Statistical Analysis Plan

A Phase 1 / 2 , Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of AstroStem, Autologous Adipose Tissue Derived Mesenchymal Stem Cells, in Patients with Alzheimer's Disease

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JS-OAP2-US01 Phase 2

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Glossary and Abbreviations

Aβ	Amyloid beta
AD	Alzheimer's Disease
ADAS-Cog	Alzheimer's Disease Assessment Scale-cognitive subscale
ADCS-ADL	Alzheimer's Disease Cooperative Study Activities of Daily Living
AdMSC	Adipose Tissue Derived Mesenchymal Stem Cell
AE	Adverse Event
AICD	Amyloid precursor protein Intracellular Domain
AIDS	Acquired Immunodeficiency Syndrome
ALT (SGPT)	Alanine Aminotransferase (Serum Glutamic Pyruvic Transaminase)
APP	Amyloid Precursor Protein
AST (SGOT)	Aspartate Aminotransferase (Serum Glutamic Oxaloacetic Transaminase)
BUN	Blood Urea Nitrogen
CDR-SOB	Clinical Dementia Rating-Sum of Boxes
CFR	Code of Federal Regulations
C-SSRS	Columbia Suicide Severity Rating Scale
CREDOS	Clinical Research Center for Dementia of South Korea
ECG	Electrocardiography
eCRF	Electronic Case Report Form
GCP	Good Clinical Practice
GDNF	Glial cell-derived Neurotrophic Factor
GDS	Geriatric Depression Scale
hASCs	Human Adipose-derived Stem Cells
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
ICH	International Conference of Harmonization
IRB	Institutional Review Board
ITT	Intent-to-Treat
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MMSE	Mini-mental status examination
NINCDS-ADRDA	National Institute of Neurological and Communicative Disorders and Stroke; Alzheimer's Disease and Related Disorders Association
NPI	Neuropsychiatric Inventory
NT3	Neurotrophin 3
PP	Per Protocol
PT-INR	Prothrombin Time - International Normalized Ratio
RBC	Red Blood Cell Count
SAE	Serious Adverse Event
SD	Standard Deviation
sNRG-1	Soluble Neuregulin-1
VDRL	Venereal Disease Research Laboratory
VEGF	Vascular Endothelial Growth Factor
WBC	White Blood Cell Count
WMH	White Matter Hyperintensity

1. Revision History

SAP Version 1 was created and approved prior to first patient visit and any unblinding of the study team.

2. Study Objectives

2.1. Primary Objective

Table 1 shows the primary objectives and endpoints used to determine the safety and efficacy of AstroStem in patients with Alzheimer's disease.

Table 1. Primary Objectives and Endpoints

Objectives	Endpoints
Primary Efficacy • To evaluate the efficacy of AstroStem in patients with Alzheimer's disease	• Change of ADAS-Cog (Alzheimer's Disease Assessment Scale-cognitive subscale) from baseline (Visit 3) to Visit 13 (Week 30)
Primary Safety • To evaluate the safety of AstroStem in patients with Alzheimer's disease	• Number of subjects with treatment related adverse events as assessed by analysis of adverse events including symptoms, and abnormal findings on physical examination, vital signs, ECG, and standard laboratory examination results

2.2. Secondary Objectives

Table 2 shows the secondary objectives and endpoints used to determine the safety and efficacy of AstroStem.

Table 2. Secondary Objectives and Endpoints

Objectives	Endpoints
Secondary Efficacy • To evaluate the efficacy of AstroStem in patients with Alzheimer's disease	• Change of MMSE (Mini-mental status examination) from baseline at Week 30 (Visit 13) • Changes of CDR-SOB (Clinical Dementia Rating-Sum of Boxes) from baseline at Week 30

	• Changes of NPI (Neuropsychiatric Inventory) from baseline at Week 30 • Changes of GDS (Geriatric Depression Scale) from baseline at Week 30 • Change of ADCS-ADL (Alzheimer's Disease Cooperative Study Activities of Daily Living) from baseline at Week 30
Secondary Safety • To evaluate the safety of AstroStem in patients with Alzheimer's disease	• Changes of C-SSRS (Columbia Suicide Severity Rating Scale) from baseline at Week 30 • Change of MRI imaging results from baseline at Week 30

2.3. Exploratory Objectives

Table 3 shows the exploratory objectives and endpoints used to determine the safety and efficacy of AstroStem.

Table 3. Exploratory Objectives and Endpoints

Objectives	Endpoints
Exploratory Efficacy • To evaluate the efficacy of AstroStem in patients with Alzheimer's disease	• Change of ADAS-Cog from baseline at Visit 6, 9, 12 and 14 or Early Termination • Change of MMSE from baseline at Visit 6, 9, 12 and 14 or Early Termination • Changes of CDR-SOB from baseline at Visit 6, 9, 12 and 14 or Early Termination • Changes of NPI from baseline at Visit 6, 9, 12 and 14 or Early Termination • Changes of GDS from baseline at Visit 6, 9, 12 and 14 or Early Termination • Change of ADCS-ADL from baseline at Visit 6, 9, 12 and 14 or Early Termination • Summary of Biomarkers in blood: Amyloid beta 40, Amyloid beta 42, Amyloid precursor protein intracellular domain (AICD), soluble neuregulin-1 (sNRG-1) at baseline, Visit 13 and 14 or Early Termination
Exploratory Safety • To evaluate the efficacy of AstroStem in patients with Alzheimer's disease	• Changes of C-SSRS from baseline at Visit 6, 9, 12 and 14 or Early Termination • Change of MRI imaging results from baseline at Visit 9 and 14 or Early Termination

3. Study Design

3.1. Summary of Study Design

This is a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of AstroStem for the treatment of Alzheimer's Disease. Three investigational centers in the United States may be utilized so that a total of approximately 22 subjects will be randomized. At Week -4, 30 mL of abdominal adipose tissue will be taken by liposuction from subjects. The adipose tissue samples will be sent to Biostar Stem Cell Research Institute to isolate AdMSCs. The isolated AdMSCs or saline will be sent to the clinical sites with identical syringes to preserve double-blinding of the study. A total $2x10^8$ AdMSCs in 220 mL of saline or the same volume of saline will be administered via I.V. at Week 0. This procedure will be repeated 9 times at 2-week interval. Subjects will be scheduled for two follow-up visits at Weeks 30 and 52 to evaluate primary and secondary outcome endpoints. The schedule of Assessments is illustrated in Table 4.

Table 4. Schedule of Assessments

Procedure	Screen		Treatment										Follow-up		Early Termination
	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	
Tested Group	-W8	-W4	W0	W2	W4	W6	W8	W10	W12	W14	W16	W18	W30	W52	
Informed Consent[1]	V														
Inclusion/Exclusion Criteria	V														
Demographic information	V														
Medical/medication history	V														
Physical examination	V		V			V			V			V	V	V	V
Vital signs	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V
Hematology, serum chemistry, and urinalysis [2]	V		V			V			V			V	V	V	V
Pregnancy test [3]	V		V									V	V	V	V
Electrocardiogram	V		V			V			V			V	V	V	V
Chest X-ray	V														
Liposuction		V													
Serum for IP		V	V		V		V		V						
ADAS-Cog			V			V			V			V	V	V	V
MMSE	V		V			V			V			V	V	V	V
CDR-SOB			V			V			V			V	V	V	V
NPI			V			V			V			V	V	V	V
GDS			V			V			V			V	V	V	V
C-SSRS			V			V			V			V	V	V	V
ADCS-ADL			V			V			V			V	V	V	V
MRI Scan	V								V				V	V	V

Biomarker [4]			V										V	V	V
Drug administration			V	V	V	V	V	V	V	V	V	V			
Concomitant medications		V	V	V	V	V	V	V	V	V	V	V	V	V	V
Adverse events		V	V	V	V	V	V	V	V	V	V	V	V	V	V

[1] Informed Consent Form should be signed prior to any clinical trial related activities

[2] See Appendix 1 for the complete list of laboratory tests

[3] Serum pregnancy test is performed for all females of childbearing potential.

[4] Amyloid beta 40, Amyloid beta 42, Amyloid precursor protein intracellular domain (AICD), soluble neuregulin-1 (sNRG-1)

3.2. Determination of Sample Size

There was no formal sample size calculation since this is a phase 1/2 study and is not a hypothesis-driven study. The number of enrolled subjects is predefined approximately at n=22, about 11 subjects per group

3.3. Method of Assignment to Treatment

Patients who meet all criteria for enrollment will be randomized to double-blind treatment at visit 2. Assignment to treatment group will be determined by a computer-generated randomization code using the electronic data capture (EDC) system on Visit 2 (Week -4).

Blinding of the drug contents from the subjects, investigators, and other study personnel at each clinical site is necessary. Because two syringes of AstroStem and control are different, one physician must be only assigned to the role of syringe injection in order to maintain the double-blinding against other site physicians and staffs.

4. Statistical Methods

4.1. General Considerations

This document describes the statistical analyses planned prior to final treatment assignment unblinding of the aggregate database. Any change to the data analysis methods described in the protocol will require an amendment ONLY if it changes a principal feature of the protocol. Any other change to the data analysis methods described in the protocol and the justification for making the change will be described in the clinical study report (CSR). Additional exploratory analyses of the data will be conducted as deemed appropriate.

All tests of treatment effects will be conducted at a two-sided alpha level of 0.05 unless

otherwise stated, and all confidence intervals (CI's) will be given at a two-sided 95% level, unless otherwise stated. Statistical analysis will be performed using SAS software (SAS, Version 9.1.2 or higher).

The following general terms will be used globally in the SAP:

- Unless otherwise specified, the statistical analyses will be reported using summary tables and data listings.
- Continuous variables will be summarized with n, mean, standard deviation, median, minimum, and maximum.
- Categorical variables will be summarized by counts and by percentages of subjects in corresponding categories.
- All summary tables will be presented by treatment.
- Individual subject data obtained from the case report form (CRFs) and any derived data will be presented by subject in data listings. Data listings will be sorted by subject, and visit date and time, if applicable.

4.2. Adjustments for Covariates

There will be no adjustment for covariates.

4.3. Analysis Populations

4.3.1. Intent-to-Treat Population

An intent-to-treat (ITT) population will include subjects who received at least one intravenous injection and have post-injection efficacy measurements. This population will be evaluated for all efficacy variables.

4.3.2. Per-Protocol Population

All subjects valid for ITT who complete Visit 13 (Week 30) will be 'valid per protocol' (also called 'valid for efficacy'). Additional criteria may be added prior to unblinding the study database. As with the ITT population, this per-protocol (PP) cohort will also be evaluated for all efficacy variables.

4.3.3. Safety Population

A safety population will include subjects who received at least one intravenous injection and have post-injection safety measurements. This population will be evaluated for all safety variables.

4.4. Baseline and Postbaseline Definition

Table 5 describes the rules for determining the patient population and baseline and postbaseline observations for study and type of analysis.

Table 5. Patient Population with Baseline and Postbaseline Definitions by Type of Analysis

Study Period/Analysis	Patient Population	Baseline Observation	Postbaseline Observation(s)
Treatment Period			
Primary Efficacy analyses	ITT Population with a baseline and at least 1 postbaseline observation	Visit 3	Visit 13
TEAEs	Safety Population	All Visits 1-3	All Visits 3.01-14
Serious Adverse Events, Discontinuations due to Adverse Events	Safety Population	N/A	
C-SSRS analyses	Patients with a baseline and at least 1 postbaseline C-SSRS assessment	All Prior History: Visits 1-3 including	All Visits 3.01-14
Treatment-emergent abnormal laboratory values	Safety Population with normal laboratory values at all nonmissing baseline visits (with respect to direction being analyzed) and who have at least 1 postbaseline observation	Low: Minimum from Visits 1-3 High: Maximum from Visits 1-3 Abnormal: All Visits 1-3	Low: Minimum from Visits 3.01-14 High: Maximum from Visits 3.01-14 Abnormal: All Visits 3.01-14
Treatment-emergent immunogenicity	Safety Population	Visit 3	All Visits 3.01-14
Treatment-emergent changes in temperature and weight	Safety Population with a baseline and at least 1 postbaseline observation	Low: Minimum from Visits 1-3 High: Maximum from Visits 1-3	Low: Minimum from Visits 3.01-14 High: Maximum from Visits 3.01-14
Treatment-emergent changes in blood pressures, pulse, and ECGs	Safety Population with a baseline and at least 1 postbaseline observation	Low: Last nonmissing from Visits 1-3 High: Last nonmissing from Visits 1-3	Low: Minimum from Visits 3.01-14 High: Maximum from Visits 3.01-14
Continuous safety analyses	Safety Population with a baseline and at least 1 postbaseline observation	Last of Visits 1-3	All scheduled visits 3< Visits ≤14

ECGs = electrocardiograms; eCRF = electronic case report form; ITT = intent-to-treat; N/A = not applicable; TEAEs = treatment-emergent adverse events

Note: Visit 3.01 indicates the first unscheduled visit occurring after Visit 3 and prior to Visit 4.

4.5. Handling of Dropouts or Missing Data

No adjustments for missing data and no imputation methods are planned for this study.

4.6. Treatment Group Comparability

4.6.1. Patient Disposition

Subject disposition information will be summarized for all subjects. Summaries will include: the number of subjects in each analysis population, the number of subjects completed the study, and the number of subjects discontinued study and its reason. All subjects randomized in the study will be included in the summary table. Patient allocation by investigator or site will be summarized. Patient allocation by investigator or site will also be listed as well.

4.6.2. Protocol Deviations

Listings of subjects with significant protocol deviations or violations will be provided. The following list of significant protocol violations will be determined from the clinical database and from the study clinical/medical group:

- Lack of informed consent or late informed consent
- Violations of inclusion/exclusion criteria
- Significant violations of prohibited concomitant medication usage as determined by the clinical/medical group
- Other significant protocol violations as determined by the clinical/medical group

4.6.3. Patient Characteristics

The following patient characteristics at baseline will be summarized by treatment group for all ITT patients:

- Demographic (age, gender, ethnic origin, height, weight, BMI)
- Medical history and Pre-existing condition

Medical history and pre-existing conditions will be summarized by preferred term (PT) within system organ class (SOC). Medical history is defined as illness(es) that ended prior to the signing of informed consent. Pre-existing conditions and AEs at baseline are those AEs occurring during the baseline/screening visits that is Visit 1, 2 and 3.

4.6.4. Prior and Concomitant Therapy

Verbatim terms on eCRFs will be mapped to Anatomical Therapeutic Chemical (ATC) class and Generic Drug Names using the World Health Organization (WHO) Drug Dictionary Enhanced (WHODDE) B2 format, March 1, 2015 release.

Prior medications are defined as medications started to take prior to the first injection. Concomitant medications are defined as medications started on or after the day of first injection of the study drug during the study.

Prior and concomitant medications will be tabulated for the ITT population by WHODDE ATC level 2 classifications, preferred term, and treatment. If a subject reports the same preferred term multiple times, then the frequency of that preferred term will only be incremented by one. As with the preferred term, if a subject reports multiple medications within the same ATC level 2 classification, then the frequency of that ATC level 2 classification will only be incremented by one. Percentages will be calculated using the total number of subjects in the safety population. Each summary will be ordered by descending order of incidence of preferred term within each ATC class. Prior and concomitant medications will be included in a data listing.

4.6.5. Treatment Compliance

Not applicable.

4.7. Efficacy Analyses

The primary efficacy hypothesis test will be performed using a 5% significance level. For the secondary efficacy endpoints, hypothesis tests will be performed individually at the 5% significance level. All hypothesis tests will be performed with two-sided alternative hypotheses. No adjustments on the significance level for multiple comparisons are planned, as this is a phase 1/2 study. All efficacy analyses will be based on the ITT population.

4.7.1. Primary Efficacy Analysis

The primary objective of this study is to test the hypothesis that AstroStem is superior to placebo in the improvement on neurological/neurocognitive assessment from baseline to week 30 in patients with Alzheimer's Disease.

The primary analysis will evaluate the efficacy of AstroStem compared with placebo on the overall mean change from baseline to week 30 in ADAS-Cog score. The primary efficacy variable will be summarized with means, standard deviations, medians and ranges, overall and by group. The change from Baseline ADAS-Cog score will be analyzed with Student's t-test or Kruskal-Wallis test depending on the violation of normality assumption.

4.7.2. Secondary Efficacy Analyses

The secondary efficacy analyses will be summarized with means, standard deviations, medians and ranges for continuous variables including the changes from baseline at Week 30 in MMSE, CDR-SOB, NPI, GDS and ADCS-ADL.

These changes score from baseline at week 30 will be analyzed with Student's t-test or Kruskal-Wallis test depending on the violation of normality assumption. .

4.7.3. Exploratory Efficacy Analyses

Change from baseline scores at Visits 6, 9, 12 and 14 or Early Termination for: ADAS-Cog, MMSE, CDR-SOB, NPI, GDS, and ADCS-ADL will be summarized with means, standard deviations, medians and ranges by treatment group and visit. These changes score from baseline at Visits 6, 9, 12 and 14 or Early Termination will be analyzed with Student's t-test or Kruskal-Wallis test depending on the violation of normality assumption.

Biomarkers in blood [Amyloid beta 40, Amyloid beta 42, Amyloid precursor protein intracellular domain (AICD), soluble neuregulin-1 (sNRG-1)] will be summarized with means, standard deviations, medians and ranges for continuous variables and with counts and percentages for categorical variables. at baseline, Visit 13 and 14 or Early Termination

4.8. Safety Analyses

The safety and tolerability of treatment will be assessed by summarizing the following:

- AEs
- Treatment-emergent adverse events (TEAEs)
    - By PT
    - By SOC
    - By maximum severity
    - By considered to be related to investigational produce by investigator
- Serious Adverse Events (SAEs)
- AE leading to discontinuation
- Suicide-Related Thoughts and Behaviors
- Vital signs and weight
- Laboratory measurements
- Electrocardiograms (ECGs)

All safety analyses will be based on the safety population. AE rates will be summarized by treatment group and overall, and will be broken down by severity, seriousness and relation to study drug. Change of MRI, C-SSRS, physical examinations, vital signs, ECG

and standard laboratory results will be summarized with means, standard deviations, medians and ranges for continuous variables and with counts and percentages for categorical variables. Statistical tests are not planned for safety.

4.8.1. Adverse Events

An AE is defined as any untoward medical occurrence in a subject who is administered a medicinal product and that does not necessarily have a causal relationship to the treatment. All AEs will be included in the data listings. Verbatim terms on case report forms will be mapped to preferred terms and system organ classes (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA) (version 19.1).

A Treatment Emergent Adverse Event (TEAE) is defined as an adverse event that occurs on or after the treatment dose. TEAE summary will be displayed by treatment. Unless otherwise specified, summaries that are displayed by SOC and preferred terms will be ordered alphabetically by SOC, and within each SOC, preferred terms will also be ordered alphabetically. Summaries of the following types will be presented:

- Subject incidence of TEAEs by MedDRA SOC and preferred term.
- Subject incidence of TEAEs by MedDRA SOC, preferred term, and severity. Severity will be recorded as deemed by investigator. At each level of subject summarization, a subject is classified according to the highest severity if the subject reported one or more events.
- Subject incidence of study drug related TEAEs by MedDRA SOC and preferred term.
- Subject incidence of TEAEs by descending incidence of preferred terms.
- Subject incidence of serious TEAEs by MedDRA SOC and preferred term, if applicable.
- Subject incidence of TEAE leading to early termination by MedDRA SOC and preferred term, if applicable.

For each subject and for each adverse event, the duration of the event will be calculated as:

Duration of AE = AE stop date - AE start date + 1

The duration of AEs will be displayed in the data listing.

4.8.2. Potential Hypersensitivity Events (Serious Adverse Events)

A serious adverse event (SAE) is any AE or suspected adverse reaction that in the view of either the investigator or Sponsor, results in any of the following outcomes:

- Death

- A life-threatening AE: it is defined as an AE or suspected adverse reaction that in the view of the investigator or Sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an AE or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.
- Inpatient hospitalization or prolongation of existing hospitalization
  A persistent or significant incapacity or substantial disruption of the ability to conduct normal life function.
- A congenital anomaly/birth defect
- Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of outcomes listed in the above definition

Life threatening:
An adverse event or suspected adverse reaction is considered “life-threatening” if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Hospitalization:
Any adverse event leading to hospitalization or prolongation of hospitalization will be considered as ‘serious’, UNLESS at least one of the following exceptions is met:

- the admission results in a hospital stay of less than 24 hours OR
- the admission is pre-planned (i.e., elective or scheduled surgery arranged prior to the start of the study)

However, it should be noted that invasive treatment during any hospitalization may fulfill the criteria of ‘medically important’ and as such may be reportable as a SAE dependent on clinical judgment.

Disability means a substantial disruption of a person’s ability to conduct normal life functions.

Important medical event:
As guidance for determination of important medical events see the ‘WHO Adverse Reaction Terminology – Critical Terms List’. These terms either see or might be indicative of a serious disease state. Such reported events warrant special attention because of their possible association with a serious disease state and may lead to more decisive action than reports on other terms.

4.8.3. Clinical Laboratory Evaluation

Abnormal laboratory findings without clinical significance (based on the investigator's judgment) should not be recorded as adverse events; however, laboratory value changes requiring therapy or adjustment in prior therapy are considered adverse events.
Adverse events will be reviewed continuously throughout the study.

Laboratory results (hematology, serum chemistry and urinalysis) will be presented in data listing. Abnormal values will be flagged as high or low relative to the local lab normal ranges, where applicable. Values that are deemed as abnormal, clinically significant will also be flagged.

Laboratory results will be summarized using descriptive statistics at baseline and post-dose. Changes from baseline will also be summarized. Only non-missing assessments at baseline and post-dose will be analyzed.

Any clinically significant lab abnormalities will be determined by the Principal Investigator and will be reported in the AE table summaries.

4.8.4. Suicide-Related Thoughts and Behaviors

Suicidal ideation, suicidal behavior, and self-injurious behavior without suicidal intent occurring during treatment, based on the C SSRS, will be summarized by treatment. In particular, for each of the following events, the number and percent of patients with the event will be enumerated by treatment: completed suicide, nonfatal suicide attempt, interrupted attempt, aborted attempt, preparatory acts or behavior, active suicidal ideation with specific plan and intent, active suicidal ideation with some intent to act without specific plan, active suicidal ideation with any methods (no plan) without intent to act, nonspecific active suicidal thoughts, wish to be dead, and self-injurious behavior without suicidal intent.

In addition, the number and percent of patients who experienced at least one of various composite measures will be presented and compared. These include suicidal behavior (completed suicide, non-fatal suicidal attempts, interrupted attempts, aborted attempts, and preparatory acts or behavior), suicidal ideation (active suicidal ideation with specific plan and intent, active suicidal ideation with some intent to act without specific plan, active suicidal ideation with any methods [no plan] without intent to act, non-specific active suicidal thoughts, and wish to be dead), and suicidal ideation or behavior.

4.8.5. Vital Signs

Vital signs will be summarized using descriptive statistics at baseline and at each post-

dose time point. Changes from baseline will also be summarized.

4.8.6. Electrocardiogram

ECG parameters (numeric) will be summarized using descriptive statistics at baseline and at each post-dose time point. Changes from baseline will also be summarized.

4.9. Interim Analysis and Data Monitoring

An unblinded interim safety analysis was done when there the first 4 subjects complete Visit 4 at Week 2 by an independent safety monitor. Change of vital sign, concomitant medications and adverse events(AEs) were evaluated to monitor the safety of the AstroStem.

Vital sign measured at Visit 3 and 4 were within normal ranges and no AEs were reported. In addition, all 4 subjects were found to be taking concomitant medications before and after administration of the treatment.

4.10. Handling of Dropouts or Missing Data

No imputations will be made for missing values.

4.11. Subgroup Analysis

There are no planned subgroup efficacy analyses.

4.12. Multiple Comparison/Multiplicity

No adjustments for multiplicity or multiple testing will be made.

5. Changes to Protocol-Specified Analyses

No changes to protocol-specified analyses are planned.

6. References

Alzheimer’s Association. 2016 Alzheimer's disease facts and figures. Alzheimers Dement. 2016 April;12(4):459-509.

7. Appendices

7.1. Appendix 1. Laboratory Parameters

Blood and urine samples for complete laboratory evaluation (hematology, serum chemistry, biomarker analysis and urinalysis) at Visits 1, 3, 6, 9, 12, 13 and 14 or Early Termination.

HEMATOLOGY	CHEMISTRY	URINALYSIS	BIOMARKER***
Hemoglobin	Total bilirubin	Color	Amyloid beta 40
Hematocrit	Alkaline phosphatase	Appearance	Amyloid beta 42
RBC	ALT (SGPT)	Specific gravity	Amyloid
WBC	AST (SGOT)	pH	precursor protein
MCV	Blood urea nitrogen	Protein	intracellular
MCH	(BUN)	Glucose	domain (AICD)
MCHC	Creatinine	Ketones	soluble
Neutrophils (absolute)	Glucose	Bilirubin	neuregulin-1
Lymphocytes (absolute)	Albumin	Blood	(sNRG-1)
Monocytes (absolute)	Total protein	Leukocyte esterase	
Eosinophils (absolute)	Sodium	WBC	
Basophils (absolute)	Potassium	RBC	
Platelets	Chloride	Epithelial cell	
PT-INR	Bicarbonate	Bacteria	
	Calcium	Hyaline casts	
	HCG *		
	HIV **		
	HBV**		
	HCV**		
	VDRL**		

* HCG (pregnancy test) only for all females of childbearing potential at Visits 1, 3, 12, 13 and 14 or Early Termination

** Visit 1 only

*** Visits 3 and 13, 14 or Early Termination