1.0 Title Page

Statistical Analysis Plan

Study M15-563

An Extension Study of ABBV-8E12 in Progressive Supranuclear Palsy (PSP)

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1.1 List of Abbreviations and Definition of terms

AE	Adverse Event
ALT	Alanine Aminotransferase
aPTT	Activated Partial Thromboplastin Time
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CGI-C	Clinical Global Impression of Change
CGI-S	Clinical Global Impression of Severity
CMC	Chemistry Manufacturing and Control
CPK	Creatine Phosphokinase
CRF	Case Report Form
CSF	Cerebrospinal Fluid
CSR	Clinical Study Report
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common Terminology Criteria for Adverse Events
CTT	Color Trails Test
DBP	Diastolic Blood Pressure
DMC	Data Monitoring Committee
DNA	Deoxyribonucleic Acid
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EQ-5D	EuroQol-5D
GABA	Gamma-Aminobutyric Acid
HR	Heart Rate
IA	Interim Analysis
ITT	Intent-to-Treat
INR	International Normalized Ratio
LFT	Letter Fluency Test
LLN	Lower Limit of Normal
LP	Lumbar Puncture
LTE	Long-term Extension
LS	Least Square

LSLV	Last Subject Last Visit
MAPT	Microtubule Associated Protein Tau
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MD	Mean Diffusivity
MMRM	Mixed-effect Model Repeated-Measures
MRI	Magnetic Resonance Imaging
NFL	Neurofilament Light Protein
NNIPPS-PPS	Natural History and Neuroprotection in Parkinson Plus Syndromes-Parkinson Plus Scale
PBO	Placebo
PCS	Potentially Clinically Significant
PGI-C	Patient Global Impression of Change
PK	Pharmacokinetic
PSP	Progressive Supranuclear Palsy
PSP-QoL	Progressive Supranuclear Palsy Health Related Quality of Life Scale
PSPRS	Progressive Supranuclear Palsy Rating Scale
PT	Prothrombin Time
PT/INR	Prothrombin Time/International Normalized Ratio
PTT	Partial Thromboplastin Time
PTAE	Post-treatment AE
PTs	Preferred Terms
QRS	ECG QRS Complex
QT	Measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle
QTcF	QT corrected for heart rate using Fridericia's Method
RBANS	Repeatable Battery for Assessment of Neuropsychological Status
RBC	Red Blood Cell Count
RD	Radial Diffusivity
RNA	Ribonucleic Acid
SAE	Serious Adverse Event
SBP	Systolic Blood Pressure
SDAC	Statistical and Data Analysis Center
SEADL	Schwab and England Activities of Daily Living Scale
SOC	System Organ Class

TEAE	Treatment-emergent Adverse Event
ULN	Upper Limit of Normal
UPDRS	Unified Parkinson's Disease Rating Scale
VAS	Visual Analog Scale

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3.0 Introduction

This analysis plan describes the statistical analyses to be completed by AbbVie Statistical Science and Programming for ABBV-8E12 Study Protocol M15-563, that incorporates two amendments (original Protocol, Amendment 1, Administrative Change 1, Amendment 2, Administrative Change 2).

This statistical analysis plan (SAP) provides details to further elaborate statistical methods as outlined in the protocol and describes analysis conventions to guide the statistical programming work. Population pharmacokinetic and exposure-response analysis for this study, if performed, will be conducted separately and are not included in this SAP.

Analyses will be performed using SAS version 9.3 or higher (SAS Institute Inc., Cary, NC 27513) under the UNIX operating system.

4.0 Study Objectives, Design and Procedures

4.1 Objectives

The primary objectives of this study are:

- To assess the long-term safety and tolerability of ABBV-8E12 in subjects with progressive supranuclear palsy (PSP).
- To assess the long-term efficacy of ABBV-8E12 in slowing disease progression in subjects with PSP as measured by the PSP Rating Scale (PSPRS).

The secondary objectives of this study are:

- To assess the long-term efficacy of ABBV-8E12 in slowing disease progression and functional impairment in subjects with PSP as measured by secondary endpoints.
- To assess the pharmacokinetics of ABBV-8E12 in subjects with PSP.

- To assess the long-term efficacy of ABBV-8E12 in slowing regional and/or whole brain atrophy in subjects with PSP as measured by volumetric magnetic resonance imaging (MRI).

The exploratory objectives of this study are:

- To assess the long-term efficacy of ABBV-8E12 in slowing disease progression and functional impairment in subjects with PSP as measured by exploratory endpoints.
- To assess the long-term effect of ABBV-8E12 on cerebrospinal fluid (CSF) and plasma tau protein levels.
- To assess the long-term effect of ABBV-8E12 on other potential CSF and plasma biomarkers of disease progression.
- To assess body position and gait in a subset of participating subjects using BioStamp digital sensors.

4.2 Study Design

This study is a long-term extension of the Phase 2, double-blind study, Study M15-562. Subjects who completed the 52-week Treatment Period in Study M15-562 will be eligible for enrollment into Study M15-563. All subjects in Study M15-563 will receive ABBV-8E12 as follows: 1) subjects who received placebo in Study M15-562 will be randomized, in a 1:1 ratio, to 1 of 2 ABBV-8E12 doses (2000 or 4000 mg); and 2) subjects who received ABBV-8E12 2000 or 4000 mg in Study M15-562 will continue on the same dose. Investigators and subjects will remain blinded to the treatment assignments in Study M15-562 after database lock and will be blinded to the dose level of ABBV-8E12 in Study M15-563.

Subjects who enroll in Study M15-563 from Study M15-562 will complete baseline procedures and receive their first infusion of study drug on Day 1 of Study M15-563. For subjects who do not have interruptions in study drug administration between Study M15-562 and Study M15-563, i.e., the duration between the last dose of study drug

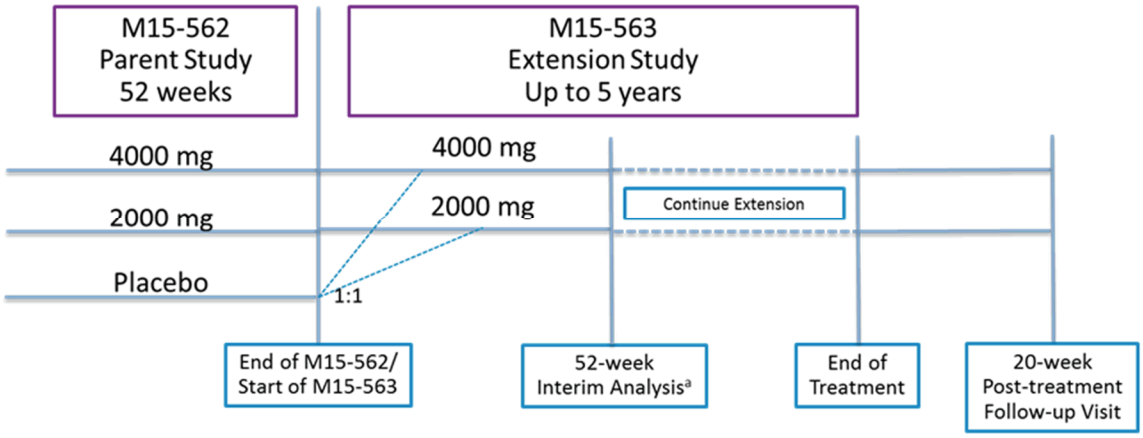
infusion in Study M15-562 and the first dose of study drug in Study M15-563 is no more than 45 days, assessments that were performed at the Week 52 Visit in Study M15-562 will be used for the Day 1 Visit assessments in Study M15-563. If a subject enrolled in Study M15-563 is more than 45 days but less than 8 weeks since the subject's last dose of study drug in Study M15-562; in that case, Day 1 activities for Study M15-563 must be performed.

Subjects will receive 3 infusions of study drug during the first 4 weeks of Study M15-563, the first on Day 1, the second on Day 15 (subjects who received placebo in Study M15-562 will receive ABBV-8E12 on Day 15 of Study M15-563, and subjects who received ABBV-8E12 in Study M15-562 will receive placebo on Day 15 of Study M15-563 to maintain the blind in Study M15-562), and the third on Day 29. After Day 29, subjects will receive study drug infusions every 28 days and will continue to receive ABBV-8E12 until one of the discontinuation criteria is met, until the study is discontinued by the Sponsor, or until the study reaches completion. Subjects will return to the site approximately 20 weeks after their last dose for a post-treatment Follow-up Visit.

A Data Monitoring Committee (DMC) will review unblinded safety data and make recommendations to the Sponsor based on the totality of available clinical data. The DMC memberships, responsibilities, and operating logistics are documented in a DMC charter.

A schematic of the study design is shown below in Figure 1, and a schedule of study procedures is shown in Table 2.

Figure 1. Study Schematic



a. Additional interim analyses may be performed.

4.3 Sample Size

The sample size for this study is dependent on the number of subjects who complete Study M15-562 and are qualified for enrollment into Study M15-563. A total of 330 subjects were planned for Study M15-562. Enrollment of M15-562 has been completed with totally 378 subjects randomized. The number of subjects who enroll in Study M15-563 could be up to 378.

4.4 Interim Analyses

Safety Interim Reviews

Regular interim safety reviews will be performed for this study by the DMC. An independent statistical and data analysis center (SDAC) will be responsible for generating and providing unblinded statistical tables, figures, and listings to the DMC for the interim safety reviews. To maintain the integrity of the trial, a specific data access plan with a strict firewall will be in place to protect the unblinded data and the details will be described in the DMC charter.

Before database lock of Study M15-562, safety reviews of Study M15-563 will follow the same schedules as Study M15-562. DMC safety reviews after subjects from Study M15-562 roll over to Study M15-563. After the last scheduled DMC safety review meeting for Study M15-562, independent DMC safety review meetings for Study M15-563 will occur every 6 months. The database snapshots will be taken for the safety interim reviews.

The DMC will communicate their recommendations to the AbbVie Contact regarding continuing, modifying or terminating the trial due to safety concerns in accordance with the DMC charter.

The following analyses will be conducted for the safety interim reviews:

- Subject disposition and baseline demographics (gender, race, ethnicity, age, weight, height, body mass index)
- Treatment emergent adverse events analysis: overview, by system organ class (SOC) and preferred term (PT), SAE by SOC and PT, AEs leading to discontinuation, AEs with reasonable possibility
- Laboratory mean change analysis and summary of potentially clinically significant (PCS) events
- Mean change analysis of vital signs and summary of PCS events of vital sign values
- Mean change analysis of electrocardiogram (ECG) and summary of PCS events of ECG values
- Summary of concomitant medications
- Summary of PK parameters (as available)
- Exposure-response analyses on any safety endpoint if necessary
- Summary of Columbia Suicide Severity Rating Scale (C-SSRS)
- Summary of MRI results

More details of safety interim analyses will be specified in the DMC Charter.

4.5 Efficacy Variables

Efficacy variable PSP Rating Scale (PSPRS) total score will be used to assess the treatment effect of ABBV-8E12 in slowing disease progression.

Other efficacy variables include Unified Parkinson's Disease Rating Scale (UPDRS) Part II score, Clinical Global Impression of Severity and Change (CGI-S, CGI-C) score, the Schwab and England Activities of Daily Living Scale (SEADL) score, Patient Global Impression of Change (PGI-C), PSP Staging System (PSP-SS) (composite of items from PSPRS), Time from first dose of M1-562 to loss of ability to walk independently as measured by PSPRS item 26.

Exploratory efficacy variables include the time from first dose of M1-562 to death, EuroQuality of Life (EQ-5D), Letter Fluency Test (LFT) score, Repeatable Battery for Assessment of Neuropsychological Status (RBANS) score, Color Trails Test (CTT) (Parts 1 and 2) score, Natural History and Neuroprotection in Parkinson Plus Syndromes-Parkinson Plus Scale (NNIPPS-PPS) total score, and Frequency of hospitalizations related to PSP.

4.6 Safety Variables

The following safety variables will be analyzed for the study: adverse event (including infusion and allergic reactions), vital signs, C-SSRS, laboratory abnormalities, ECG, and MRI safety evaluations.

4.7 Pharmacokinetic Variables

The concentration of ABBV-8E12 in serum and CSF samples will be summarized at each collection time point in the study. Data from this study may be combined with data from other ABBV-8E12 studies for pharmacokinetic analyses.

4.8 Biomarker and Pharmacogenetic Research Variables

4.8.1 Biomarker Research Variables

Blood and CSF samples will be collected to conduct research to investigate disease-related and drug-related biomarkers. The biomarkers to be analyzed may include, but are not limited to, the following:

- CSF and Plasma Biomarkers:
  - Tau in CSF and plasma
  - Additional exploratory CSF and plasma-based pharmacodynamic variables for which concentration data are reported
- Imaging Biomarkers:
  - Regional and/or whole brain volume derived from MRI
  - Fractional anisotropy and diffusivity measures in brain regions of interest derived from DTI
- Digital Biomarkers:
  - BioStamp sensor motor outcomes including posture, gait, and step count

4.8.2 Pharmacogenetic Research Variables

Optional samples may be collected to conduct exploratory investigations into known and novel biomarkers. The types of biomarkers to be analyzed may include, but are not limited to, nucleic acids, proteins, lipids or metabolites. The samples may be analyzed as part of a multi-study assessment of factors influencing the subjects' response to the study drug (or drugs of the same or similar class) or the development and progression of the subjects' disease or related conditions. The samples may also be used to develop new diagnostic tests, therapies, research methods or technologies.

If such data are obtained, the results from these analyses would be exploratory in nature and may not be included with the study report. The analysis for such data is not addressed in this SAP.

5.0 Analysis Populations

5.1 Analysis Data Sets

Data Sets for Efficacy Analyses

Two data sets will be created for the efficacy analysis: an intent-to-treat (ITT) data set and a delayed-start data set.

ITT Data Set: the ITT data set consists of all subjects who received any dose of study drug in Study M15-563. All efficacy analyses will be conducted on the ITT data set using data from Study M15-563 alone unless otherwise specified.

Delayed-Start Data Set: The Delayed-Start data set includes all subjects from the Study M15-562 ITT data set who received placebo or ABBV-8E12 in Study M15-562 regardless of whether they enroll in Study M15-563 or not. For the Delayed-Start analysis, efficacy data for PSPRS total score from both Study M15-562 and Study M15-563 studies will be included.

Data Sets for Safety Analyses

The safety data set will consist of all subjects who received any dose of study drug infusion in Study M15-563. For safety analyses, the actual treatment received will be used instead of the treatment assignment at enrollment. There are two safety data sets: a Stand-Alone data set and a Cumulative data set.

Stand-Alone Data Set: The Stand-Alone data set is the primary data set for safety analyses, and will contain data from Study M15-563 only, regardless of the treatment received in Study M15-562. Baseline for the Stand-Alone data set will be the last observation on or before the first dose of ABBV-8E12 in Study M15-563. If no Baseline is recorded in Study M15-563, the last value in Study M15-562 will be used as the Baseline.

Cumulative Data Set: The Cumulative data set will consist of data from both Study M15-562 and Study M15-563. It is the secondary data set for safety analyses. For subjects who were in the placebo group in Study M15-562, their safety data from Study M15-562 will not be included in the Cumulative data set but their safety data from Study M15-563 will be included. For subjects who were in the placebo group in Study M15-562, Baseline will be the last observation prior to the first dose of study drug in Study M15-563. For subjects who were in ABBV-8E12 treatment groups in Study M15-562, Baseline for the Cumulative data set will be their Baseline in Study M15-562.

Data Sets for Biomarker Analyses

For the analysis of biomarker data, the actual treatment received will be used rather than the treatment assignment at enrollment. Descriptive statistics will be provided for all scheduled post-baseline times of measurement in Study M15-563, with all subjects who were administered a dose in Study M15-563 included. The descriptive statistics will also be provided for the baseline measurement. For subjects whose treatment in Study M15-562 was one of the ABBV-8E12 doses, the baseline value for Study M15-563 will be the baseline value of Study M15-562. For subjects whose treatment in Study M15-562 was placebo, the baseline value will be the last measurement obtained before the first dose of Study M15-563, which might be the last measurement of Study M15-562 as explained in Section 4.2.

Longer-Term Biomarker Data Set: Only data of subjects whose treatment in Study M15-562 was with one of the ABBV-8E12 dose levels will be included in this data set. The data set will include the data for all scheduled times of measurement of Study M15-563. The baseline value for this data set will be the baseline value of Study M15-562.

6.0 Demographics, Baseline Characteristics, Medical History, and Previous/Concomitant Medications

The data analysis will be conducted among treatment groups defined as Studies M15-562/M15-563: 2000/2000 mg, 4000/4000 mg, placebo/2000 mg, and placebo/4000 mg.

6.1 Demographic and Baseline Characteristics

The following demographic and baseline characteristics will be summarized for each treatment group, and for overall subjects the Stand-Alone data set.

- Gender (male, female)
- Race (white, black, American Indian/Alaska native, Native Hawaiian or another Pacific Islander, Asian, Other, Multi-Race)
- Ethnicity (Hispanic or Latino)
- Age (years)
- Age group (≤ 65, > 65)
- Weight for all subjects (kg)
- Weight for all male subjects (kg)
- Weight for all female subjects (kg)
- Height (cm)
- Body mass index (BMI, kg/m^2)
- Body mass index category (BMI, kg/m^2) (≤ 25, > 25)

Alcohol and tobacco use will be summarized for each treatment group and overall subjects for the Stand-Alone safety data set. For alcohol use, the number and percentage of subjects who are drinkers, ex-drinkers and non-drinkers (defined as those who have never been a drinker) will be presented. For tobacco use, the number and percentage of users, ex-users and non-users (defined as those who have never been a user) will be presented. A subject reporting multiple use category for the different types of tobacco (cigarette, pipe, cigar and chewing tobacco) will be counted in the tobacco user category.

The following baseline efficacy and clinical variables will be summarized for each treatment group and overall subjects for the ITT data set and Delayed-Start data set (if Delayed-Start analysis will be conducted).

- PSPRS total and domain scores
- UPDRS Part II score
- SEADL score
- CGI-S score
- RBANS total scale score
- Color Trails Test (Parts 1 and 2) score
- Letter Fluency Test score
- NNIPPS-PPS total score
- EQ-5D index score and VAS score

Categorical variables will be summarized by the number and percentage of subjects in each category. No comparisons of treatment groups will be performed for alcohol and nicotine uses. Continuous variables will be summarized with descriptive statistics (number of non-missing observations, mean, standard deviation, median, minimum and maximum). No statistical comparisons of treatment groups will be performed.

6.2 Medical History

Medical history of this study is transferred from medical history in Study M15-562. The conditions/diagnoses recorded in medical/surgical history data will be coded using the most current version of the Medical Dictionary for Regulatory Activities (MedDRA). Data will be summarized and presented using system organ classes (SOCs) and preferred terms (PTs). The SOC will be presented in alphabetical order and the PTs will be presented in alphabetical order within each SOC. The number and percentage of subjects with any condition/diagnosis and condition/diagnosis in a particular SOC and PT will be summarized for each treatment group and overall subjects for the safety Stand-Alone data set. Subjects reporting more than one PT within a SOC will be counted only once for that SOC. No comparison among treatment groups will be performed.

The following progressive supranuclear palsy disease history variables will be summarized for each treatment group and overall subjects for the Stand-Alone data set.

- Age at onset of symptoms of PSP (years)
- Age when first diagnosed as having PSP (years)
- Years since onset of PSP symptoms (Age at study – Age at onset)
- Years since PSP diagnosis (Age at study – Age at diagnosis)
- Family history of PSP (None, biological mother, biological father, full sibling, biological child)

Categorical variables will be summarized with the number and percentage of subjects in each category. Continuous variables will be summarized with descriptive statistics (number of non-missing observations, mean, standard deviation, median, minimum, and maximum). No comparisons of treatment groups will be performed.

6.3 Previous and Concomitant Medications

Previous medications are defined as all medications with a start date before the first study drug administration date. Concomitant medications are defined as all medications, other than study drug, taken during the treatment period (i.e., from the first day of study drug administration through 45 days after the last day of study drug administration). Previous and concomitant medications will be coded using the World Health Organization (WHO) dictionary and will be summarized by generic name and Anatomical Therapeutic Chemical (ATC) classification system level 3. The number and percentage of subjects who take at least 1 medication and who take at least 1 dose of each specific medication in the following categories will be summarized for each treatment group and overall subjects for the Stand-Alone data set.

- Previous medications for PSP (CMCAT = "PROGRESSIVE SUPRANUCLEAR PALSY MEDICATIONS") will be summarized by the following categories:
  - Antipsychotic medication

- Antidepressants
- Medications for Parkinsonian symptoms (including levodopa/carbidopa, dopamine agonists, monoamine oxidase inhibitors, COMT inhibitors, and amantadine).
- Anti-dementia drugs (CMCLAS3 = ANTI-DEMENTIA DRUGS): cholinesterase inhibitors (donepezil, rivastigmine, galantamine) or memantine for cognitive impairment.
- Selective benzodiazepines and gamma-aminobutyric acid (GABA) agonists (zolpidem, zaleplon, eszopiclone, alprazolam, clonazepam and lorazepam for sleep and anxiety). Other medications

- Other previous medications
- Concomitant medications for PSP (CMCAT = "PROGRESSIVE SUPRANUCLEAR PALSY MEDICATIONS") will be summarized by the same categories as previous medications for PSP.
- Concomitant non-medicinal therapy.
- Other concomitant medications.

No comparisons of treatment groups will be performed.

7.0 Subject Disposition

For subjects who are enrolled in the study, the number and percentage of subjects in each disposition category (prematurely discontinued and completed) will be summarized for each treatment group and overall subjects. The interim analyses, the disposition category "ongoing" will also be included.

The number and percentage of subjects who prematurely discontinued study drug or prematurely discontinued from the study will be summarized by reason (primary or any reason) for each treatment group and overall subjects.

In addition, the following additional summaries will be presented for all enrolled subjects:

- The number and percentage of subjects who are enrolled at each site.

- The number and percentage of subjects who prematurely discontinued at each site.

8.0 Study Drug Exposure and Compliance

Summaries of study drug exposure and compliance will be prepared for the Stand-Alone data set.

Study drug exposure will be summarized for each treatment group and overall subjects. Duration of exposure is calculated as the last study drug administration date minus the first study drug administration date + 30. Total subject years of exposure is calculated by summing the duration of exposure across all subjects and dividing this sum by 365 (1 year will be considered as 365 days). The number and percentage of subjects who have taken a total of ≤ 6, 7 to 12, 13 to 18, 19 to 24, 25 to 30, 31 to 36, 37 to 42, 43 to 48, 49 to 54, 55 to 60, and ≥ 61 doses of study drug will be summarized. No comparisons of treatment groups will be performed for this summary. In addition, duration of exposure will be summarized with descriptive statistics (number of non-missing observations, mean, standard deviation, median, minimum and maximum duration and total years).

At each scheduled dosing visit, the investigator will document whether the subject has received entire infusion and the volume administered will be recorded in the eCRF if the entire dose is not administered. The percentage of the assigned dose administered will be calculated. The mean of this percentage across infusions for each subject will be obtained. The descriptive statistics (number of non-missing observations, minimum, mean, median, standard deviation, maximum) based on each subject's mean volume percentage of study drug infusion will be summarized for each treatment group and overall subjects.

9.0 Efficacy Analysis

No efficacy analyses will be conducted. Baseline values and change from baseline of the following primary and secondary efficacy variables will be summarized on both ITT data set and Delayed-start data set:

- PSPRS total score
- UPDRS Part II score
- CGI-C score
- SEADL score
- CGI-S score
- PGI-C score
- PSP-SS (composite of items from PSPRS) score

A Figure of mean of PSPRS total score for each visit will be displayed by treatment groups 2000/2000 mg, 4000/4000 mg, placebo/2000 mg, and placebo/4000 mg. This will be conducted on delayed-start data set.

10.0 Safety Analysis

10.1 General Considerations

Comparisons between treatment groups (Studies M15-562/M15-563) of interest will not be performed.

All other safety assessments that are taken no more than 45 days after the last dose of study drug will be included in the safety evaluation of the Treatment Period, and all safety assessments that are taken more than 45 days but not more than 20 weeks after the last dose of study drug will be included in the safety evaluation for the Post-treatment Follow-up Visit.

10.2 Analysis of Adverse Events

The Stand-Alone data set will be the primary data set for adverse event summaries. Analyses that will also be performed on the Cumulative data set are as follows: adverse event overview, adverse event incidence by system organ class (SOC) and preferred term, adverse event incidence in descending frequency by overall subjects, and SAE incidence by SOC and preferred term.

All adverse events will be coded using the most current version of the Medical Dictionary for Regulatory Activities (MedDRA). A treatment-emergent adverse event (TEAE) is defined as any adverse event that begins or worsens in severity on or after the first study drug dose date and no more than 20 weeks after the last study drug dose date. Analysis of adverse events will also be conducted by geographical region (North America including US and Canada, European countries plus Australia, and Japan).

10.2.1 Adverse Event Overview

The number and percentage of subjects experiencing one or more adverse events in the following adverse event categories will be summarized for each treatment group and overall subjects in both Stand-Alone data set and the Cumulative data set. No comparisons of treatment groups will be performed.

- Any TEAE
- Any TEAE that was rated reasonable possibility of being related to study drug by the investigator
- Any severe TEAE
- Any serious TEAE
- Any TEAE that led to discontinuation of study drug
- Any fatal TEAE
- All deaths

10.2.2 Adverse Event Incidence

TEAE incidence will be summarized and presented using primary MedDRA system organ classes (SOCs) and preferred terms (PTs). The system organ classes will be presented in alphabetical order and the preferred terms will be presented in the alphabetical order within each system organ class. Subjects reporting more than one adverse event for a given MedDRA PT will be counted only once for that term. Subjects reporting more than one adverse event within a SOC will be counted only once for the SOC total. Subjects reporting more than one adverse event will be counted only once in the overall adverse event total.

The number and percentage of subjects experiencing one or more TEAEs will be summarized by PT for each treatment group and overall subjects. The PTs will be presented by decreasing frequency in overall subjects.

The number and percentage of subjects experiencing one or more adverse events in the following adverse event categories will be summarized by primary SOC and PT for each treatment group and overall subjects.

- Any TEAE
- Any serious TEAE
- Any TEAE that led to discontinuation of study drug
- Any TEAE assessed by the investigator to be Reasonable Possibility of Being Related to study drug

The number of subjects experiencing one or more TEAEs will also be summarized by maximum severity category (mild, moderate, severe and unknown) and primary SOC and PT for each treatment group and overall subjects. Subjects reporting more than one TEAE for a given PT will be counted only once for that term in the most severe category reported. If a subject has an adverse event with unknown severity, then the subject will be counted in the severity category of "unknown" even if the subject has another occurrence of the same event with a severity present. The only exception is if the

subject has another occurrence of the same adverse event with the most extreme severity – "Severe." In this case, the subject will be counted under the "Severe" category. No comparisons of treatment groups will be performed.

The number of subjects experiencing one or more TEAEs will also be summarized by maximum relationship category (Reasonable Possibility of Being Related, No Reasonable Possibility of Being Related and Unknown), as assessed by the investigator, and primary SOC and PT for each treatment group and overall subjects. Subjects reporting more than one TEAE for a given PT will be counted only once for that term in the most related category reported. If a subject has an adverse event with unknown relationship, then the subject will be counted in the relationship category of "unknown," even if the subject has another occurrence of the same event with a relationship present. The only exception is that if a subject has another occurrence of the same adverse event with a relationship assessment of "Reasonable Possibility of Being Related." In this case, the subject will be counted under the "Reasonable Possibility of Being Related." No comparisons between treatment groups will be performed.

10.2.3 Listing of Adverse Events

The following additional summaries of adverse events will be prepared only on Stand-Alone data set.

- List of subject numbers associated with each PT for all TEAEs
- List of subject numbers associated with each PT for all TEAEs assessed by the investigator as Reasonable Possibility of Being Related.
- Listing of all serious adverse events
- Listing of all adverse events that led to discontinuation of study drug
- Listing of all fatal adverse events
- Listing of all deaths

10.3 Analysis of Laboratory Tests

Analyses of Laboratory tests will be performed on the Stand-Alone data set.

The laboratory tests are described in the following table.

Table 1. Laboratory tests

Hematology	Clinical Chemistry	Urinalysis
Hematocrit Hemoglobin Red blood cell (RBC) count White blood cell (WBC) count Neutrophils Bands (if detected) Lymphocytes Monocytes Basophils (if detected) Eosinophils (if detected) Platelet count (estimate not acceptable) Mean corpuscular volume (MCV) Mean corpuscular hemoglobin concentration (MCHC) Prothrombin time (PT) Activated partial thromboplastin time (aPTT) PT/INR (Prothrombin Time/International Normalized Ratio)	Blood urea nitrogen (BUN) Creatinine Total bilirubin Albumin Aspartate aminotransferase (AST) Alanine aminotransferase (ALT) Alkaline phosphatase Sodium Potassium Calcium Inorganic phosphate Uric acid Cholesterol Total protein Glucose Triglycerides Bicarbonate/Carbon Dioxide (CO2) Chloride	Specific gravity pH

10.3.1 Analysis of Mean Changes for Laboratory Tests

The following summaries of laboratory data will be included in the output: mean change from baseline to each double-blind visit value and to the minimum, maximum and final double-blind value for each continuous hematology, chemistry and urinalysis variable, mean change from final double-blind value to final post-treatment value presented for each continuous hematology, chemistry and urinalysis variable, shift tables, and potentially clinically significant laboratory values.

10.3.2 Shifts Between Normal and Abnormal for Laboratory Tests

Laboratory observations will be categorized as normal, low, or high relative to the reference (normal) range associated with the laboratory that performed the assay. For each hematology, chemistry and urinalysis variable with a reference range, shift tables will be prepared for shifts from baseline to lowest, highest and final value during the entire study for each treatment group and overall subjects. No comparisons of treatment groups will be performed. Shift tables will also be prepared by geographical region. The tables will present:

- The numbers and percentages of subjects with low or normal observations at baseline who have a high observation at any post-baseline visit
- The numbers and percentages of subjects with normal or high observations at baseline who have a low observation at any post-baseline visit
- The numbers and percentages of subjects with low or normal observations at baseline who have a high observation at the final visit
- The numbers and percentages of subjects with normal or high observations at baseline who have a low observation at the final visit

10.3.3 Potentially Clinically Significant Laboratory Values

Criteria for potentially clinically significant (PCS) values have been predefined for selected laboratory variables as outlined in Appendix A. For each variable, a summary of the number and percentage of subjects in each treatment group who have at least one double-blind observation that meets the PCS criteria and is more extreme than their baseline value will be provided. A listing will also be prepared that will include, for each variable, all observations for each subject that met the PCS criteria for that variable at any time during the study.

10.4 Analysis of Vital Signs and Weight

Vital sign and weight data analyses will be performed on Stand-Alone data set. Vital sign variables include: diastolic blood pressure, systolic blood pressure and pulse rate at

supine and standing positions, orthostatic diastolic blood pressure, orthostatic systolic blood pressure, orthostatic pulse rate, and body temperature. The calculations of orthostatic vital sign values are:

- Orthostatic SBP (mmHg) = Standing SBP – Supine SBP
- Orthostatic DBP (mmHg) = Standing DBP – Supine DBP
- Orthostatic Pulse Rate (bpm) = Standing Pulse Rate – Supine Pulse Rate.

Weight variables include weight and BMI.

10.4.1 Analysis of Mean Changes for Vital Sign and Weight

Diastolic blood pressure, systolic blood pressure and pulse will be analyzed separately for each position of measurement. Analyses of mean change from baseline to each double blinded visit value and to the minimum, maximum and final double-blind value will be presented for each vital sign and weight variable. Analysis of orthostatic SBP, DBP and pulse rate will be conducted similarly.

10.4.2 Potentially Clinically Significant Vital Sign and Weight Values

Criteria for potentially clinically significant values have been predefined for selected vital sign and weight variables as outlined in Appendix. For each variable, a summary of the number and percentage of subjects in each treatment group who have at least one double blind observation that meets the PCS criteria and is more extreme than their baseline value will be provided. A listing will also be prepared that will include, for each variable, all observations for each subject that met the PCS criteria for that variable at any time during the study.

10.5 Analysis of Electrocardiogram (ECG) Variables

Electrocardiogram (ECG) variables include: heart rate (HR), PR interval, QRS interval, uncorrected QT interval, and QT interval corrected for heart rate using Fridericia's

formula (QTcF). Analyses of ECG variables will be performed on the Stand-Alone data set.

10.5.1 Analysis of Mean Changes for ECG

Analyses of mean change from baseline to each double-blind visit value and to the minimum, maximum and final double-blind value will be presented for each ECG variable. Analyses of mean change from final double-blind value to final post-treatment value will also be presented for each ECG variable.

10.5.2 Potentially Clinically Significant ECG Values

Criteria for potentially clinically significant values have been predefined for selected ECG variables as outlined in Appendix C. For each variable, a summary of the number and percentage of subjects in each treatment group who have at least one double-blind observation that meets the PCS criteria and is more extreme than their baseline value will be provided. Listings will also be prepared to include all observations for each variable for each subject that met the PCS criteria for that variable at any time during the study. No comparisons of treatment groups will be performed.

10.6 Analysis for Other Safety Variables

10.6.1 Analysis of Columbia-Suicide Severity Rating Scale (C-SSRS)

Analyses of C-SSRS will be performed on the Stand-Alone data set.

Number and percentage of subjects in the following categories will be summarized for each treatment group and overall subjects by visit and for the entire study:

- Answered 'Yes' to each C-SSRS item
- Had suicidal ideation (defined as answering 'Yes' to one or more suicidal ideation items)
- Had suicidal ideation only (defined as answering 'Yes' to one or more suicidal ideation items and answering 'No' to all suicidal behavior items)

- Had suicidal behavior (defined as answering 'Yes' to one or more suicidal behavior items)
- Had suicidal ideation or behavior (defined as answering 'Yes' to one or more suicidal ideation or behavior items)

10.6.2 Summary of MRI Safety Evaluations

MRI safety evaluations will be summarized by treatment group based on MRI evaluations in the double blinded period. The summaries include the number and percentage of subjects pertaining cerebral edema, micro- and macro-haemorrhages, white matter hyperintensities (ARWMC score) across visits; number and percentage of subjects with presence and increasing severity of cerebral edema; number and percentage of subjects with new micro- and macro-haemorrhage lesions; number and percentage of subject with white matter hyperintensities change (ARWMC score) from previous time point. Descriptive statistics (mean, median, minimum, maximum) of number of new micro- and macro-hemorrhages or new lesions, as well as changes in ARWMC score in the double-blinded period will be presented.

11.0 Pharmacokinetic Analysis

For ABBV-8E12 serum and/or CSF concentration data, descriptive statistics will be provided for each scheduled time of measurement with a breakdown by groups defined by treatment in Study M15-562 and treatment in this study.

12.0 Analysis of Biomarker Research Variables

12.1 Descriptive Statistics

For CSF and plasma concentrations of tau and volumetric MRI variables, descriptive statistics will be provided for each scheduled time of measurement for each treatment group. The descriptive statistics will be provided for the baseline measurement also. The data set for which the descriptive statistics will be provided is described in Section 5.1 under the heading "Data Sets for Biomarker Analyses." The four treatment groups are

those defined in the first paragraph of Section 4.2. That is, the treatments of the 4 groups are:

- Subjects who received ABBV-8E12 2000 mg in Study M15-562 and continue on the same dose in Study M15-563
- Subjects who received ABBV-8E12 4000 mg in Study M15-562 and continue on the same dose in Study M15-563
- Subjects who received placebo in Study M15-562 and receive ABBV-8E12 2000 mg doses in Study M15-563
- Subjects who received placebo in Study M15-562 and receive ABBV-8E12 4000 mg doses in Study M15-563

The descriptive statistics for a post-baseline time will be provided for both the data of the given time and the changes from baseline.

Time of measurement will be indicated for two different reference points. The first reference point will simply be the day of the first dose of Study M15-563. The second reference point is the time relative to the first dose of ABBV-8E12, which will be the first dose of Study M15-562 or the first dose in Study M15-563, depending upon whether the subject was administered ABBV-8E12 or placebo in Study M15-562. For subjects who were treated with ABBV-8E12 in Study M15-562, the time relative to the second reference point will be 52 weeks longer than the time relative to the first reference point. For the subjects whose treatment in Study M15-562 was placebo, the time relative to both reference points will be the same.

The statistics will consist of: number of observations (n), mean, standard deviation, coefficient of variation as a percentage (quotient of standard deviation and mean, multiplied by 100), minimum, median and maximum. If the logarithmic transformation is employed for a variable in the statistical analysis that is described in Section 12.2, the geometric mean will also be reported. All of these descriptive statistics except for the coefficient of variation and the geometric mean will be provided for the change from baseline at each scheduled time of measurement in Study M15-563.

12.2 Analysis on Treatment by ABBV-8E12 for at Least One Year

The data set on which this analysis will be performed is the Longer-Term Biomarker Data Set described in Section 5.1. All the measurements in this data set were obtained after a subject was on treatment with ABBV-8E12 for 52 weeks or longer.

Transformation of Variables for Analysis

If the probability distribution for a variable appears to have considerable non-symmetry (e.g., skewness coefficient > 1.00 in magnitude), a transformation will be sought that has an approximately normal distribution. If a transformation is employed, estimates of central values on the original scale (back transformation of SAS least squares means) will be provided. If the logarithmic transformation is used, the comparison of the treatments will be in terms of the ratio of central values.

Analysis of CSF and Plasma Concentration Variables

For CSF and plasma concentrations of tau, an MMRM analysis will be performed to compare the effects of the 2000 and 4000 mg doses of ABBV-8E12. The model will include classification by ABBV-8E12 dose and time of measurement. There will be an effect for the interaction of ABBV-8E12 dose and time of measurement. The subjects in each treatment group will be viewed as a random sample. The baseline value will be a covariate. The model will also initially have a term for the interaction of baseline value and visit.

After the structure of the covariance matrix is decided upon, as discussed below, a test will be performed on the term for the interaction of baseline value and visit. The term for this interaction will be removed from the model if the statistic is not significant at level 0.100.

Within the framework of the final model, the mean across the scheduled times of measurement will be estimated for each ABBV-8E12 dose level. The hypothesis of no difference between the main effects of the two ABBV-8E12 dose levels (i.e., a composite

assessment for the several times of times of evaluation) will be tested at significance level 0.050. The SAS least squares means (LS means) for the two ABBV-8E12 dose levels across time will be provided and presented graphically.

There will be three candidates for the structure of the covariance matrix for the conditional distribution of the vector of scheduled responses, given the values of the covariate(s). The simplest model will be the compound symmetry model (SAS option CS with the REPEATED statement), and another option will be the one that imposes no conditions on the covariance matrix (SAS option UN with the REPEATED statement). The third model will allow the variances for the several times of response to differ, but impose the condition that all pairs of the response variables have the same correlation coefficient (SAS option CSH with the REPEATED statement). An approximate test will be performed to compare the model with no restrictions to the compound symmetry model, with a multivariate normal distribution assumed for the conditional distribution. Such a test will also be performed to compare the model of intermediate complexity (SAS CSH option) to the compound symmetry model. The approximate test will be that based upon the difference in the values of –2log(likelihood) for the two models, using the chi-square approximation for the null distribution, with degrees of freedom being the difference in the number of parameters required for the two structures of the covariance matrix. If the test statistic is not significant at level 0.050 for either test, the compound symmetry model will be used. If the statistic is significant at level 0.050 for one of the two tests, the compound symmetry model will not be used, and the two more complex models will be compared using the approximate test. If the statistic for this test is significant at level 0.050, the model with no restrictions will be used. Otherwise, the model of intermediate complexity will be used.

Analysis of Imaging Variables

For imaging variables, an MMRM analysis corresponding to that described for the tau variables will be performed. However, for the volumetric MRI variables, there will be two covariates. In addition to the baseline value, a variable reflecting head size

(e.g., intracranial volume) will be a covariate. For this second covariate, interaction with visit will not be included in the model.

For other variables for which data are reported, descriptive statistics will be provided, and appropriate analyses will be performed.

13.0 Table and Appendix

Table 2. Study Activities

Visits & Procedures[b]	Treatment Period[a]																20 Wks Post Last Dose F/U
	Year 1																
	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7	Dose 8	Dose 9	Dose 10	Dose 11	Dose 12	Dose 13	Dose 14	Dose 15	D/C	
	Day 1	Day 15	Day 29	Day 57	Day 85	Day 113	Day 141	Day 169	Day 197	Day 225	Day 253	Day 281	Day 309	Day 337	Day 365		
	Day 1	Wk 2	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48	Wk 52		
Subject/study partner ICF[c]	X																
Medical history update[d]	X																
Randomization	X																
Physical examination	X																
Symptom-driven physical examination[e]								X							X	X	X
Orthostatic vital signs[f,g]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Vital signs[g]																X	X
Body weight (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (WOCBP)[h]	U				U			U							U	S	U
Neurological examination	X				X			X							X	X	X
12-lead ECG	X				X			X							X	X	
Clinical laboratory tests	X				X			X							X	X	
Brain MRI[i]	X				X			X							X	X	X
LP/CSF collection[j]	X							X							X	X	X

Table 2. Study Activities (Continued)

Visits & Procedures[b]	Treatment Period[a]																20 Wks Post Last Dose F/U
	Year 1																
	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7	Dose 8	Dose 9	Dose 10	Dose 11	Dose 12	Dose 13	Dose 14	Dose 15		
	Day 1	Day 15	Day 29	Day 57	Day 85	Day 113	Day 141	Day 169	Day 197	Day 225	Day 253	Day 281	Day 309	Day 337	Day 365		
	Day 1	Wk 2	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48	Wk 52	D/C	
Blood PK sample	X				X			X							X	X	X
ADA Sample collection	X				X			X							X	X	X
Plasma biomarkers	X				X			X							X	X	X
CSF biomarkers	X							X							X	X	X
Optional exploratory PGx DNA and RNA blood sample	X				X			X							X	X	
Administer IV Study Drug	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
PSPRS	1				1			1							1	1	1
CGI-S	2				2			2							2	2	2
CGI-C	3				3			3							3	3	3
SEADL	4				4			4							4	4	4
UPDRS Part II	5				5			5							5	5	5
RBANS															6	6	
CTT Parts 1 & 2															7	7	
Letter Fluency Test (wpm)															8	8	

Table 2. Study Activities (Continued)

Visits & Procedures[b]	Treatment Period[a]																20 Wks Post Last Dose F/U
	Year 1																
	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7	Dose 8	Dose 9	Dose 10	Dose 11	Dose 12	Dose 13	Dose 14	Dose 15		
	Day 1	Day 15	Day 29	Day 57	Day 85	Day 113	Day 141	Day 169	Day 197	Day 225	Day 253	Day 281	Day 309	Day 337	Day 365		
	Day 1	Wk 2	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48	Wk 52	D/C	
NNIPPS-PPS[k]															9	9	
PGI-C[l]	X				X			X							X	X	X
EQ-5D[l]	X														X	X	
C-SSRS[m]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BioStamp Digital[n]	X		X	X	X												
PSP Caregiver Questionnaires	X							X							X	X	X
TSQM-9	X							X							X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE assessment (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Telephone contact[o]	X				X			X							X	X	X

AE = adverse event; ICF = informed consent form; LP = lumbar puncture; PK = pharmacokinetic; PGx = pharmacogenetic; S = serum; U = urine

a. Study drug will be administered on Days 1, 15, and 29, then every 28 days thereafter until 1 of the discontinuation criteria is met, until the Sponsor discontinues the study, or until the study reaches completion. For those Visits that include both study drug infusion and other activities, the Visits may be completed over 2 consecutive days with the second day to include the start and end of the infusion.

Table 2. Study Activities (Continued)

b. Audio recordings/central review of the administration/assessment of selected scales may be conducted.
c. Subject informed consent, or as applicable, legally authorized representative informed consent, and study partner informed consent must be obtained prior to Study M15-563 Day 1 dosing.
d. Review medical history to confirm subject does not meet exclusion criteria prior to randomization.
e. Additional symptom-driven physical examinations may be performed as needed.
f. All supine and standing blood pressure and pulse rate measurements are to be measured as part of an orthostatic assessment.
g. An attempt should be made to obtain all vital sign measurements at the same time of day and using the same arm.
h. For all females of childbearing potential, a negative urine pregnancy test result is also required prior to any radiological procedures.
i. If a subject cannot undergo MRI due to a clinical reason, the AbbVie TA MD should be consulted for approval.
j. Subjects who are not able to undergo an LP may be enrolled with permission of the AbbVie TA MD without the requirement of an LP during the study.
k. The NNIPPS-PPS will not be administered in Japan.
l. Scale may be administered/assessed at any time during the visit, after the other procedures are completed, with the exception of the scheduled infusion time.
m. Scale may be administered/assessed at any time during the visit with the exception of the scheduled infusion time.
n. Device to be worn for 7 days.
o. Only applicable to subjects who prematurely discontinue. Verify consent was obtained prior to making contact.

Note: Numbering listed in the table provides a pre-defined order of administration that these scales should occur during each visit.

Visits & Procedures[b]	Treatment Period[a]														20 Wks Post Last Dose F/U
	Year 2														
	Dose 16	Dose 17	Dose 18	Dose 19	Dose 20	Dose 21	Dose 22	Dose 23	Dose 24	Dose 25	Dose 26	Dose 27	Dose 28		
	Day 393	Day 421	Day 449	Day 477	Day 505	Day 533	Day 561	Day 589	Day 617	Day 645	Day 673	Day 701	Day 729		
	Wk 56	Wk 60	Wk 64	Wk 68	Wk 72	Wk 76	Wk 80	Wk 84	Wk 88	Wk 92	Wk 96	Wk 100	Wk 104	D/C	
Symptom-driven physical examination[c]						X							X	X	X
Vital signs[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body weight (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (WOCBP)[e]						U							U	S	U
Neurological examination						X							X	X	X
12-lead ECG													X	X	
Clinical laboratory tests													X	X	
Brain MRI[f]						X							X	X	X
LP/CSF collection						O							X	X	X
Blood PK sample						X							X	X	X
ADA Sample collection						X							X	X	X
Plasma biomarkers													X	X	X
CSF biomarkers						O							X	X	X
Optional exploratory PGx DNA and RNA sample													X	X	
Administer IV Study Drug	X	X	X	X	X	X	X	X	X	X	X	X	X		
PSPRS						1							1	1	1

Visits & Procedures[b]	Treatment Period[a]														20 Wks Post Last Dose F/U
	Year 2														
	Dose 16	Dose 17	Dose 18	Dose 19	Dose 20	Dose 21	Dose 22	Dose 23	Dose 24	Dose 25	Dose 26	Dose 27	Dose 28		
	Day 393	Day 421	Day 449	Day 477	Day 505	Day 533	Day 561	Day 589	Day 617	Day 645	Day 673	Day 701	Day 729		
	Wk 56	Wk 60	Wk 64	Wk 68	Wk 72	Wk 76	Wk 80	Wk 84	Wk 88	Wk 92	Wk 96	Wk 100	Wk 104	D/C	
CGI-S						2							2	2	2
CGI-C						3							3	3	3
SEADL						4							4	4	4
UPDRS Part II						5							5	5	5
RBANS													6	6	
CTT Parts 1 & 2													7	7	
Letter Fluency Test (wpm)													8	8	
NNIPPS-PPS[g]													9	9	
PGI-Ch						X							X	X	X
EQ-5D[h]													X	X	
C-SSRS[i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PSP Caregiver Questionnaires						X							X	X	X
TSQM-9						X							X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE assessment (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Telephone contact[j]						X							X	X	X

AE = adverse event; LP = lumbar puncture; PK = pharmacokinetic; PGx = pharmacogenetic; S = serum; U = urine

a. Study drug will be administered on Days 1, 15, and 29, then every 28 days thereafter until 1 of the discontinuation criteria is met, until the Sponsor discontinues the study, or until the study reaches completion. For those Visits that include both study drug infusion and other activities, the Visits may be completed over 2 consecutive days with the second day to include the start and end of the infusion.
b. Audio recordings/central review of the administration/assessment of selected scales may be conducted.
c. Additional symptom-driven physical examinations may be performed as needed.
d. An attempt should be made to obtain all vital sign measurements at the same time of day and using the same arm.
e. For all females of childbearing potential, a negative urine pregnancy test result is also required prior to any radiological procedures.
f If a subject cannot undergo MRI due to a clinical reason, the AbbVie TA MD should be consulted for approval.
g. The NNIPPS-PPS will not be administered in Japan.
h. Scale may be administered/assessed at any time during the visit, after the other procedures are completed, with the exception of the scheduled infusion time.
i. Scale may be administered/assessed at any time during the visit with the exception of the scheduled infusion time.
j. Only applicable to subjects who prematurely discontinue. Verify consent was obtained prior to making contact.

Note: Numbering listed in the table provides a pre-defined order of administration that these scales should occur during each visit.

Visits & Procedures[b]	Treatment Period[a]														20 Weeks Post Last Dose F/U
	Year 3														
	Dose 29	Dose 30	Dose 31	Dose 32	Dose 33	Dose 34	Dose 35	Dose 36	Dose 37	Dose 38	Dose 39	Dose 40	Dose 41	D/C	
	Day 757	Day 785	Day 813	Day 841	Day 869	Day 897	Day 925	Day 953	Day 981	Day 1009	Day 1037	Day 1065	Day 1093		
	Wk 108	Wk 112	Wk 116	Wk 120	Wk 124	Wk 128	Wk 132	Wk 136	Wk 140	Wk 144	Wk 148	Wk 152	Wk 156		
Symptom-driven physical examination[c]						X							X	X	X
Vital signs[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body weight (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (WOCBP)[e]						U							U	S	U
Neurological examination						X							X	X	X
12-lead ECG													X	X	
Clinical laboratory tests													X	X	
Brain MRI[f]						X							X	X	X
LP/CSF collection						O							X	X	X
Blood PK sample						X							X	X	X
ADA Sample collection						X							X	X	X
Plasma biomarkers													X	X	X
CSF biomarkers						O							X	X	X
Optional exploratory PGx DNA and RNA sample													X	X	
Administer IV Study Drug	X	X	X	X	X	X	X	X	X	X	X	X	X		
PSPRS						1							1	1	1

Visits & Procedures[b]	Treatment Period[a]														20 Weeks Post Last Dose F/U
	Year 3														
	Dose 29	Dose 30	Dose 31	Dose 32	Dose 33	Dose 34	Dose 35	Dose 36	Dose 37	Dose 38	Dose 39	Dose 40	Dose 41	D/C	
	Day 757	Day 785	Day 813	Day 841	Day 869	Day 897	Day 925	Day 953	Day 981	Day 1009	Day 1037	Day 1065	Day 1093		
	Wk 108	Wk 112	Wk 116	Wk 120	Wk 124	Wk 128	Wk 132	Wk 136	Wk 140	Wk 144	Wk 148	Wk 152	Wk 156		
CGI-S						2							2	2	2
CGI-C						3							3	3	3
SEADL						4							4	4	4
UPDRS Part II						5							5	5	5
RBANS													6	6	
CTT Parts 1 & 2													7	7	
Letter Fluency Test (wpm)													8	8	
NNIPPS-PPS[g]													9	9	
PGI-C[h]						X							X	X	X
EQ-5D[h]													X	X	
C-SSRS[i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PSP Caregiver Questionnaires						X							X	X	X
TSQM-9						X							X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE assessment (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Telephone contact[j]						X							X	X	X

AE = adverse event; LP = lumbar puncture; PK = pharmacokinetic; PGx = pharmacogenetic; S = serum; U = urine

a. Study drug will be administered on Days 1, 15, and 29, then every 28 days thereafter until 1 of the discontinuation criteria is met, until the Sponsor discontinues the study, or until the study reaches completion. For those Visits that include both study drug infusion and other activities, the Visits may be completed over 2 consecutive days with the second day to include the start and end of the infusion.
b. Audio recordings/central review of the administration/assessment of selected scales may be conducted.
c. Additional symptom-driven physical examinations may be performed as needed.
d. An attempt should be made to obtain all vital sign measurements at the same time of day and using the same arm.
e. For all females of childbearing potential, a negative urine pregnancy test result is also required prior to any radiological procedures.
f. If a subject cannot undergo MRI due to a clinical reason, the AbbVie TA MD should be consulted for approval.
g. The NNIPPS-PPS will not be administered in Japan.
h. Scale may be administered/assessed at any time during the visit, after the other procedures are completed, with the exception of the scheduled infusion time.
i. Scale may be administered/assessed at any time during the visit with the exception of the scheduled infusion time.
j. Only applicable to subjects who prematurely discontinue. Verify consent was obtained prior to making contact.

Note: Numbering listed in the table provides a pre-defined order of administration that these scales should occur during each visit.

Visits & Procedures[b]	Treatment Period[a]														20 Weeks Post Last Dose F/U
	Year 4														
	Dose 42	Dose 43	Dose 44	Dose 45	Dose 46	Dose 47	Dose 48	Dose 49	Dose 50	Dose 51	Dose 52	Dose 53	Dose 54	D/C	
	Day 1121	Day 1149	Day 1177	Day 1205	Day 1233	Day 1261	Day 1289	Day 1317	Day 1345	Day 1373	Day 1401	Day 1429	Day 1457		
	Wk 160	Wk 164	Wk 168	Wk 172	Wk 176	Wk 180	Wk 184	Wk 188	Wk 192	Wk 196	Wk 200	Wk 204	Wk 208		
Symptom-driven physical examination[c]						X							X	X	X
Vital signs[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body weight (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (WOCBP)[e]						U							U	S	U
Neurological examination						X							X	X	X
12-lead ECG													X	X	
Clinical laboratory tests													X	X	
Brain MRI[f]						X							X	X	X
LP/CSF collection						O							X	X	X
Blood PK sample						X							X	X	X
ADA Sample collection						X							X	X	X
Plasma biomarkers													X	X	X
CSF biomarkers						O							X	X	X
Optional exploratory PGx DNA and RNA sample													X	X	
Administer IV Study Drug	X	X	X	X	X	X	X	X	X	X	X	X	X		
PSPRS						1							1	1	1
CGI-S						2							2	2	2

Visits & Procedures[b]	Treatment Period[a]														20 Weeks Post Last Dose F/U
	Year 4														
	Dose 42	Dose 43	Dose 44	Dose 45	Dose 46	Dose 47	Dose 48	Dose 49	Dose 50	Dose 51	Dose 52	Dose 53	Dose 54		
	Day 1121	Day 1149	Day 1177	Day 1205	Day 1233	Day 1261	Day 1289	Day 1317	Day 1345	Day 1373	Day 1401	Day 1429	Day 1457		
	Wk 160	Wk 164	Wk 168	Wk 172	Wk 176	Wk 180	Wk 184	Wk 188	Wk 192	Wk 196	Wk 200	Wk 204	Wk 208	D/C	
CGI-C						3							3	3	3
SEADL						4							4	4	4
UPDRS Part II						5							5	5	5
RBANS													6	6	
CTT Parts 1 & 2													7	7	
Letter Fluency Test (wpm)													8	8	
NNIPPS-PPS[g]													9	9	
PGI-C[h]						X							X	X	X
EQ-5D[h]													X	X	
C-SSRS[i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PSP Caregiver Questionnaires						X							X	X	X
TSQM-9						X							X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE assessment (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Telephone contact[j]						X							X	X	X

AE = adverse event; LP = lumbar puncture; PK = pharmacokinetic; PGx = pharmacogenetic; S = serum; U = urine

a. Study drug will be administered on Days 1, 15, and 29, then every 28 days thereafter until 1 of the discontinuation criteria is met, until the Sponsor discontinues the study, or until the study reaches completion. For those Visits that include both study drug infusion and other activities, the Visits may be completed over 2 consecutive days with the second day to include the start and end of the infusion.
b. Audio recordings/central review of the administration/assessment of selected scales may be conducted.
c. Additional symptom-driven physical examinations may be performed as needed.
d. An attempt should be made to obtain all vital sign measurements at the same time of day and using the same arm.
e. For all females of childbearing potential, a negative urine pregnancy test result is also required prior to any radiological procedures.
f. If a subject cannot undergo MRI due to a clinical reason, the AbbVie TA MD should be consulted for approval.
g. The NNIPPS-PPS will not be administered in Japan.
h. Scale may be administered/assessed at any time during the visit, after the other procedures are completed, with the exception of the scheduled infusion time.
i. Scale may be administered/assessed at any time during the visit with the exception of the scheduled infusion time.
j. Only applicable to subjects who prematurely discontinue. Verify consent was obtained prior to making contact.

Note: Numbering listed in the table provides a pre-defined order of administration that these scales should occur during each visit.

Visits & Procedures[b]	Treatment Period[a]														
	Year 5														
	Dose 55	Dose 56	Dose 57	Dose 58	Dose 59	Dose 60	Dose 61	Dose 62	Dose 63	Dose 64	Dose 65	Dose 66/ Final	No Dose	D/C	20 Weeks Post Last Dose F/U
	Day 1485	Day 1513	Day 1541	Day 1569	Day 1597	Day 1625	Day 1653	Day 1681	Day 1709	Day 1737	Day 1765	Day 1793	Day 1821		
	Wk 212	Wk 216	Wk 220	Wk 224	Wk 228	Wk 232	Wk 236	Wk 240	Wk 244	Wk 248	Wk 252	Wk 256	Wk 260		
Symptom-driven physical examination[c]						X							X	X	X
Vital signs[d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body weight (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (WOCBP)[e]						U							S	S	U
Neurological examination						X							X	X	X
12-lead ECG													X	X	
Clinical laboratory tests													X	X	
Brain MRI[f]						X							X	X	X
LP/CSF collection						O							X	X	X
Blood PK sample						X							X	X	X
ADA Sample collection						X							X	X	X
Plasma biomarkers													X	X	X
CSF biomarkers						O							X	X	X
Optional exploratory PGx DNA and RNA sample													X	X	
Administer IV Study Drug	X	X	X	X	X	X	X	X	X	X	X	X			
PSPRS						1							1	1	1

Visits & Procedures[b]	Treatment Period[a]														
	Year 5														
	Dose 55	Dose 56	Dose 57	Dose 58	Dose 59	Dose 60	Dose 61	Dose 62	Dose 63	Dose 64	Dose 65	Dose 66/ Final	No Dose	D/C	20 Weeks Post Last Dose F/U
	Day 1485	Day 1513	Day 1541	Day 1569	Day 1597	Day 1625	Day 1653	Day 1681	Day 1709	Day 1737	Day 1765	Day 1793	Day 1821		
	Wk 212	Wk 216	Wk 220	Wk 224	Wk 228	Wk 232	Wk 236	Wk 240	Wk 244	Wk 248	Wk 252	Wk 256	Wk 260		
CGI-S						2							2	2	2
CGI-C						3							3	3	3
SEADL						4							4	4	4
UPDRS Part II						5							5	5	5
RBANS													6	6	
CTT Parts 1 & 2													7	7	
Letter Fluency Test (wpm)													8	8	
NNIPPS-PPS[g]													9	9	
PGI-C[h]						X							X	X	X
EQ-5D[h]													X	X	
C-SSRSi	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PSP Caregiver Questionnaires						X							X	X	X
TSQM-9						X							X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE assessment (prior to infusion)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Telephone contact[j]						X							X	X	X

AE = adverse event; LP = lumbar puncture; PK = pharmacokinetic; PGx = pharmacogenetic; S = serum; U = urine

a. Study drug will be administered on Days 1, 15, and 29, then every 28 days thereafter until 1 of the discontinuation criteria is met, until the Sponsor discontinues the study, or until the study reaches completion. For those Visits that include both study drug infusion and other activities, the Visits may be completed over 2 consecutive days with the second day to include the start and end of the infusion.
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Note: Numbering listed in the table provides a pre-defined order of administration that these scales should occur during each visit.

Appendix A. Potentially Clinically Significant (PCS) Laboratory Value

Clinical Laboratory Tests	Very Low (VL)	Very High (VH)
Hematology		
Activated partial thromboplastin time	NA	> ULN
Hemoglobin	< 100 g/L (6.2 mmol/L)	> 40 g/L above ULN
Prothrombin Intl. Normalized Ratio	NA	> ULN
Leukocytes	$< 2 \times 10^9$/L	$> 100 \times 10^9$/L
Lymphocyte	$< 0.5 \times 10^9$/L	$> 20 \times 10^9$/L
Neutrophil	$< 1 \times 10^9$/L	NA
Platelets	$< 75 \times 10^9$/L	NA
Chemistry		
Bilirubin	NA	> 1.5 × ULN
Cholesterol	NA	> 12.92 mmol/L (500 mg/dL)
Creatinine	NA	> 1.5 × ULN
Calcium (corrected serum)	< 1.75 mmol/L (7.0 mg/dL)	> 3.1 mmol/L (12.5 mg/dL)
Glucose (fasting)	< 2.2 mmol/L (40 mg/dL)	> 13.9 mmol/L (250 mg/dL)
Potassium	< 3.0 mmol/L	> 6.0 mmol/L
Triglycerides	NA	> 5.7 mmol/L (500 mg/dL)
Urate	NA	> 590 umol/L (10 mg/dL)
Albumin	< 20 g/L	NA
Sodium	< 130 mmol/L	> 155 mmol/L
Phosphate	< 0.6 mmol/L (2.0 mg/dL)	NA
Enzymes		
Alanine aminotransferase (ALT)	NA	> 3 × ULN
Alkaline phosphatase	NA	> 2.5 × ULN
Aspartate aminotransferase (AST)	NA	> 3 × ULN

Appendix B. Criteria for Potentially Clinically Significant Vital Sign and Weight Values

Vital Signs	Very Low (VL)	Very High (VH)
Systolic Blood Pressure (SBP) (mmHG)	≤ 90 and decreased ≥ 30 from baseline	≥ 180 and increased ≥ 40 from baseline
Diastolic Blood Pressure (DBP) (mmHG)	≤ 50 and decreased ≥ 20 from baseline	≥ 105 and increased ≥ 30 from baseline
Pulse (bpm)	≤ 50 and decreased ≥ 30 from baseline	≥ 100 and increased ≥ 30 from baseline
Temperature (C)	≥ 1.1 decrease from baseline	> 38.5 or increase ≥ 1.1 from baseline
Orthostatic SBP (Hypotension) (mmHg)	Decrease of ≥ 30 in SBP (supine to standing)	NA
Orthostatic DBP (Hypotension) (mmHg)	Decrease of ≥ 20 in DBP (supine to standing)	NA
Weight (kg)	Decreased ≥ 7% from baseline	Increased ≥ 7% from baseline

Appendix C. Criteria for Potentially Clinically Significant ECG Values

ECG Parameters	Significant Values
QTcF Interval (msec)	> 499
QTcF Interval Increased from Baseline (msec)	> 60