

STATISTICAL ANALYSIS PLAN (SAP)

Protocol Number: SBT101-CT101

Protocol Title: A Phase 1/2 Randomized, Blinded, Dose-escalation Study to Evaluate the Safety and Efficacy of Intrathecal Administration of AAV9-ABCD1 Gene Therapy (SBT101) in Adult Patients with Adrenomyeloneuropathy (AMN)

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SAP APPROVAL

A Phase 1/2 Randomized, Blinded, Dose-escalation Study to Evaluate the Safety and Efficacy of Intrathecal Administration of AAV9-ABCD1 Gene Therapy (SBT101) in Adult Patients with Adrenomyeloneuropathy (AMN)

I approve the Statistical Analysis Plan, Version 0.4, dated 15 August 2025.

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SAP VERSION HISTORY

SAP Version	Approval Date	Based on Protocol (Version, Approval Date)	Brief Description of Change(s)/Revision(s) and Rationale
0.1		Version 9.0, 13 December 2023	Original document creation.
0.2		Version 9.0, 13 December 2023, as modified according to an e-mail request for a study design change from the Sponsor in October 2024	Update to study design: In the Dose Escalation phase, there will be a total of 4 patients in Dose Level 1 and a total of 5 patients in Dose Level 2. Following this phase, there will be no dose expansion phase.
0.3		Version 9.0, 13 December 2023	Updates from Sponsor review of 0.2.
0.4	15 Aug 2025	Version 9.0, 13 December 2023	The study is closing for business reasons. The study design, objectives, and endpoints are scaled back as described in Section 1. The analyses are similarly modified.

TABLE OF CONTENTS

SAP APPROVAL	2
SAP VERSION HISTORY	3
LIST OF TABLES	6
LIST OF ABBREVIATIONS	7
1. INTRODUCTION	10
1.1 Study Objectives and Endpoints	11
1.2 Study Design	12
1.2.1 Treatment Blinding	12
1.2.2 Central Review	12
1.2.3 Data Monitoring	13
2. STATISTICAL HYPOTHESES AND MULTIPLICITY ADJUSTMENT	13
3. ANALYSIS SETS	13
3.1 Definition of Analysis Sets	13
3.2 Violations and Deviations	13
4. STATISTICAL ANALYSIS	13
4.1 General Considerations	13
4.1.1 Definitions, Derivations and Classifications	14
4.1.2 Windowing, Unscheduled Visits and Repeat Test Results	15
4.1.3 Dropouts, Missing/Incomplete Data, and Outliers	15
4.2 Participant Disposition	15
4.2.1 Demographic and Baseline Characteristics	16
4.2.2 Medical History	16
4.2.3 Medications, Therapies and Procedures	17
4.2.3.1 Prior and Concomitant Medications	17
4.2.3.2 Planned Immunosuppressants	17
4.3 Primary Endpoints Analysis	17
4.3.1 Definition of Endpoints	17
4.3.2 Main Analytical Approach	17
4.3.2.1 Adverse Events	17
4.3.2.2 Grade III or IV Laboratory Values	20
4.3.2.3 Physical Examination	21
4.3.2.4 Neurological Examination	21
4.3.2.5 Electrocardiogram	22
4.3.2.6 Vital Signs	22
4.3.2.7 Magnetic Resonance Imaging (MRI)	23
4.4 Exploratory Endpoints Analysis	23
4.4.1 Somatosensory Evoked Potentials (SSEP)	23

4.4.1.1	Definition of Endpoints.....	23
4.4.1.2	Main Analytical Approach.....	23
4.4.2	AEs Related to the IMP Procedure Catheter	23
4.4.2.1	Definition of Endpoints.....	23
4.4.2.2	Main Analytical Approach.....	23
4.5	Safety Analyses.....	23
4.5.1	Extent of Exposure	23
4.5.2	Pregnancy Test	24
5.	SAMPLE SIZE DETERMINATION.....	24
6.	CHANGES FROM AND ADDITIONS TO METHODS PLANNED IN THE PROTOCOL	24
7.	REFERENCE	25
8.	SUPPORTING DOCUMENTATION	26
	Appendix 1 Schedule of Procedures/Assessments.....	26
	Appendix 2 NCI-CTCAE V5.0 Toxicity Grading	32

LIST OF TABLES

Table 1	Objectives and Endpoints.....	11
Table 2	Treatment Group Label	14
Table 3	Criteria for Potentially Clinically Significant Lab Parameters	20
Table 4	Criteria for Potentially Clinically Significant Vital Sign Parameters	22
Table 5	Schedule of Assessments for Screening to Day 90 (Month 3).....	26
Table 6	Schedule of Assessments for Day 97 to Day 720 (Month 24)	30
Table 7	Laboratory Grading Scale – CTCAE version 5.0.....	32

LIST OF ABBREVIATIONS

Abbreviation	Description
2MWT	2-minute Walk Test
5XSST	5 times Sit-to-Stand Test
6MWT	6-minute Walk Test
AAV	adeno-associated virus
ANCOVA	analysis of covariance
AE	adverse event
ALD	adrenoleukodystrophy
ALT	Alanine aminotransferase
AMN	adrenomyeloneuropathy
AP	Anteroposterior
AST	Aspartate aminotransferase
ATP	Adenosine triphosphate
ATC	Anatomic Therapeutic Chemical coding dictionary
BMI	body mass index
CI	confidence interval
CGI	Clinical Global Impression
CGI-C	Clinical Global Impression-Change
CNS	central nervous system
CRF	case report form
CSF	Cerebrospinal fluid
DSMB	Data Safety Monitoring Board
ECG	electrocardiogram
ELISpot	enzyme-linked immunosorbent spot
EP	Electrophysiological
eCRF	electronic case report form
EDSS	Expanded Disability Status Score
ECG	electrocardiogram
FAS	Full Analysis Set
IMP	Investigational medicinal product

LIST OF ABBREVIATIONS

Abbreviation	Description
IT	intrathecal
ITT	intent to treat
LPC-VLCFA	Lysophosphatidylcholine very long chain fatty acid
MedDRA	Medical Dictionary for Regulatory Activities
miniBESTest	Balance Evaluation System Test
ML	Mediolateral
MMRM	mixed-effect model with repeated measures
MRI	Magnetic resonance imaging
MSQoL-54	Multiple Sclerosis Quality of Life-54
MSWS-12	Multiple Sclerosis Walking Scale
MTD	maximum tolerated dose
NCS	Nerve conduction study
PE	Physical examination
PGI	Patient Global Impression
PGI-S	Patient Global Impression of Severity
PGI-C	Patient Global Impression of Change
PRO	patient reported outcome
PT	preferred term
SAE	serious adverse event
SAP	Statistical Analysis Plan
SAS	Safety Analysis Set
SAS	Statistical Analysis System
SD	standard deviation
SE	standard error
SOC	system organ class
SSEP	Somatosensory Evoked Potentials
SSPROM	Severity Score System for Progressive Myelopathy
TEAE	treatment emergent adverse event
TFL	table, figure, listing

LIST OF ABBREVIATIONS

Abbreviation	Description
TUG	Timed Up and Go
TUG-DT	Dual-task TUG
vg	Vector genome
VLCFA	Very long chain fatty acid
WHODD	World Health Organization Drug Dictionary

1. INTRODUCTION

Adrenoleukodystrophy (ALD) is an inherited progressive neurodegenerative disorder caused by a mutation in the adenosine triphosphate (ATP)-binding cassette transporter subfamily D member 1 (ABCD1) gene. This gene is localized to the X chromosome and encodes a peroxisomal ATP-binding cassette half-transporter responsible for transporting very long chain fatty acids (VLCFAs) from the cytosol into the peroxisome for degradation¹⁻². A mutation in the ABCD1 gene results in reduced degradation and accumulation of saturated VLCFAs in tissues and body fluids (i.e., brain, nervous system, adrenal glands), which in turn leads to demyelination, central nervous system (CNS) deterioration, and neurologic defects¹⁻³.

The principal phenotypes observed in males with ALD are AMN, the cerebral demyelinating form of ALD (cerebral ALD), and adrenal insufficiency (Addison's disease)⁴. Among these disease states, AMN is the most common. It is characterized by a slowly progressive axonopathy affecting sensory ascending and motor descending spinal cord tracts that manifests in aging patients, with 100% penetrance in men⁴.

There are no curative treatments available for AMN. Current therapeutic strategies are aimed at eliminating or ameliorating symptoms that affect functional abilities and/or impair quality of life. These therapies can somewhat improve the quality of life of patients; however, without addressing the genetic root cause of AMN, patients are left with a progressive disorder that leads to lifelong disability.

In vivo gene therapy offers the possibility of a one-time treatment for an inherited disease, with the prospect of life-long benefits⁵. Recombinant adeno-associated virus (AAV) gene therapies directed at the CNS, particularly recombinant AAV serotype 9 (AAV9), have produced promising pre-clinical results, indicating great potential in recombinant AAV9 gene therapy as treatment for AMN, and are increasingly being translated from the bench to clinical trials⁶, and even marketing authorization (e.g., Zolgensma®, approved for the treatment of the genetic disease of spinal muscular atrophy).

The Sponsor is defined as SwanBio Therapeutics, Ltd (SwanBio) doing business as Spur Therapeutics, Ltd.

SwanBio is developing SBT101, a recombinant AAV9 vector encoding the functional human ABCD1 gene (hABCD1; AAV9 hABCD1), for use as a single dose administered via intrathecal (IT) infusion to treat AMN by correcting for the underlying genetic defect in the CNS.

Safety and efficacy have been demonstrated in animal studies, and the SBT101-CT101 Phase I/II study represents the first time SBT101 has been evaluated in humans. This study was originally designed to evaluate the safety, tolerability, and efficacy of one time IT administration of SBT101 on disease progression in adult patients with AMN. However, the Sponsor has made a business decision to discontinue the SBT101 program, including termination of SBT101-CT101 prior to study completion. This decision was not based on any safety or scientific concerns. As such, the statistical analysis plan (SAP) has been amended to support study termination and will prioritize describing the safety of the study at the time of study termination. This version of the SAP describes the safety of 8 participants in Dose Levels 1 and 2. There was no dose expansion phase at the time of study termination.

Shells for the planned tables, figures, and listings (TFL) will be included in a separate document, entitled "SAP Table, Figure and Listing Shells".

1.1 Study Objectives and Endpoints

Table 1 Objectives and Endpoints

Objective	Endpoint
PRIMARY	
To characterize the safety and tolerability of one-time IT administered SBT101 in adults diagnosed with AMN at the time of study early termination.	• Incidence, severity, and relationship of treatment-emergent adverse events (TEAEs), • Incidence and relationship of treatment emergent serious adverse events (SAEs) • Severity, and relationship of deaths • Post-Baseline Newly Occurring or Worsening Potentially Clinically Significant Laboratory Values • Shift from baseline: ECG • Post-Baseline Newly Occurring or Worsening Potentially Clinically Significant Vital Signs • Incidence of treatment emergent brain MRI parameters related to inflammation post-treatment. Describe clinically significant observations in full spine MRI.
EXPLORATORY	
To characterize the effect of SBT101 on SSEPs	Describe clinically significant changes in somatosensory evoked potentials (SSEPs) after SBT101 administration compared to Baseline.
To evaluate the safety of the catheter used to infuse SBT101 intrathecally in Europe (European only objective)	Frequency and severity of adverse events related to the catheter used for infusion of SBT101 intrathecally in Europe (European only endpoint).

1.2 Study Design

The Sponsor has made a business decision to discontinue development of the SBT101 program including discontinuation of the SBT101-CT101 study. The study design below reflects the status of the study at the time of discontinuation.

This is a Phase 1/2 randomized, blinded, sham-controlled, multicenter, dose escalation study to evaluate the safety and efficacy of one-time IT administration of SBT101 in adult male patients with AMN aged 18-65 years.

Dose escalation consists of two dose levels. Patients will receive a single dose of SBT101 via IT route and will be followed for safety and efficacy for 5 years:

- Dose Level 1 Cohort – 1.0E14 vector genomes (vg)
- Dose Level 2 Cohort – 3.0E14 vg

The Sponsor will review the available safety data each time a patient completes the Day 30 Visit. The review of safety data will be completed before the next patient receives SBT101. After completion of a minimum of 2 patients in each Dose Level Cohort, the independent Data Safety Monitoring Board (DSMB) will review the available safety data of all patients in the cohort that complete the Day 30 visit. The decision to proceed with the next Dose Level Cohort will be made after the independent DSMB and the Sponsor have reviewed the safety data. Refer to Section 1.2.3 for additional details of data monitoring.

Long-term Safety Follow-up

Long-term safety follow-up after all participants have completed Month 6 of dosing will be managed locally.

Table 6 and **Table 7** in Appendix 1 display the original protocol-planned schedule of assessments for the study prior to study termination. The assessments performed at each visit were as predefined by the schedule of assessments until the time of study termination.

Informed consent will be obtained from all patients at the Screening Visit (Visit 1) prior to conducting any screening procedures to assess study eligibility.

Safety follow-up and efficacy assessments will be completed at clinic visits or remote visits.

Patients enrolled at the University of Massachusetts Chan Medical School will undergo an additional blood draw to assess the T-cell reactivity to the AAV capsid, as measured by enzyme-linked immunosorbent spot (ELISpot), per the Schedule of Assessments. These results are exploratory and will not be captured in the abbreviated CSR/

The End of Study Visit will be conducted at study termination.

1.2.1 Treatment Blinding

This study will not be blinded to treatment.

1.2.2 Central Review

All MRIs will be assessed and a Loes score will be assigned to any brain MRI performed by the clinical site by an independent reviewer. If a patient is diagnosed with or suspected of a cerebral disease by the clinical site, blinded independent experts will assess/confirm the presence of the cerebral disease. The Imaging Review Charter, which describes the procedures for image blinding, reading, and scoring, will be used by the central reviewers.

1.2.3 Data Monitoring

An independent DSMB will be established to review safety data throughout the study. Members will include at least 3 independent physicians with expertise in neurological diseases and/or gene therapy and an independent statistician.

The DSMB will review the safety data of the patients completing the Day 30 visit within each Dose Level Cohort, and subsequent meetings every 6 months until the completion of the study.

The decision to proceed to the next Dose Level Cohort will be made after review of safety data by the independent DSMB and the Sponsor.

The Sponsor, in consultation with the DSMB, may:

- Elect to increase or decrease the number of patients in a Dose Level Cohort during the study.

Further details will be provided in the DSMB Charter.

The DSMB has been notified of Sponsors decision to terminate the study due to business reasons.

2. STATISTICAL HYPOTHESES AND MULTIPLICITY ADJUSTMENT

No formal hypothesis testing will be conducted in this study. All analyses will be descriptive in nature. Any modeling that is performed will focus on parameter estimation. P-values may be included to characterize associations and trends but will not be used inferentially and will not be adjusted for multiplicity.

3. ANALYSIS SETS

3.1 Definition of Analysis Sets

The following populations are defined for this study:

Population	Definition
Full Analysis Set (FAS)	All participants who signed informed consent and were treated.
Safety Analysis Set (SAS)	All participants who received any amount of SBT101 as part of this study.

3.2 Violations and Deviations

Protocol deviations are failures to adhere to the inclusion/exclusion criteria and protocol requirements and will be classified as important or not important protocol deviations.

Important protocol deviations will be identified and categorized by medical review before each milestone database lock for analysis. There is no intention to perform a per-protocol analysis in this study.

4. STATISTICAL ANALYSIS

4.1 General Considerations

All relevant safety data to support early termination collected will be provided in listings. Data collected only for confirmation of study entry criteria and for study administrative purposes will not be listed. If any

enrolled participant is found to not have valid documented informed consent, that participant's data will be excluded from the report, except as necessary to document the error. Partner pregnancy test results will be verified by the Sponsor according to what was reported in the safety database. Exploratory biomarker data will be collected but are beyond the scope of this updated SAP.

Unless specified otherwise, TFLs will be presented by study treatment group including dose level, and visit as applicable. The treatment group labels by study part analysis period are displayed in Table 2.

Table 2 Treatment Group Label

Study Part	Treatment Group Label	Instruction
Part 1	Cohort 1 SBT101 1.0E14 vg	
	Cohort 2 SBT101 3.0E14 vg	
	Combined SBT101	Pooled SBT101 doses from all SBT101 Cohorts.

Unless specified otherwise, the participant listings will be based on FAS; all safety analyses will be performed in the Safety Analysis Set; all analyses will be based on the actual treatment received.

All medical history and adverse events will be coded using MedDRA; the primary system organ class (SOC) and preferred term (PT) will be used for analyses. All medications will be coded using the WHO drug dictionary. The version of the dictionaries will be the dictionary current at the time of analysis.

Except where specified otherwise, all continuous variables will be summarized with descriptive statistics (the number of non-missing values, mean, standard deviation (SD), median, lower quartile (Q1), upper quartile (Q3), minimum and maximum). In some cases, the standard error of the mean and/or confidence intervals (CIs) may be presented. All CIs will be two-sided 95% CIs.

All categorical variables will be summarized with frequency counts and percentages in each category by treatment group and study part. If applicable, the number of events will be summarized.

For conversion of days to years, months, or weeks, the following conversion factors will be used:

- 1 year = 365.25 days
- 1 month = $365.25/12 = 30.4375$ days
- 1 week = $365.25/52 = 7.024$ days

All analyses will be conducted using SAS version 9.4 or higher.

4.1.1 Definitions, Derivations and Classifications

Definition of Baseline

The baseline value will be the last available value prior to the administration of investigational medicinal product (IMP) on Study Day 1.

Definition of Study Day

Study Day will be computed as follows:

- Study Day = (Date of event/assessment – Date of IMP administration) + 1 if the date of the event/assessment is on or after the date of IMP administration.

- Study Day = (Date of event/assessment – Date of IMP administration) if the date of the event/assessment is prior to the date of the IMP administration.

Definition of Study Day 1

Study Day 1 is defined as the day of IMP administration.

Calculations of Change and Percent Change from Baseline

Change from baseline (CHG) will be calculated as:

Change from baseline = Actual (observed) value at post baseline visit – baseline value

Percent change from baseline (PCHG) will be calculated as:

Percent change from baseline (%) = $100 * (\text{Change from baseline at post baseline visit} / \text{Baseline value})$

If baseline is not available, the change from baseline and percent change from baseline will not be calculated and will remain missing.

4.1.2 Windowing, Unscheduled Visits and Repeat Test Results

Data Collected at Visits

Data will be summarized based on the nominal visits; analysis windows will not be defined. All assessments collected at scheduled and unscheduled visits will be included in the by-participant data listings. Only the results collected at scheduled visits per protocol will be included in the by-visit summary tables. Unscheduled visits are eligible to be used as the worst/last assessments for analysis such as analysis of abnormality for the whole study.

4.1.3 Dropouts, Missing/Incomplete Data, and Outliers

Missing data occurs when any requested data are not provided, leading to blank fields on the collection instrument. These data will be indicated using a “blank” in participant listing displays. Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.

Uncoded events and procedures at the time of analysis will be assigned the string “UNCODED” as the system organ class, and the reported term will be used as the preferred term so they can be included in the summary tables. In the final dataset, all the adverse events and procedures should be coded.

Uncoded medications at the time of analysis will be assigned the string “UNCODED” as the Anatomical-Therapeutic-Chemical (ATC) summary level and the verbatim term will be used as the preferred name, so they can be included in the summary tables. In the final dataset, all the medications will be coded.

4.2 Participant Disposition

The summary of participant disposition will be tabulated for all screened participants by treatment group and overall for the following categories:

- Number of participants screened (who signed informed consent – total column only)
- Number and percentage of participants who failed screening and screen failure reasons (total column only)

- Number and percentage of participants who were treated in the Dose Escalation Phase (the numbers in this row will be used as denominators of the following rows)
 - Number and percentage of participants who completed key visits: Month 6, Month 12 (Year 1), Month 24 (Year 2)
 - Number and percentage of Part 1 Dose Escalation Phase participants who discontinued from Part 1 of the study
 - Reason for early discontinuation from the Part 1 Dose Escalation Phase of the study
- Number and percentage of all participants completing end of study visit

All disposition data and randomization data will be provided in participant listings for the FAS.

Protocol deviations will be listed, including the deviation category and an indicator for important or not important for the FAS.

The participants excluded from analysis sets and reasons for exclusion will be listed for all screened participants.

4.2.1 Demographic and Baseline Characteristics

Descriptive statistics will be used to summarize demographic and baseline characteristics by treatment group and overall. Demographic data include:

- Age (years)
- Sex
- Race
- Ethnicity

Baseline characteristics include:

- Weight (kg)
- Height (cm)
- Body Mass Index (BMI; kg/m²)
- BMI Category (< 18.5, 18.5 - < 25, 25 - < 30, 30 - <35, 35 - < 40, > = 40)
- Baseline EDSS Score
- Confirmed Mutation in the ACBD1 Gene (yes/no)
- Adrenal Insufficiency (yes/no)
- Time Since AMN Diagnosis (years) = (date of SBT101 administration – date of AMN diagnosis + 1)/365.25. Demographic and baseline characteristics will be summarized for the Safety Analysis Set.

Demographic and baseline characteristics will be listed for the FAS.

4.2.2 Medical History

The medical history will be listed for the FAS.

4.2.3 Medications, Therapies and Procedures

4.2.3.1 Prior and Concomitant Medications

Prior medications are defined as medications which stopped before initiation of the administration of IMP. Concomitant medications are defined as medications taken at any time during or after the administration of IMP. If a medication or therapy cannot be classified due to completely missing dates, it will be classified as concomitant.

The prior and concomitant medications, including concomitant medication to treat ALD and concomitant medication to treat spasticity, will be listed for the FAS.

4.2.3.2 Planned Immunosuppressants

The immunosuppressive medications administration data will be listed for the FAS and categorized as Prior or Concomitant. Prior medications are defined as medications which stopped before initiation of the administration of IMP. Concomitant medications are defined as medications taken at any time during or after the administration of IMP.

4.3 Primary Endpoints Analysis

4.3.1 Definition of Endpoints

The primary endpoints of the study are defined in Table 1.

4.3.2 Main Analytical Approach

All analyses will be based on the Safety Analysis Set and will be summarized by treatment group unless otherwise stated.

4.3.2.1 Adverse Events

An AE is any untoward medical occurrence in a patient administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. Any AE (i.e., a new event or an exacerbation of a preexisting condition) with an onset date after the patient provides informed consent through the patient's End of Study Visit will be collected. AEs will be characterized by seriousness, severity, and relationship to study procedure.

Treatment-Emergent Adverse Events (TEAEs)

TEAEs will be defined as those AEs which started during or after the administration of SBT101 or the immunosuppressant pre-medication. If an AE cannot be classified due to missing date or time, it will be classified as TEAE.

Serious Adverse Events (SAEs)

An SAE is defined as any AE that meets at least 1 of the following criteria:

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization for the AE

- Is a persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions
- Is a congenital anomaly/birth defect
- Is an important medical event or reaction

A serious TEAE is defined as a TEAE that meets any SAE criterion above.

Severity of Adverse Events

The severity of all AEs and SAEs will be graded by the Investigator according to the version of the Common Terminology Criteria for Adverse Events (CTCAE) that is current at the time of study conduct. Missing grades will not be imputed. AEs with missing grade will be summarized into the category of 'Not Reported' in the tabulation summary.

Relationship of Adverse Events to IMP Procedure/ IMP Procedure Catheter/ other study procedure (except IMP Procedure)/ IMP Study Drug/ Immunosuppression/ Disease

The relationship of AE to IMP procedure, IMP procedure catheter, other study procedure (except IMP procedure, European only), IMP study drug, immunosuppression, and diseases will be determined by the Investigator. The relatedness categories include Unrelated, Unlikely, Possible, Probable, and Definite.

For any analyses of AE data in which only two categories of "related" and "unrelated" are used, the assessments of "unrelated" and "unlikely" will be combined into the category of "unrelated", and the assessments of "possible", "probable", and "definite" will be combined into the category of "related". Missing relationships will not be imputed. An AE will be considered as related to "study procedure" if at least one relationship to IMP procedure, IMP procedure catheter, or other study procedure is "related".

AE Date and Duration

Partial or missing AE dates will not be imputed. The duration of an AE is defined as the end date of AE minus the start date of the AE, plus 1.

AE Summary

Only treatment emergent events are included in summaries. The TEAE summaries will be presented using the number and percentage of participants with TEAEs, by dose level and overall for each SOC, PT, and severity grade, as well the number of events as described below.

An overall summary of adverse events will include:

- TEAEs
- TEAEs related to study procedure or study drug
- TEAEs related to IMP procedure catheter (European only)
- TEAEs related to immunosuppression
- TEAEs related to disease progression
- Serious TEAEs
- Serious TEAEs related to study procedure or study drug

The following summaries will also be presented:

- TEAEs by SOC, PT, and Maximum Severity Grade
- TEAEs Related to Study Procedure or Study Drug by SOC, PT, and Maximum Severity Grade
- TEAEs Related to IMP Procedure Catheter (European only) by SOC, PT, and Maximum Severity Grade
- TEAEs Related to Immunosuppression by SOC, PT, and Maximum Severity Grade
- TEAEs Related to Disease Progression by SOC, PT, and Maximum Severity Grade
- Serious TEAEs by SOC, PT, and Maximum Severity Grade
- Serious TEAEs Related to Study Procedure or Study Drug by SOC, PT, and Maximum Severity Grade

For AE counts at the event level: all AEs appearing in the dataset will be treated as individual events.

For AE counts at the participant level: A participant having the same event (SOC or PT) more than once will be counted only once. When summarizing events by causality and severity by participants, each participant will be counted only once within a SOC or a PT by using the event with the greatest relationship and highest severity within each classification.

For uncoded events, refer to Section 4.1.4 for the data handling rules.

For TEAE tables by SOC and PT, the AEs will be presented in descending order of total frequency of both SOC and PT within each SOC. If multiple SOC or PTs have the same frequency, then they will be sorted in alphabetical order. For TEAE tables by PT only, the AEs will be listed in the descending order of total frequency.

All AEs will be presented in a listing. Separate listings will also be provided for the following:

- AEs
- SAEs
- AEs related to study procedure or study drug
- AEs related to IMP procedure catheter (European only)
- AEs related to immunosuppression
- AEs related to disease progression
- AEs with Grade III or IV

Incidence rates will be calculated for specific SOC and PTs. Rates will be computed every 12 months or every 3 months starting from the time of informed consent, depending on the frequency of the identified AEs. This analysis will be conducted if a sufficient number of AEs are observed.

4.3.2.1.1 Deaths

Deaths will be captured as a part of SAE collection. If there are deaths, they will be listed, including the admission date if the subject was hospitalized, the date the event became serious, and the date of last study assessment before the SAE became serious.

4.3.2.2 Grade III or IV Laboratory Values

The central laboratory assessments will include parameters from hematology, blood chemistry, coagulation (PT, INR, and aPTT), and urinalysis. The hemoglobin A1c, viral tests (HIV, HBV, and HCV), and adrenal function test (cortisol, plasma ACTH, plasma renin, and aldosterone) are also performed only at the Screening Visit to support the inclusion/exclusion eligibility criteria assessment. Assessments of T-cell immunity to AAV9 and hABCD1 will be performed by ELISpot.

All lab tests and results collected will be listed. The parameters from hematology, chemistry, coagulation, and urinalysis will be summarized in tables and figures. T-cell immunity summaries are described in section 4.5.8.

Lab Data Handling Rules

Laboratory data in summary tables and participant data listings will be presented in the International System of Units (SI units; *Système International d'Unités*).

Laboratory data include both the continuous lab tests results (including all parameters from hematology, chemistry, coagulation, and parameters pH and specific gravity from urinalysis), and qualitative lab tests results (collected in other urinalysis parameters).

Normal ranges established by the central laboratory will be used to determine the 'Normal Range Indicator' by comparing the lab test result with the reference range of that parameter. For continuous lab tests, the possible 'Normal Range Indicator' value is Low (below the normal range), Normal (within the normal range) and High (above the normal range). For the qualitative lab tests, the possible 'Normal Range Indicator' value is 'Normal' (within the categorical ranges) and 'Abnormal' (outside the categorical ranges).

Hematology, chemistry, and coagulation tests will be programmatically graded according to NCI-CTCAE v5.0 toxicity grading as detailed in Table 8 in Appendix 2. The worst post-baseline CTCAE grade will be identified for each lab parameter by participants. If there are the same worst grades at multiple different time points, the earliest one will be selected for analysis.

For any continuous laboratory variable reported using a non-numeric qualifier (e.g., less than (<xx.x) a certain value, or greater than (>yy.y) a certain value, or <=, >=), the inequality sign will be removed and the resulting numeric value used as the observed value, or for change from baseline calculations. As an example, a value of <10 may be converted to 10. Such substitutions will be clearly documented in the footnotes of relevant tables and/or figures outputs. For participant listing, the qualifiers collected will be presented. When evaluating the value to determine the normal range indicator or CTCAE severity grade, the numeric values will be used; however, if the numeric value is equal to a cutoff value, the inequality signs will be considered.

Potentially Clinically Significant (PCS) Lab Tests Result Summary

The post-baseline lab tests values are PCS if they meet both the observed value criteria and/or the change from baseline criteria listed in Table 3.

Table 3 Criteria for Potentially Clinically Significant Lab Parameters

Lab Panel	Lab Parameter	Flag	Criteria
Hematology	Hemoglobin (g/L)	Low	< 80

Lab Panel	Lab Parameter	Flag	Criteria
	White Blood Cell Count ($10^9/L$)	High	> ULN and increase > 40
		Low	< 2
		High	> 35
	Platelet Count ($10^9/L$) [a]	Low	< 50
		High	> 999
Chemistry	AST (U/L)	High	> 2 x baseline
	ALT (U/L)	High	> 2 x baseline
	Alkaline Phosphatase (U/L)	High	> 2 x ULN
	Total Bilirubin (umol/L)	High	> 2 x ULN
	Potassium (mmol/L)	Low	< 3.0
	Creatinine (umol/L)	High	> 6.0
		High	> 2 x ULN

ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; ULN = Upper Limit of Normal Value.

[a] Low platelet counts are counted as being clinically significant only if they occur $\geq$ 4 weeks post administration of IMP.

The number and percentage of participants with PCS post-baseline values will be summarized by treatment group. The percentages will be calculated relative to the number of participants with at least one post-baseline assessment of the parameter, and a baseline assessment when the criteria involve comparison with baseline value. The numerator is the total number of participants with at least one PCS post-baseline value. Supportive listings of participants with PCS hematology and chemistry values will be provided including all the lab data collected in specific lab tests. Supportive listings of coagulation and urinalysis parameters will also be provided.

Spaghetti plots for ALT will be provided.

4.3.2.3 Physical Examination

A full physical examination (PE) will be conducted at the Screening Visit. A brief PE will be conducted at other scheduled timepoints starting from Day -1. For each body system, the result will be judged by the Investigator as “Normal” or “Abnormal” with clinical significance information collected.

Each body system will be assessed (“Normal”, “Abnormal (NCS)”, “Abnormal (CS)”), and will be listed.

4.3.2.4 Neurological Examination

Neurological Examinations will include the assessment of mental status, cranial nerve examination, motor examination, reflexes, coordination, sensory examination, and gait. The neurologic test results will be judged by the Investigator as “Normal” and “Abnormal” with clinical significance information collected.

Each neurologic test will be assessed (“Normal”, “Abnormal (NCS)”, “Abnormal (CS)”), and will be listed.

4.3.2.5 Electrocardiogram

ECG parameters include heart rate (beats/min), RR interval (msec), PR interval (msec), QRS complex (msec), uncorrected QT interval (msec), Fredericia corrected QT interval (QTcF) (msec) and other parameters per clinical judgement. All the ECG results will be reviewed by the Investigator and be judged as “Normal” and “Abnormal”. If the overall ECG assessment is “Abnormal”, then the individual ECG parameter’s clinical significance will be documented on the CRF. When the overall assessment is “Abnormal” and there is any clinically significant ECG parameter, then the overall assessment will be presented as ‘Abnormal, Clinically Significant (CS)’; otherwise, the overall assessment will be presented as “Abnormal, Not Clinically Significant (NCS)”.

For ECG overall assessment by the Investigator, a shift table from baseline to post-baseline will be provided for each post-baseline timepoint.

All ECG data including the overall assessment and individual parameters’ clinical significance when collected will be listed.

4.3.2.6 Vital Signs

Vital sign parameters include systolic blood pressure (mmHg), diastolic blood pressure (mmHg), pulse rate (beats/min), respiration rate (breath/min), temperature (C), height (cm), weight (kg), and BMI (kg/m²).

The post-baseline vital sign values are PCS if they meet both the observed value criteria and the change from baseline criteria listed in **Table 4**.

Table 4 Criteria for Potentially Clinically Significant Vital Sign Parameters

Vital Sign Parameter	Flag	Criteria
Systolic Blood Pressure (mmHg)	High	≥ 180 and increase from baseline ≥ 20
	Low	≤ 90 and decrease from baseline ≥ 20
Diastolic Blood Pressure (mmHg)	High	≥ 105 and increase from baseline ≥ 15
	Low	≤ 50 and decrease from baseline ≥ 15
Pulse Rate (beats/min) Tachycardia Event	High	≥ 110 beats/min and increase $\geq 15\%$ from baseline
Pulse Rate (beats/min) Bradycardia Event	Low	≤ 50 beats/min and decrease $\geq 15\%$ from baseline

The number and percentage of participants with PCS post-baseline values will be summarized by treatment group. The percentages will be calculated relative to the number of participants with baseline and at least one post-baseline assessment. The numerator is the total number of participants with at least one PCS post-baseline value. A supportive listing of participants with PCS values by study will be provided including all the vital sign data collected.

4.3.2.7 Magnetic Resonance Imaging (MRI)

An MRI of the brain will be performed at Screening Visit, and at other scheduled post-baseline timepoints. MRI of the full spine and cervical spine will also be performed. Clinical MRI monitoring for signs of inflammatory cerebral disease and clinical MRI monitoring for signs of dorsal root ganglion toxicity will be listed. Brain and full spine results will be included in the listings. Cervical spine results are exploratory in nature and are outside of the scope of this SAP.

4.4 Exploratory Endpoints Analysis

4.4.1 Somatosensory Evoked Potentials (SSEP)

4.4.1.1 Definition of Endpoints

The endpoint is the change from baseline in SSEPs. The SSEPs are collected at the clinical sites and then reviewed by an independent reviewer. The independent reviewer evaluates the SSEPs for abnormalities which are categorized as normal/abnormal and, if abnormal, as clinically significant/not clinically significant.

4.4.1.2 Main Analytical Approach

The independent reviewer evaluations as well as any data for the components/parameters collected by the site will be listed.

4.4.2 AEs Related to the IMP Procedure Catheter

4.4.2.1 Definition of Endpoints

The endpoint is the frequency and severity of AEs related to the catheter used for infusion of SBT101 intrathecally (European only endpoint).

4.4.2.2 Main Analytical Approach

AEs, TEAEs, and relatedness of AEs are defined in Section 4.3.2.1. Summaries and a listing of AEs related to the IMP procedure catheter will be provided, as described in Section 4.3.2.1.

4.5 Safety Analyses

Additional safety data that will be summarized includes drug exposure and pregnancy reports of the study participant's partners. All safety analyses will be based on the Safety Analysis Set and will be summarized by treatment group unless otherwise stated.

4.5.1 Extent of Exposure

For the participants enrolled in the Part 1 dose escalation phase, the SBT101 infusion procedure will be performed on Day 1. The IMP procedure data includes the IMP procedure date, start and end time, total duration, total volume administered, whether the full or partial dose is administered, the interruption if any during the procedure, whether the IMP procedure is completed and reason if not, and related AE(s) which occurred during or after the IMP procedure.

All collected data from the IMP procedure will be provided in listings.

The following parameters will be tabulated with descriptive statistics by treatment group for participants who receive SBT101 on Day 1 of Part 1.

- Total Volume Administered (mL): Continuous variable
- Dose Administered (Full/Partial): Categorical variable
- IMP Procedure Interrupted (Yes/No): Categorical variable
- IMP Procedure Completed (Yes/No): Categorical variable
- Number of Participants with a related AE during or after the IMP Procedure: Categorical variable

4.5.2 Pregnancy Test

In the event of any pregnancies in study participants' partners, consent will be requested to follow the mother and child after delivery. All pregnancies that occur or become confirmed during the study must be reported in a Pregnancy Form.

5. SAMPLE SIZE DETERMINATION

Please note that the sample size described below is from protocol version 9.0. Per Sponsor request in October 2024, the Dose Expansion Phase will no longer be included in the study and analyses pertaining to the Dose Expansion Phase are removed from this version of the SAP.

No formal sample size calculation was performed for this study.

6. CHANGES FROM AND ADDITIONS TO METHODS PLANNED IN THE PROTOCOL

Per Sponsor request in October 2024, the Dose Expansion Phase will no longer be included in the study and analyses pertaining to the Dose Expansion Phase are removed from this version of the SAP.

As of 29 May 2025, the Sponsor has made the decision to close the study. The SAP has been updated to remove many of the endpoints, and update others, and to modify the analyses accordingly.

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8. SUPPORTING DOCUMENTATION

Appendix 1 Schedule of Procedures/Assessments

Table 5 Schedule of Assessments for Screening to Day 90 (Month 3)

Activity/Assessment	Screening	Day -1		Day 1		Day 2		Day 4	Day 8	Day 15	Day 22	Day 30 (M1)	Day 38, 52, 68, and 82	Day 45	Day 60 (M2)	Day 75	Day 90 (M3)
		Admission		Pre Dose	Post Dose	Discharge											
<i>Visit Window</i>	-120 days							±1 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±7 days
<i>Visit Number</i>	<i>Visit 1</i>	<i>Visit 2</i>		<i>Visit 3</i>	<i>Visit 4</i>	<i>Visit 4</i>		<i>Visit 5</i>	<i>Visit 6</i>	<i>Visit 7</i>	<i>Visit 8</i>	<i>Visit 9</i>	<i>ELISpot^{1,3}</i>	<i>Visit 10</i>	<i>Visit 11</i>	<i>Visit 12</i>	<i>Visit 13</i>
<i>Visit Type</i>	<i>Clinic</i>	<i>Clinic</i>		<i>Clinic</i>		<i>Clinic</i>		<i>Phone Call</i>	<i>Clinic</i>	<i>Remote¹</i>	<i>Remote¹</i>	<i>Clinic</i>	<i>Remote</i>	<i>Remote¹</i>	<i>Clinic</i>	<i>Remote¹</i>	<i>Clinic</i>
Informed Consent	X																
Inclusion/Exclusion Criteria	X	X															
Medical History and Demographics	X																
Physical Examination ²	X	X				X			X			X			X		X
Adrenal Function Laboratory Test	X																
HIV, HBV, and HCV Testing	X																
Genetic Testing for <i>ABCD1</i> Mutation	X																
Vital Signs	X		X			X			X			X			X		X
Height and Weight	X	X										X			X		X
Electrocardiogram	X					X			X			X			X		X
Neurological Examination	X											X			X		X
Electrophysiological Exam	X											X			X		X
Somatosensory Evoked Potentials	X																X
MRI of the Full Spine ^{3, 14}	X																X
MRI of the Brain ³	X											X					X

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Activity/Assessment	Screening	Day -1		Day 1		Day 2		Day 4	Day 8	Day 15	Day 22	Day 30 (M1)	Day 38, 52, 68, and 82	Day 45	Day 60 (M2)	Day 75	Day 90 (M3)
		Admission		Pre Dose	Post Dose	Discharge											
Visit Window	-120 days							±1 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±7 days
Visit Number	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15	Visit 16	Visit 17
Visit Type	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic	Clinic
MRI of the Cervical Spine ¹³	X																
Expanded Disability Status Score	X																
SSPROM	X																
Balance Evaluation System Test (MiniBEST)	X																
6-minute Walk Test, Dual-task Timed Up and Go ⁴	X																
2-minute Walk Test, 5 Times Sit-to-Stand Test, Timed Up and Go ⁴	X																
Postural Body Sway ⁴	X																
Clinical Global Impression Scale	X																
MSWS-12, MSQoL-54, PGI Scales, and Urinary and Bowel Questionnaire	X																
Randomization ⁵	X																
IMP Procedure ⁶					X												
IV Methylprednisolone Infusion ⁷		X			X	X											
Oral Prednisone Treatment ⁸																	
Blood Chemistry	X ⁹	X				X		X	X	X	X	X			X	X	X
Hematology	X	X				X		X	X	X	X	X			X	X	X
Urinalysis	X																
Neutralizing Antibody Titer Testing	X									X	X	X			X	X	X

Everyday starting on Day 3

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Page 27 of 33

Activity/Assessment	Screening	Day -1		Day 1		Day 2		Day 4	Day 8	Day 15	Day 22	Day 30 (M1)	Day 38, 52, 68, and 82	Day 45	Day 60 (M2)	Day 75	Day 90 (M3)
		Admission	Post Dose	Pre Dose	Post Dose	Discharge											
Visit Window	-120 days							±1 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±7 days
Visit Number	Visit 1	Visit 2		Visit 3		Visit 4		Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	ELLISpot ¹³	Visit 10	Visit 11	Visit 12	Visit 13
Visit Type	Clinic	Clinic		Clinic		Clinic		Phone Call	Clinic	Remote ¹	Remote ¹	Clinic	Remote ¹	Remote ¹	Clinic	Remote ¹	Clinic
Enzyme-linked Immunosorbent Spot ¹²		X								X	X	X	X	X	X	X	X
Plasma Biomarkers ⁹	X	X															
Cerebrospinal Fluid Biomarkers ¹⁰			X														
Viral Shedding ¹¹	X									X	X	X			X	X	X
CentrePoint Watch Data Collection																	
Continuous data collection (everyday)																	
Concomitant Medications	X	X	X	X	X	X		X	X	X	X	X		X	X	X	X
Adverse Events Monitoring		X	X	X	X	X		X	X	X	X	X		X	X	X	X
Instrumented Gait Analysis (sub-study)	X																

Abbreviations: HBV = hepatitis B virus; HBC = hepatitis C virus; HIV = human immunodeficiency virus; IMP = investigational medicinal product; IV = intravenous; MRI = magnetic resonance imaging; M = month; MSQoL-54 = Multiple Sclerosis Quality of Life-54; MSWS-12 = Multiple Sclerosis Walking Scale; PGI = Patient Global Impression; SSPROM = Severity Score System for Progressive Myelopathy.

1. A qualified professional will conduct a home healthcare visit for sample collection in conjunction with the site staff, who will conduct assessments virtually. Patients will be contacted by the clinical site to review and record concomitant medications, AEs and functional progress since the last visit. The phone calls will be conducted until the patient has completed immunosuppression regimen tapering.
2. A full physical examination will be conducted at Screening. All other physical examinations will be brief physical examinations.
3. With and without contrast.
4. Completed using the Mobility Lab (OPAL) sensors.
5. IMP Request and randomization (Dose Level 2 Cohort and Dose- Expansion Cohort) should occur after patient's eligibility has been confirmed, but before Day 1.
6. Patients receiving SBT101 will be administered SBT101 via IT infusion; patients randomized to the control arm will undergo an imitation (sham) procedure. All patients must remain at the study site for a 24-hour observational period prior to discharge.
7. The first dose of IV methylprednisolone will be administered on Day -1 and should be completed at least 6 hours before IMP infusion, the second IV methylprednisolone should be administered approximately 2 hours after completion of the IMP procedure, and the third infusion on Day 2 prior to discharge.
8. Maintenance immunosuppressant medication will be dispensed to patients prior to discharge. Patients will be on prednisone/prednisolone (0.5 mg/kg orally once a day) starting on Day 2 for a minimum of 3 months.
9. Patients should be fasted.
10. The CSF sample will be collected after the IMP catheter has been inserted and prior to the IMP infusion (i.e., SBT101 infusion or imitation (sham) procedure). Collection of the CSF sample will be performed via gravity. Patients should refrain from air travel for at least 2 days after cerebrospinal fluid collection.
11. Viral shedding (serum, saliva, urine) assessments are to be performed until 3 consecutive negative results are obtained after Visit 13 (Day 90).

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Activity/Assessment	Screening	Day -1		Day 1		Day 2		Day 4	Day 8	Day 15	Day 22	Day 30 (M1)	Day 38, 52, 68, and 82	Day 45	Day 60 (M2)	Day 75	Day 90 (M3)
		Admission	Pre Dose	Post Dose	Discharge												
Visit Window	-120 days							±1 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±2 days	±7 days
Visit Number	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15	Visit 16	Visit 17
Visit Type	Clinic	Clinic	Clinic	Clinic	Phone Call	Clinic	Remote ¹	Remote ¹	Clinic	Remote ¹	Remote ¹	Clinic	Remote	Remote ¹	Clinic	Remote ¹	Clinic

12. Patients enrolled at UMass Chan will have an additional ELISpot collection at Day -1, 15, 22, 30, 45, 60, 75, and 90.

13. ELISpot collection at Day 38, 52, 68, and 82 is only for UMass Chan patients.

14. Full Spine MRI (inclusive of Cervical, Thoracic and Lumbar Spine). Cervical Spine MRIs should be completed based on Cervical Spine Protocol.

Table 6 Schedule of Assessments for Day 97 to Day 720 (Month 24)

Activity/Assessment	Day 97, Day 104, and Day 111	Day 120 (M4)	Day 150 (M5)	Day 180 (M6)	Day 270 (M9)	Day 360 (M12)	Day 450 (M15)	Day 540 (M18)	Day 630 (M21)	Day 720 (M24)
<i>Visit Window</i>	± 2 days	± 2 days	± 2 days	± 7 days	± 2 days	± 7 days	± 2 days	± 7 days	± 2 days	± 7 days
<i>Visit Number</i>	Visits 14 to 16	Visit 17	Visit 18	Visit 19	Visit 20	Visit 21	Visit 22	Visit 23	Visit 24	Visit 25
<i>Visit Type</i>	Remote ¹	Clinic	Remote ¹	Clinic	Clinic	Clinic	Remote ²	Clinic	Remote ²	Clinic
Vital Signs		X		X	X	X		X		X
Electrocardiogram		X		X		X		X		X
Brief Physical Examination		X		X	X	X		X		X
Height and Weight		X			X	X		X		X
Neurological Examination		X		X		X		X		X
Electrophysiological Exam		X		X		X				X
Somatosensory Evoked Potentials						X				
MRI of the Full Spine ^{3,9}				X		X				
MRI of the Brain ³				X		X		X		X
MRI of the Cervical Spine						X				X
Blood Chemistry	X	X	X	X	X	X		X		X
Hematology		X	X	X	X	X		X		X
Urinalysis				X		X				X
Neutralizing Antibody Titer Testing		X	X	X	X	X				
Enzyme-linked Immunosorbent Spot		X	X	X	X	X				
Plasma Biomarkers ⁸				X		X				X
Lumbar Puncture and Cerebrospinal Fluid Collection for Biomarkers ⁴						X				X
Viral Shedding ⁵		X	X	X	X	X				
Extended Disability Status Score				X		X		X		X
SSPROM				X		X		X		X

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Activity/Assessment	Day 97, Day 104, and Day 111	Day 120 (M14)	Day 150 (M15)	Day 180 (M16)	Day 270 (M19)	Day 360 (M12)	Day 450 (M15)	Day 540 (M18)	Day 630 (M21)	Day 720 (M24)
<i>Visit Window</i>	±2 days	±2 days	±2 days	±7 days	±2 days	±7 days	±2 days	±7 days	±2 days	±7 days
<i>Visit Number</i>	Visits 14 to 16	Visit 17	Visit 18	Visit 19	Visit 20	Visit 21	Visit 22	Visit 23	Visit 24	Visit 25
<i>Visit Type</i>	Remote ¹	Clinic	Remote ¹	Clinic	Clinic	Clinic	Remote ²	Clinic	Remote ²	Clinic
Balance Evaluation System Test (MiniBEST)				X		X		X		X
2-minute Walk Test, 5 Times Sit-To-Stand Test, and Timed Up and Go ^{6,7}				X	X	X	X	X	X	X
6-minute Walk Test and Dual-task Timed Up and Go ⁶				X		X		X		X
Postural Body Sway ^{6,7}				X	X	X	X	X	X	X
Clinical Global Impression and CGI-C				X		X		X		X
MSWS-12, MSQoL-54, PGI Scales, and Urinary and Bowel Questionnaire				X		X				X
CentrePoint Watch Data Collection					Continuous data collection (everyday)					
Concomitant Medications	X	X	X	X	X	X	X	X	X	X
Adverse Events Monitoring	X	X	X	X	X	X	X	X	X	X

Abbreviations: M = month; MRI = magnetic resonance imaging; MSQoL-54 = Multiple Sclerosis Quality of Life-54; MSWS-12 = Multiple Sclerosis Walking Scale; PGI = Patient Global Impression; SSPROM= Severity Score System for Progressive Myelopathy.

1. A qualified professional will conduct a home healthcare visit for sample collection in conjunction with the site staff, who will conduct assessments virtually. Patients will be contacted by the clinical site to review and record concomitant medications, AEs and functional progress since the last visit. The phone calls will be conducted until the patient has completed immunosuppression regimen tapering.
2. Patients will be contacted by the study site staff to conduct assessments virtually.
3. With and without contrast.
4. Patients should refrain from air travel at least 2 days after cerebrospinal fluid collection.
5. Viral shedding (serum, saliva, urine) assessments are to be performed until 3 consecutive negative results are obtained after Visit 13 (Day 90).
6. Completed using the Mobility Lab (OPAL) sensors.
7. The qualified professional will not routinely conduct these assessments with the patients during home healthcare visits.
8. Patients should be fasted.
9. Full Spine MRI inclusive of cervical, thoracic and lumbar Spine. Cervical Spine MRIs should be completed based on Cervical Spine Protocol.

Appendix 2 NCI-CTCAE V5.0 Toxicity Grading

Table 7 Laboratory Grading Scale – CTCAE version 5.0

Serum ⁽¹⁾	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life-threatening (Grade 4) ⁽²⁾
Sodium – Hyponatremia mEq/L or mmol/L	<LLN - 130	125-129 and asymptomatic	125-129 and symptomatic; 120-124 regardless of symptoms	<120; life-threatening consequences
Sodium – Hypernatremia mEq/L or mmol/L	>ULN - 150	>150 - 155; intervention initiated	>155 - 160; hospitalization indicated	>160; life-threatening consequences
Potassium – Hyperkalemia mEq/L or mmol/L	>ULN - 5.5	>5.5 - 6.0; intervention initiated	>6.0 - 7.0; hospitalization indicated	>7.0; life-threatening consequences
Potassium – Hypokalemia mEq/L	<LLN - 3.0	Symptomatic with <LLN - 3.0; intervention indicated	<3.0 - 2.5; hospitalization indicated	<2.5; life-threatening consequences
Glucose – Hypoglycemia mg/dL	<LLN - 55	<55 - 40	<40 - 30	<30
Creatinine increased – mg/dL	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN
Calcium – hypocalcemia mg/dL	<LLN - 8.0	<8.0 - 7.0	<7.0 - 6.0	<6.0
Calcium – hypercalcemia mg/dL	>ULN - 11.5	>11.5 - 12.5	>12.5 - 13.5	>13.5
Magnesium – hypomagnesemia mg/dL	<LLN - 1.2	<1.2 - 0.9	<0.9 - 0.7	<0.7
Magnesium – hypermagnesemia mg/dL	>ULN - 3.0	NA	>3.0 - 8.0	>8.0 mg/dL
CPK – mg/dL	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN
Albumin – Hypoalbuminemia g/dL	<LLN - 3	<3 - 2	<2 g/dL	NA
Alkaline phosphate –increase by factor	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Liver Function Tests – ALT, AST increase by factor	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
GGT increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal

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Serum [1]	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life-threatening (Grade 4) [2]
Blood bilirubin increased	>ULN - 1.5 x ULN if baseline was normal; > 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x ULN if baseline was normal; >1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x ULN if baseline was normal; >3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal
Cholesterol mg/dL	>ULN - 300	>300 - 400	>400 - 500	>500
Pancreatic enzymes – amylase, lipase increased	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN; >2.0 - 5.0 x ULN and asymptomatic	>2.0 - 5.0 x ULN with signs or symptoms; >5.0 x ULN and asymptomatic	>5.0 x ULN and with signs or symptoms
Hemoglobin decreased (Anemia), g/dL	<LLN - 10.0	<10.0 - 8.0	<8.0	NA
Hemoglobin increased, g/dL	Increase in >0 - 2	Increase in >2 - 4	Increase in >4	NA
Lymphocyte count decreased, 10 ⁹ /L	<LLN - 0.8	<0.8 - 0.5	<0.5 - 0.2	<0.2
Lymphocyte count increased, 10 ⁹ /L	NA	>4 - 20	>20	NA
Neutrophil count decreased, 10 ⁹ /L	<LLN - 1.5	<1.5 - 1.0	<1.0 - 0.5	<0.5
Platelet count decreased, 10 ⁹ /L	<LLN - 75.0	<75.0 - 50.0	<50.0 - 25.0	<25.0
White blood cell decreased, 10 ⁹ /L	<LLN - 3.0	<3.0 - 2.0	<2.0 - 1.0	<1.0

“ULN” is the upper limit of the normal range.

[1] The laboratory values provided in the tables serve as guidelines and are dependent upon institutional normal parameters. Institutional normal reference ranges should be provided to demonstrate that they are appropriate.

[2] The clinical signs or symptoms associated with laboratory abnormalities might result in characterization of the laboratory abnormalities as potentially life-threatening (Grade 4). For example, a low sodium value that falls within a Grade 3 parameter (125-129 mEq/L) should be recorded as a Grade 4 hyponatremia event if the participant had a new seizure associated with the low sodium value.