Stage A	SAF-A	
14.3.1.24	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class, Preferred Term and Worst Severity – Stage B	SAF-B	
14.3.1.25	Treatment-Emergent Injection-Related Reactions by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.26	Treatment-Emergent Injection-Related Reactions by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.27	Serious Treatment-Emergent Injection-Related Reactions by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	
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14.3.1.29	Injection Site Reactions Overview – Stage A	SAF-A	TLR
14.3.1.30	Injection Site Reactions Overview – Stage B	SAF-B	TLR
14.3.1.31	Injection Site Reactions Overview by 3-monthly Periods – Stage B	SAF-B	
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14.3.1.33	Treatment-Emergent Injection Site Reactions by MedDRA System Organ Class and Preferred Term – Stage A	SAF-A	TLR
14.3.1.34	Treatment-Emergent Injection Site Reactions by MedDRA System Organ Class and Preferred Term – Stage B	SAF-B	TLR
14.3.1.35	Treatment-Emergent Injection Site Reactions by MedDRA System Organ Class and Preferred Term by 3-monthly Periods – Stage B	SAF-B	
14.3.1.36	Treatment-Emergent Injection Site Reactions by MedDRA System Organ Class and Preferred Term by 3-monthly Periods – Stage A+B	SAF-AB	
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14.3.1.41	COVID-19 Events Overview – Stage A	SAF-A	
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14.3.1.43.1	Adverse Events Overview by Quartile of AUCss – Stage A	SAF-A	
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14.3.2.3	Cross-Tabulation of Laboratory Abnormalities Versus Stage A Baseline – Stage A	SAF-A	
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14.3.2.5	Cross-Tabulation of Laboratory Toxicity Grades Versus Stage A Baseline – Stage A	SAF-A	TLR
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14.3.3.3	Cross-Tabulation of Vital Signs Abnormalities Versus Stage A Baseline – Stage A	SAF-A	
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14.3.4.1	Descriptive Statistics of ECG Actual Values and Changes from Stage A Baseline – Stage A	SAF-A	
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14.3.4.3	Cross-Tabulation of ECG Abnormalities Versus Stage A Baseline – Stage A	SAF-A	
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14.3.4.5	Tabulation of QTc Change Abnormalities Compared to Stage A Baseline – Stage A	SAF-A	
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16.2.6.1	ECI	SAF-A
16.2.6.2	First Improvement	SAF-A
16.2.6.3	INCAT Disability Score	SAF-A
16.2.6.4	Adjusted INCAT Deterioration	mITT
16.2.6.5	I-RODS	SAF-A
16.2.6.6	CIDP Disease Progression, Improved Functional Level and 10% Decrease in I-RODS	mITT
16.2.6.7	Mean Grip Strength	SAF-A
16.2.6.8	MRC Sum Score	SAF-A
16.2.6.9	TUG Test	SAF-A
PHARMACODYNAMICS		
16.2.6.10	Total IgG	PD-A
IMMUNOGENICITY		
16.2.6.11	Anti-Drug Antibodies and Neutralizing Antibodies Against Efgartigimod	IMM-A

16.2.6.12	Antibodies and Neutralizing Antibodies Against rHuPH20	IMM-A
PATIENT REPORTED OUTCOMES		
16.2.6.13	EQ-5D-5L	SAF-A
16.2.6.14	[redacted]	SAF-A
16.2.6.15	[redacted]	SAF-A
16.2.6.16	[redacted]	SAF-A
16.2.6.17	[redacted]	SAF-A
16.2.6.18	[redacted]	SAF-A
SAFETY		
ADVERSE EVENTS		
16.2.7.1	Adverse Events	SAF-A
16.2.7.2	Run-in Adverse Events	SCR
16.2.7.3	Serious Adverse Events	SAF-A
16.2.7.4	Fatal Adverse Events	SAF-A
16.2.7.5	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug	SAF-A
16.2.7.6	Adverse Events of Special Interest	SAF-A
16.2.7.7	COVID-19 Events	SAF-A
16.2.7.8	Adverse Events: Coding Information	SAF-A
LABORATORY DATA		
16.2.8.1	Laboratory Test Results for Participants with Abnormal Values	SAF-A
16.2.8.2	Urinalysis and Lipid Laboratory Test Results	SAF-A
VITAL SIGNS		
16.2.8.3	Vital Signs Results for Participants with Abnormal Values	SAF-A
ECG		
16.2.8.4	ECG Results for Participants with Abnormal Values	SAF-A
PE		
16.2.8.5	Physical Examination Results for Participants with Abnormal Values	SAF-A
SUICIDALITY		
16.2.8.6	Suicidality Assessments for Participants with Abnormal Values	SAF-A

10. APPENDICES

10.1 SAS CODE

10.1.1 Exact (Clopper-Pearson) two-sided 95% CI

[redacted]

10.1.2 Kaplan-Meier (Stage A)

[redacted]

10.1.3 Cox proportional hazard regression model, Schoenfeld residual plot and test for PH

[redacted]

‘efgartigimod PH20 SC’[redacted]

[redacted]

10.1.4 Log-log plot of the survival function

[redacted]

[redacted];

10.1.5 Kaplan-Meier (Stage B) and stratified log-rank test

[redacted]

10.1.6 Logistic regression model

[redacted]

10.2 ESTIMANDS

Table 1: Stage B - Primary Estimand - Main Intercurrent Events

ICE	Strategy for primary estimand
Early withdrawal from trial for efficacy related reason (patient lost to follow-up, consent withdrawn, physician's decision, prohibited medication, lack of treatment efficacy).	While-on-treatment: data up to the ICE will be used in the analysis. Patients who do not experience adjusted INCAT deterioration before the ICE are censored at the time of last observed INCAT assessment.
Early withdrawal from trial due to COVID-19 infection.	While-on-treatment: see above.
Early withdrawal from trial for other reason, including patients who have to discontinue the trial early when the trial is stopped (when all events for the primary analysis are achieved).	While-on-treatment: see above.
Temporary treatment interruption (see section 3.6.2) or early treatment discontinuation (but patient continues trial).	Treatment policy: data will be used in the analysis regardless of whether a patient experienced the ICE or not.
Use of prohibited medications (see section 3.4.2) (but patient continues trial).	Treatment policy: see above.
Death.	While-on-treatment (while-alive): see above.
COVID-19 infection (but patient continues trial).	Treatment policy: see above.

10.3 TOXICITY GRADES

Below table shows how the Common Terminology Criteria for Adverse Events CTCAE, v5.0: November 27, 2017 will be implemented in the analysis.

PARAMETER	Unit	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Amylase (pancreatic)		>1.0-1.5 *ULN	>1.5-2.0 *ULN	>2.0-5.0 *ULN	>5.0 *ULN
Alanine amino transferase		>1-3 *ULN	>3-5 *ULN	>5-20 *ULN	>20 *ULN
Albumin	g/L	<LLN-30	<30-20	<20	-
	g/dL	<LLN-3	<3-2	<2	-
Alkaline phosphatase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-20.0 *ULN	>20.0 *ULN
Aspartate amino transferase		>1-3 *ULN	>3-5 *ULN	>5-20 *ULN	>20 *ULN
Bilirubin (total)		>1.0-1.5 *ULN	>1.5-3.0 *ULN	>3.0-10.0 *ULN	>10.0 *ULN
Calcium (ionized) low	mmol/L	<LLN-1.0	<1.0-0.9	<0.9-0.8	<0.8
	mg/dL	<LLN-4.0	<4.0-3.6	<3.6-3.2	<3.2
Calcium (ionized) high	mmol/L	>ULN-1.5	>1.5-1.6	>1.6-1.8	>1.8
	mg/dL	>ULN-6.0	>6.0-6.4	>6.4-7.2	>7.2
Calcium (corrected) low	mmol/L	<LLN-2.00	<2.00-1.75	<1.75-1.50	<1.50
	mg/dL	<LLN-8	<8-7	<7-6	<6
Calcium (corrected) high	mmol/L	>ULN-2.9	>2.9-3.1	>3.1-3.4	>3.4
	mg/dL	>ULN-11.5	>11.5-12.5	>12.5-13.5	>13.5
Cholesterol	mmol/L	>ULN-7.75	>7.75-10.34	>10.34-12.92	>12.92

	mg/dL	>ULN-300	>300-400	>400-500	>500
Creatine kinase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-10.0 *ULN	>10.0 *ULN
Creatinine		>1.0-1.5 *ULN	>1.5-3.0 *ULN	>3.0-6.0 *ULN	>6.0 *ULN
Gamma-glutamyl transferase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-20.0 *ULN	>20.0 *ULN
Glucose (fasting) low	mmol/L	<LLN-3.0	<3.0-2.2	<2.2-1.7	<1.7
	mg/dL	<LLN-55	<55-40	<40-30	<30
Lipase		>1.0-1.5 *ULN	>1.5-2.0 *ULN	>2.0-5.0 *ULN	>5.0 *ULN
Magnesium low	mmol/L	<LLN-0.5	<0.5-0.4	<0.4-0.3	<0.3
	mg/dL	<LLN-1.2	<1.2-0.9	<0.9-0.7	<0.7
Magnesium high	mmol/L	>ULN-1.23	-	>1.23-3.30	>3.30
	mg/dL	>ULN-3.0	-	>3.0-8.0	>8.0
Potassium low	mmol/L	-	<LLN-3.0	<3.0-2.5	<2.5
	mEq/L	-	<LLN-3.0	<3.0-2.5	<2.5
Potassium high	mmol/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
	mEq/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
Sodium low	mmol/L	<LLN-130	-	<130-120	<120
	mEq/L	<LLN-130	-	<130-120	<120
Sodium high	mmol/L	>ULN-150	>150-155	>155-160	>160
	mEq/L	>ULN-150	>150-155	>155-160	>160
Triglycerides	mmol/L	1.71-3.42	>3.42-5.70	>5.70-11.4	>11.4

	mg/dL	150-300	>300-500	>500-1000	>1000
Partial thromboplastin time (activated or not specified		>1.0-1.5 *ULN	>1.5-2.5 *ULN	>2.5 *ULN	-
CD4 count	giga/L	<LLN-0.50	<0.50-0.20	<0.20-0.05	<0.05
	counts/mm3	<LLN-500	<500-200	<200-50	<50
Fibrinogen		<1.00-0.75 *LLN	<0.75-0.50 *LLN	<0.50-0.25 *LLN	<0.25 *LLN
International normalized ratio		>1.2-1.5 *ULN	>1.5-2.5 *ULN	>2.5 *ULN	-
Lymphocytes (absolute count) low	giga/L	<LLN-0.80	<0.80-0.50	<0.50-0.20	<0.20
	counts/mm^3	<LLN-800	<800-500	<500-200	<200
Lymphocytes (absolute count) high	giga/L	-	>4-20	>20	-
	counts/mm^3	-	>4000-20000	>20000	-
Neutrophils (absolute count) low	giga/L	<LLN-1.5	<1.5-1.0	<1.0-0.5	<0.5
	counts/mm^3	<LLN-1500	<1500-1000	<1000-500	<500
Platelets	giga/L	<LLN-75	<75-50	<50-25	<25
	counts/mm^3	<LLN-75000	<75000-50000	<50000-25000	<25000
White blood cells	giga/L	<LLN-3	<3-2	<2-1	<1
	counts/mm^3	<LLN-3000	<3000-2000	<2000-1000	<1000

Note: In case ULN/LLN is higher/lower than the upper/lower limit of grade 1 (or even higher grades), ULN/LLN will be ignored and only the fixed values of CTCAE will be considered. In case ULN/LLN is missing, a grade will only be derived if the value leaves no doubt on which grade is to be assigned.

10.4 SCHEDULE OF ASSESSMENTS

10.4.1 Screening, run-in period and Stage A

	Screening[a] ≤28 days	Run-in Period ≤12 weeks[b]		Stage A: Open-Label Period ≤12 Weeks (With Optional 1 Additional Week)[c]														Unscheduled[e]	Safety Follow-up[f]
		RI-V1	RI-V2 to RI-V4	A-V1	A-V2	A-V3	A-V4	A-V5	A-V6[c]	A-V7[c]	A-V8[c]	A-V9[c]	A-V10[c]	A-V11[c]	A-V12[c]	A-V13[c] (Additional)	EOSA/ ED[d]	UnschV	28 (±3) Days After Last IMP Dose
	Up to 28 days			D1A	D8	D15	D22	D29	D36[c]	D43[c]	D50[c]	D57[c]	D64[c]	D71[c]	D78[c]	D85			
Assessment/Procedure		±0 days	±2 days	±0 days	±2 days														
Informed consent	●																		
Demographics	●																		
In-/exclusion criteria	●	●		●															
Medical history[g]	[10]																		
12-lead ECGs	●			●													●	●	●
CDAS	●																		
Physical exam and vital signs	●[h]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]	●[i]
Pregnancy test	●[j]	●[k]	●[k]	●[k]				●[k]				●[k]					●[k]	●[k]	●[k]
Adjusted INCAT score		●	●	●	●	●	●	●	(●)[l]	●	(●)[l]	●	(●)[l]	●	(●)[l]	●	●	●	
MRC Sum score		●	●	●	●	●	●	●	(●)[l]	●	(●)[l]	●	(●)[l]	●	(●)[l]	●	●	●	
I-RODS score		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
Mean grip strength		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
TUG test		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
EQ-5D-5L				●													●	●	
[redacted]																			

	Screening[a] ≤28 days	Run-in Period ≤12 weeks[b]		Stage A: Open-Label Period ≤12 Weeks (With Optional 1 Additional Week)[c]														Unscheduled[e]	Safety Follow-up[f]
		RI-V1	RI-V2 to RI-V4	A-V1	A-V2	A-V3	A-V4	A-V5	A-V6[c]	A-V7[c]	A-V8[c]	A-V9[c]	A-V10[c]	A-V11[c]	A-V12[c]	A-V13[c] (Additional)	EOSA/ED[d]	UnschV	28 (±3) Days After Last IMP Dose
	Up to 28 days			D1A	D8	D15	D22	D29	D36[c]	D43[c]	D50[c]	D57[c]	D64[c]	D71[c]	D78[c]	D85			
Assessment/Procedure		±0 days	±2 days	±0 days	±2 days														
[redacted]																			
Suicidality assessment[n]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Blood & urine clinical laboratory safety tests	●[o]			●	●	●	●	●									●	●	●
HIV, HBV, HCV, and tuberculosis testing	●																	●[p]	
Blood sampling for PK and PD analysis[q]				●[w]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Blood sampling for immunogenicity analysis[r]	●[w]			●[w]		●		●				●					●	●	●
[redacted]																			
IMP self-administration training[t]				●	●	●	●	●[t]	●[t]	●[t]	●[t]	●[t]	●[t]	●[t]	●[t]	●[t]			
IMP administration (SC)[u]				●	●	●	●	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]			
IMP accountability[u]				●	●	●	●	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●		
Adverse events[v]	←----------										●								----------→
Concomitant therapies[g,v]	←----------										●								----------→

Footnotes are on next page

ADA=anti-drug antibodies; AE=adverse event; [redacted] CDAS=CIDP disease activity status; CIDP=chronic inflammatory demyelinating polyneuropathy; D1A=baseline of Stage A; D1B=baseline of Stage B; ECG=electrocardiogram; ECI=evidence of clinical improvement; ECMD=evidence of clinically meaningful deterioration; ED=early discontinuation; EOSA=end of Stage A; EQ-5D-5L=EuroQol 5 dimensions and 5 levels health-related quality-of-life questionnaire; [redacted]; HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus; ICF=informed consent form; IgG=immunoglobulin G; IMP=investigational medical product; INCAT=inflammatory neuropathy cause and treatment; I-RODS=Inflammatory-Rasch-built Overall Disability Scale; OLE=open-label extension; PD=pharmacodynamic(s); [redacted] PK=pharmacokinetic(s); rHuPH20=recombinant human hyaluronidase PH20; [redacted]; MRC=Medical Research Council; SAE=serious adverse event; SC=subcutaneous(ly); [redacted] TUG=timed up and go; UNS=unscheduled; V=visit; W=week.

a. Within 28 days before the first day of run-in (visit RI-1). If needed a medical monitor can authorize the extension of the screening period. For treatment-naïve patients screening can occur within 28 days before D1A, if during screening documented evidence for worsening on the adjusted INCAT score within 3 months prior to screening is available compared to previous adjusted INCAT score within 6 months prior to screening.

b. Site visit every 4 weeks. R1-V1: day 1 of run-in; R1-V2:run-in week 4 (±2 days); R1-V3: run-in week 8 (±2 days), and R1-V4: run-in week 12 (±2 days). A patient showing ECMD will enter Stage A immediately. Patients will receive appropriate training and instructions to assess every week the disability status by means of I-RODS and grip strength. If the patient does not have evidence of ECMD by the end of the run-in period, then he/she should be recorded as a run-in failure.

c. Weekly administration of efgartigimod PH20 SC (±2 days). Patients, who show ECI only after the 12th IMP administration (ie, 1 week after the A-V12 visit), may be allowed to extend Stage A for a further week with an additional visit (the visit at which ECI is observed for the first time will then be A-V13) and patients will need to come back 1 week later (ie, 1 week after A-V13) to confirm ECI.
All patients with confirmed ECI following a minimum of 4 IMP administrations will have an EOSA visit and will enter Stage B. If the patient does not show confirmed ECI during Stage A, then he/she will have an EOSA visit and end the trial after a follow-up visit 28 days after the last administration of IMP.

d. The assessments in this visit are for patients who end Stage A (ie, EOSA visit; for patients with or without confirmed ECI) as well as for patients who discontinue the trial prematurely (ie, ED visit). Patients with confirmed ECI can continue the trial in Stage B (in this case, the patients will have a combination of the EOSA visit and the Baseline Stage B [D1B] visit [see Section 1.3.2]).

   Note: Patients who end Stage A with confirmed ECI and will go to Stage B, should have had at least 4 IMP administrations during Stage A.

   Note: Patients with ECI only after 12 IMP administrations in Stage A, may be allowed to extend Stage A for 1 more week (in order to determine if ECI is confirmed or not) with an additional consecutive visit (see footnote above).

e. The investigator can decide which of the assessments need to be performed at each unscheduled visit (refer to Section 5.1.5).

f. Only applicable for patients who do not continue in Stage B and for patients who prematurely discontinued IMP in case IMP was stopped less than 28 days before the last trial visit.

g. At screening, all available vaccination history will be captured as part of prior medication. For vaccines where multiple doses or boosters are received, only the most recent one must be recorded. Any vaccination received during the trial (from screening onwards) will be entered as concomitant medication.

   Note: For patients who provide separate consent, the titers of produced vaccination antibodies will be measured using retained blood samples (left over blood samples taken for other tests) during the trial.

h. Includes physical examination, height, weight, semi-supine blood pressure and heart rate, and body temperature.

i. Includes physical examination, weight, semi-supine blood pressure and heart rate, and body temperature.

j. A serum pregnancy test will be conducted at screening.

k. Urine pregnancy tests will be conducted every 4 weeks during the trial and at the follow-up visit.

l. These tests are only required for confirmation of improvement (for patients with improvement in the previous visit).

[redacted]

n. At screening, suicidality will be assessed with the Columbia-suicide severity rating scale (C-SSRS) (see Section 9.2). During the trial, suicidality will be assessed by specifically answering 1 question from the PHQ-9 depression questionnaire (see Section 9.15).

o. At screening, total IgG will be measured (by central laboratory as part of the blood chemistry tests) to determine eligibility.

p. Serology can be retested only during the screening period.

q. For PK, pre-dose (within 2 hours prior to start of IMP administration at the trial visits) samples will be taken. At these time points, blood samples will also be taken for PD analysis. PD analysis includes the measurement of IgG and IgG subtypes (IgG1, IgG2, IgG3, and IgG4).

r. Blood samples for immunogenicity testing will be taken pre-dose at the trial visits to measure ADA directed toward efgartigimod (measured in serum) and rHuPH20 (measured in plasma).

s. Optional blood samples will be taken for autoantibodies testing (serum) and serum-sample storage for future testing.

t. Patients will be trained to self-administer IMP (foreseen in the OLE trial; not in the ARGX-113-1802 trial) during the first 4 visits when IMP is administered; thereafter, training for self-administration is optional (only if needed).

u. IMP will be administered weekly at the site in Stage A (IMP administration will be after blood samples have been taken for laboratory safety, PK, PD, immunogenicity, and/or biomarker analyses and after all assessments needed for determination of ECI). Patients will receive a minimum of 4 IMP administrations in Stage A. Note that IMP in Stage A will **not** be administered if ECI is confirmed at the visit (and the patient has received at least 4 IMP administrations). When ECI is confirmed (ie, ECI observed at the second consecutive visit), the patient will be randomized and receive the first double-blind IMP administration in Stage B (ie, the visit at which ECI is confirmed will be a combination of the EOSA visit and the Stage B baseline [D1B] visit [see Section 1.3.2]).

v. AEs and intake of concomitant medication(s) will be monitored continuously from signing the ICF until the last trial-related activity. In case of early discontinuation, any AEs/SAEs should be assessed for 30 days following the ED visit or until satisfactory resolution or stabilization.

w. Blood samples may also be used to cross-validate the PK, PD, biomarker, and ADA assays in CIDP matrix (serum and plasma).

10.4.2 Screening, run-in period and Stage A (Japan amendment)

	Screening[a] ≤28 days	Run-in Period ≤12 weeks[b]		Stage A: Open-Label Period ≤12 Weeks (With Optional 1 Additional Week)[d]																Unscheduled[f]	Safety Follow-up[g]
		RI-V1	RI-V2 to RI-V4	A-V1[c]		A-V2	A-V3	A-V4[c]		A-V5	A-V6[d]	A-V7[d]	A-V8[d]	A-V9[d]	A-V10[d]	A-V11[d]	A-V12[d]	A-V13[d] (Additional)	EOSA/ED[e]	UnschV	28 (±3) Days After Last IMP Dose
	Up to 28 days			D1A	D1A + 48 to 96 hours	D8	D15	D22	D22 + 48 to 96 hours	D29	D36[d]	D43[d]	D50[d]	D57[d]	D64[d]	D71[d]	D78[d]	D85			
Assessment/Procedure		±0 days	±2 days	±0 days		±2 days	±2 days	±2 days		±2 days											
Informed consent	●																				
Demographics	●																				
In-/exclusion criteria	●	●		●																	
Medical history[h]	●																				
12-lead ECGs	●			●															●	●	●
CDAS	●																				
Physical exam and vital signs	●[i]	●[j]	●[j]	●[j]		●[j]	●[j]	●[j]		●[j]	●[j]	●[j]	●[j]	●[j]	●[j]	●[j]	●[j]	●[j]	●[j]	●[j]	●[j]
Pregnancy test	●[k]	●[l]	●[l]	●[l]						●[l]				●[l]					●[l]	●[l]	●[l]
Adjusted INCAT score		●	●	●		●	●	●		●	(●)[m]	●	(●)[m]	●	(●)[m]	●	(●)[m]	●	●	●	
MRC Sum score		●	●	●		●	●	●		●	(●)[m]	●	(●)[m]	●	(●)[m]	●	(●)[m]	●	●	●	
I-RODS score		●	●	●		●	●	●		●	●	●	●	●	●	●	●	●	●	●	
Mean grip strength		●	●	●		●	●	●		●	●	●	●	●	●	●	●	●	●	●	
TUG test		●	●	●		●	●	●		●	●	●	●	●	●	●	●	●	●	●	
EQ-5D-5L				●															●	●	
[redacted]																					

	Screening[a] ≤28 days	Run-in Period ≤12 weeks[b]		Stage A: Open-Label Period ≤12 Weeks (With Optional 1 Additional Week)[d]															Unscheduled[f]	Safety Follow-up[g]
		RI-V1	RI-V2 to RI-V4	A-V1[c]		A-V2	A-V3	A-V4[c]		A-V5	A-V6[d]	A-V7[d]	A-V8[d]	A-V9[d]	A-V10[d]	A-V11[d]	A-V12[d]	A-V13[d] (Additional)	EOSA/ED[e]	UnschV	28 (±3) Days After Last IMP Dose
	Up to 28 days			D1A	D1A + 48 to 96 hours	D8	D15	D22	D22 + 48 to 96 hours	D29	D36[d]	D43[d]	D50[d]	D57[d]	D64[d]	D71[d]	D78[d]	D85			
Assessment/Procedure		±0 days	±2 days	±0 days		±2 days	±2 days	±2 days		±2 days											
HADS				●														●	●	
PGIC						●												●	●	
Suicidality assessment[o]	●	●	●	●		●	●	●		●	●	●	●	●	●	●	●	●	●	●
Blood & urine clinical laboratory safety tests	●[p]			●		●	●	●		●				●				●	●	●
HIV, HBV, HCV, and tuberculosis testing	●																		●[q]	
Blood sampling for PK and PD analysis[r]				●[s]	●[c]	●	●	●	●[c]	●	●	●	●	●	●	●	●	●	●	●	●
Blood sampling for immunogenicity analysis[t]	●[s]			●[s]			●			●				●					●	●	●
[redacted]																					
IMP self-administration training[u]				●		●	●	●		●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]	●[u]			
IMP administration (SC)[v]				●		●	●	●		●[v]	●[v]	●[v]	●[v]	●[v]	●[v]	●[v]	●[v]	●[v]			
IMP accountability[v]				●		●	●	●		●[v]	●[v]	●[v]	●[v]	●[v]	●[v]	●[v]	●[v]	●[v]	●		
Adverse events[w]	←----------										●										----------→
Concomitant therapies[h,w]	←----------										●										----------→

Footnotes are on next page

ADA=anti-drug antibodies; AE=adverse event; [redacted] CDAS=CIDP disease activity status; CIDP=chronic inflammatory demyelinating polyneuropathy; D1A=baseline of Stage A; D1B=baseline of Stage B; ECG=electrocardiogram; ECI=evidence of clinical improvement; ECMD=evidence of clinically meaningful deterioration; ED=early discontinuation; EOSA=end of Stage A; EQ-5D-5L=EuroQol 5 dimensions and 5 levels health-related quality-of-life questionnaire; [redacted] HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus; ICF=informed consent form; IgG=immunoglobulin G; IMP=investigational medical product; INCAT=inflammatory neuropathy cause and treatment; I-RODS=Inflammatory-Rasch-built Overall Disability Scale; OLE=open-label extension; PD=pharmacodynamic(s); [redacted] PK=pharmacokinetic(s); rHuPH20=recombinant human hyaluronidase PH20; [redacted] MRC=Medical Research Council; SAE=serious adverse event; SC=subcutaneous(ly); [redacted] TUG=timed up and go; Unsch=unscheduled; V=visit; W=week.

a. Within 28 days before the first day of run-in (visit RI-1). If needed a medical monitor can authorize the extension of the screening period. For treatment-naive patients screening can occur within 28 days before D1A, if during screening documented evidence for worsening on the adjusted INCAT score within 3 months prior to screening is available compared to previous adjusted INCAT score within 6 months prior to screening.

b. Site visit every 4 weeks. R1-V1: day 1 of run-in; R1-V2:run-in week 4 (±2 days); R1-V3: run-in week 8 (±2 days), and R1-V4: run-in week 12 (±2 days). A patient showing ECMD will enter Stage A immediately. Patients will receive appropriate training and instructions to assess every week the disability status by means of I-RODS and grip strength. If the patient does not have evidence of ECMD by the end of the run-in period, then he/she should be recorded as a run-in failure.

c. Two additional PK samples will be taken; ie, one sample 48 to 96 hours after the 1st IMP injection and one sample 48 to 96 hours after the 4th IMP injection in approximately 10 Japanese patients in Stage A. Note that no additional PD samples will be taken at these timepoints.

d. Weekly administration of efgartigimod PH20 SC (±2 days). Patients, who show ECI only after the 12th IMP administration (ie, 1 week after the A-V12 visit), may be allowed to extend Stage A for a further week with an additional visit (the visit at which ECI is observed for the first time will then be A-V13) and patients will need to come back 1 week later (ie, 1 week after A-V13) to confirm ECI.
All patients with confirmed ECI following a minimum of 4 IMP administrations will have an EOSA visit and will enter Stage B. If the patient does not show confirmed ECI during Stage A, then he/she will have an EOSA visit and end the trial after a follow-up visit 28 days after the last administration of IMP.

e. The assessments in this visit are for patients who end Stage A (ie, EOSA visit; for patients with or without confirmed ECI) as well as for patients who discontinue the trial prematurely (ie, ED visit). Patients with confirmed ECI can continue the trial in Stage B (in this case, the patients will have a combination of the EOSA visit and the Baseline Stage B [D1B] visit [see Section 1.3.2]).

Note: Patients who end Stage A with confirmed ECI and will go to Stage B, should have had at least 4 IMP administrations during Stage A.

Note: Patients with ECI only after 12 IMP administrations in Stage A, may be allowed to extend Stage A for 1 more week (in order to determine if ECI is confirmed or not) with an additional consecutive visit (see footnote above).

f. The investigator can decide which of the assessments need to be performed at each unscheduled visit (refer to Section 5.1.5).

g. Only applicable for patients who do not continue in Stage B and for patients who prematurely discontinued IMP in case IMP was stopped less than 28 days before the last trial visit.

h. At screening, all available vaccination history will be captured as part of prior medication. For vaccines where multiple doses or boosters are received, only the most recent one must be recorded. Any vaccination received during the trial (from screening onwards) will be entered as concomitant medication.

Note: For patients who provide separate consent, the titers of produced vaccination antibodies will be measured using retained blood samples (left over blood samples taken for other tests) during the trial.

i. Includes physical examination, height, weight, semi-supine blood pressure and heart rate, and body temperature.

j. Includes physical examination, weight, semi-supine blood pressure and heart rate, and body temperature.

k. A serum pregnancy test will be conducted at screening.

l. Urine pregnancy tests will be conducted every 4 weeks during the trial and at the follow-up visit.

m. These tests are only required for confirmation of improvement (for patients with improvement in the previous visit).

[redacted]

o. At screening, suicidality will be assessed with the Columbia-suicide severity rating scale (C-SSRS) (see Section 9.1.1). During the trial, suicidality will be assessed by specifically answering 1 question from the PHQ-9 depression questionnaire (see Section 9.15).

p. At screening, total IgG will be measured (by central laboratory as part of the blood chemistry tests) to determine eligibility.

q. Serology can be retested only during the screening period.

r. For PK, pre-dose (within 2 hours prior to start of IMP administration at the trial visits) samples will be taken. At these time points, blood samples will also be taken for PD analysis. PD analysis includes the measurement of IgG and IgG subtypes (IgG1, IgG2, IgG3, and IgG4). IgG testing cannot be performed locally.

s. Blood samples for immunogenicity testing will be taken pre-dose at the trial visits to measure ADA directed toward efgartigimod (measured in serum) and rHuPH20 (measured in plasma).

t. Optional blood samples will be taken for autoantibodies testing (serum) and serum-sample storage for future testing.

u. Patients will be trained to self-administer IMP (foreseen in the OLE trial; not in the ARGX-113-1802 trial) during the first 4 visits when IMP is administered; thereafter, training for self-administration is optional (only if needed).

v. IMP will be administered weekly at the site in Stage A (IMP administration will be after blood samples have been taken for laboratory safety, PK, PD, immunogenicity, and/or biomarker analyses and after all assessments needed for determination of ECI). Patients will receive a minimum of 4 IMP administrations in Stage A. Note that IMP in Stage A will **not** be administered if ECI is confirmed at the visit (and the patient has received at least 4 IMP administrations). When ECI is confirmed (ie, ECI observed at the second consecutive visit), the patient will be randomized and receive the first double-blind IMP administration in Stage B (ie, the visit at which ECI is confirmed will be a combination of the EOSA visit and the Stage B baseline [D1B] visit [see Section 1.3.2]). Note: Patients will be asked to remain at the site for at least 1 hour after the end of the first 2 IMP injections (ie, at visits A-V1 and A-V2) and for at least 15 minutes after the end of the following IMP injections (from visit A-V3 onwards) in order to observe the patients for adverse events.

w. AEs and intake of concomitant medication(s) will be monitored continuously from signing the ICF until the last trial-related activity. In case of early discontinuation, any AEs/SAEs should be assessed for 30 days following the ED visit or until satisfactory resolution or stabilization.

x. Blood samples may also be used to cross-validate the PK, PD, biomarker, and ADA assays in CIDP matrix (serum and plasma).

10.4.3 Stage B

	Stage B: Randomized-Withdrawal Treatment ≤48 Weeks													UNS	Safety Follow-up[d]
	B-V1	B-V2	B-V3	B-V4	B-V5	B-V6	B-V7	B-V8	B-V9	B-V10	B-V11	B-V12	B-V13	UNS V[c]	28 (±3) Days After Last IMP Dose
	D1B[a]	W4	W8	W12	W16	W20	W24	W28	W32	W36	W40	W44	W48/ED[b]		
Assessment/Procedure	±0 days	±2 days													
Randomization	●														
12-lead ECGs	●			●			●			●			●	●	●
Physical exam and vital signs[e]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Pregnancy test[f]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Adjusted INCAT score	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
MRC sum score	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
I-RODS score	●	●	●	●	●	●	●	●	●	●	●	●	●	●	

	Stage B: Randomized-Withdrawal Treatment ≤48 Weeks													UNS	Safety Follow-up[d]
	B-V1	B-V2	B-V3	B-V4	B-V5	B-V6	B-V7	B-V8	B-V9	B-V10	B-V11	B-V12	B-V13	UNS V[c]	28 (±3) Days After Last IMP Dose
	D1B[a]	W4	W8	W12	W16	W20	W24	W28	W32	W36	W40	W44	W48/ED[b]		
Assessment/Procedure	±0 days	±2 days													
Mean grip strength	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
TUG test	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
EQ-5D-5L	●			●			●			●			●	●	
[redacted]															
PGIC													●	●	
Suicidality assessment	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Blood & urine safety tests	●			●			●			●			●	●	●
Blood sampling for PK and PD analysis[g]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Blood sampling for immunogenicity analysis[h]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
[redacted]															
IMP self-administration training[j]	●	●	●	●	●	●	●	●	●	●	●	●			
IMP administration (SC)[k]	●	●	●	●	●	●	●	●	●	●	●	●[k]			
IMP dispensation	●	●	●	●	●	●	●	●	●	●	●	●[k]			
IMP accountability	●	●	●	●	●	●	●	●	●	●	●	●	●		
Adverse events[l]	‹----------›														
Concomitant therapies[l,m]	‹----------›														

ADA=anti-drug antibody; AE=adverse event; BPI-SF=Brief Pain Inventory Short Form; D1B=baseline of Stage B; ECG=electrocardiogram; ECI=evidence of clinical improvement; ED=early discontinuation; EQ-5D-5L=EuroQol 5 dimensions and 5 levels health-related quality-of-life questionnaire; [redacted]HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus; ICF=informed consent form; IgG=immunoglobulin G; IMP=investigational medical product; INCAT=inflammatory neuropathy cause and treatment; I-RODS=Inflammatory-Rasch-built Overall Disability Scale; OLE=open-label extension; PD=pharmacodynamic(s); [redacted]rHuPH20 = recombinant human hyaluronidase PH20; [redacted]MRC=Medical Research Council; SAE=serious adverse event; SC = subcutaneous(ly); [redacted], TUG=timed up and go; UNS=unscheduled; V=visit; W=week.

a. D1B will occur at the same visit, at which ECI has been confirmed in Stage A. There is no need to schedule an additional visit for D1B. All assessments are performed prior to IMP administration.

b. The assessments in this visit are for patients who end Stage B as well as for patients who discontinue the trial prematurely (ie, ED visit). Patients who will roll over to the open-label extension trial, will have a combination this last visit in the ARGX-113-1802 trial and the first visit of the open-label extension trial ARGX-113-1902.

c. The investigator can decide which of the indicated assessments need to be performed at each unscheduled visit (refer to Section 5.1.5).

d. This visit is not applicable for patients who roll over to the open-label extension trial and for patients who prematurely discontinued IMP in case IMP was stopped less than 28 days before the last trial visit.

e. Includes physical examination, weight, semi-supine blood pressure and heart rate, and body temperature.

f. Urine pregnancy test every 4 weeks and at the follow-up visit.

g. For PK, pre-dose (within 2 hours prior to start of IMP administration at the trial visits) samples will be taken. At these time points, blood samples will also be taken for PD analysis. PD analysis includes the measurement of IgG and IgG subtypes (IgG1, IgG2, IgG3, and IgG4).

h. Blood samples for immunogenicity testing will be taken pre-dose at the trial visits to measure ADA directed toward efgartigimod (measured in serum) and rHuPH20 (measured in plasma).

i. Optional blood samples will be taken for autoantibodies testing (serum) and serum-sample storage for future testing.

j. Patients will be trained (refreshment training), if needed, to self-administer IMP (foreseen in the OLE trial; not in the ARGX-113-1802 trial).

k. IMP will be administered at the site at the scheduled visits. This will be after blood samples have been taken for laboratory safety, PK, PD, immunogenicity, and/or biomarker analyses. For IMP administrations between the scheduled visits, the patient can choose between nurse home visits or return to the trial site for the SC injection only. The last planned IMP administration is at week 47.

l. AEs and intake of concomitant medication(s) will be monitored continuously from signing the ICF until the last trial-related activity. In case of early discontinuation, any AEs/SAEs should be assessed for 30 days following the ED visit or until satisfactory resolution or stabilization.

m. Any vaccination received during the trial (from screening onwards) will be entered as concomitant medication.

Note: For patients who provide separate consent, the titers of produced vaccination antibodies will be measured using retained blood samples (left over blood samples taken for other tests) during the trial.

10.5 HISTORICAL CONTROL DATA