Statistical Analysis Plan (SAP)

A Comparison of Tc 99m Tilmanocept Quantitative Imaging with Immunohistochemical (IHC) Analysis of CD206 Expression in Synovial Tissue from Subjects Clinically Diagnosed with Rheumatoid Arthritis (RA)

Study No: NAV3-32

Version 1.0

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Approval Page

By entering into this Statistical Analysis Plan (SAP), the parties acknowledge and agree that this SAP shall be incorporated into and subject to the terms of the Master Services Agreement (MSA). Any changes requested by Client to this SAP shall be subject to Section I.C of the MSA requiring a mutually agreed upon "Change Order" prior to any modification of the procedures set forth herein.

I agree to the format and content of this document.

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Revision History

N/A

List of Abbreviations and Definitions of Terms

Term	Definition
μg	microgram
ACR/EULAR	American College of Rheumatology/European League Against Rheumatism
ADR	adverse drug reaction
AE	adverse event
Anti TNF-α bDMARD	Anti-Tumor Necrosis Factor α biological Disease Modifying Anti-Rheumatic Drug
CDAI	Clinical Disease Activity Index
CRF	case report form
CSR	clinical study report
CT	X-ray computed tomography
DAS28	Disease activity score used with the ACR/EULAR 2010 RA guidelines
ECG	electrocardiogram
FDA	Food and Drug Administration
HAQ-DI	Health Assessment Questionnaire Disability Index
HC	healthy controls
ICH	International Conference on Harmonization
ITA	intent-to-assay
IV	intravenous
mCi	milliCurie ($37x10^6$ becquerels; 37megabecquerels)
MCP	metacarpophalangeal
MedDRA	Medical Dictionary for Regulatory Activities
OA	osteoarthritis
PIP	proximal interphalangeal
PP	per protocol
PT	preferred term
RA	rheumatoid arthritis
ROI	region of interest
RR	reference region
SAE	serious adverse event
SAP	statistical analysis plan
SOC	system organ class
SPECT	single photon emission computed tomography
Tc 99m	technetium-99m metastable isotope; γ-emitting (half-life 6.02 h)
tilmanocept	DTPA Mannosyl Dextran (the US Adopted Name for the drug substance of Lymphoseek)
TUV	Tilmanocept uptake value
US	United States

Term	Definition
$\bar{X}_{ROI}$	the decay-corrected average voxel intensity of a region of interest

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INTRODUCTION

Description

This Statistical Analysis Plan (SAP) is consistent with the study protocol Amendment 6 (dated 24 June 2021) and includes the latest details of efficacy and safety summaries to be included in the clinical study report (CSR).

The preparation of this SAP is done in accordance with STATKING Clinical Services SOP SCI 02-54, Statistical Analysis Plans.

1.0 Synopsis of Study Design/Procedures

This is a Phase 2b, open-label, multi-center, multinational, non-randomized, single-dose study designed to assess the relationship between quantitative Tc 99m tilmanocept planar imaging and synovial histopathology in subjects clinically diagnosed with RA.

The objectives of the study are:

Primary Objectives:

- Assessment of the relationship between joint-specific tilmanocept uptake value (TUV_{joint}) and synovial anatomic pathology.
- IHC assessment of macrophage expression of the CD206 receptor.

Secondary Objectives:

- Assessments of CD68 and CD163 receptor expression levels through IHC microscopy.
- Classification of synovial anatomic pathology as
    - Lympho-myeloid
    - Diffuse myeloid
    - Pauci-immune fibroid

Exploratory Objectives:

- Determine the relationship between TUV_{joint} and mRNA expression profiles of CD68, CD163, and CD206 as determined by RNA sequencing (RNA-seq).
- Determine the relationship between TUV_{joint} and the number, size, and intensity of CD68, CD163, and CD206 as determined by (optional) flow cytometry.
- Evaluate synovial expression of CD3, CD20, CD55, and TE-7 and CD206 in synovial tissue biopsy specimens.

- Assessment of the relationship between global tilmanocept uptake value (TUV_{global}) and synovial anatomic pathology.

Safety Objective:

- Evaluate safety through the examination of adverse event (AE) incidence, physical examination findings, and changes over time in laboratory tests, electrocardiograms (ECGs), and vital signs.

1.1 Design and Treatment

Subjects will receive the administration of Tc 99m tilmanocept through an intravenous (IV) route of administration. All subjects will receive a 150 μg mass dose of tilmanocept radiolabeled with 10 mCi of Tc 99m and will be at study time 00:00. Following injection, a 10-mL sterile normal saline flush will be administered. The preferred site of IV placement will be the left or right antecubital vein.

Subjects will undergo an imaging assessment of the bilateral hands and wrists followed by an ultrasound-guided synovial biopsy of a select joint at a subsequent visit. Tissue samples from the synovial biopsy procedure will be used for 2 mandatory anatomic pathology evaluations, [1] IHC and [2] RNA-seq, and optional flow cytometry, to provide quantitative and semi-quantitative information regarding joint-specific disease activity. Results from each anatomic pathology evaluation will be correlated with TUV_{joint} on planar imaging to mechanistically assess the relationship between synovial anatomic pathology and TUV_{joint}.

All joints selected for biopsy will be required to have an ultrasound synovial thickness score of ≥ 2. In instances where more than 1 joint qualifies for biopsy, the candidate joint will be selected based on TUV_{joint}.

Table 1 Biopsy Selection Options

Option	Description
1	The subject has only 1 metacarpophalangeal (MCP) joint or wrist joint with an ultrasound gray-scale synovitis score of ≥ 2. This joint will be selected for biopsy.
2	The subject has 2 or more MCP and/or wrist joints with an ultrasound gray-scale synovitis score of ≥ 2. The joint for biopsy will be selected based on evaluation of corresponding TUV_{joint}. In the first subject with multiple qualifying joints, the joint with

	the highest TUV_{joint} will be selected; in the second subject with multiple qualifying joints, the joint with the lowest TUV_{joint} will be selected. Selection will proceed in this fashion, alternating between highest and lowest TUV_{joint}.

1.2 Study Procedures

Subjects will be "on study" for up to 45 days depending on the screening window (up to 30 days). The first visit is for the screening (Day -30 to -1). Screening procedures (demographics, vital signs, medical and surgical history, concomitant medications, blood and urine samples for clinical labs, RA specific labs, urine pregnancy testing for subjects of childbearing potential, ultrasound synovitis assessment, AE assessment, and physical exam) will be completed along with RA evaluations including the 2010 ACR/EULAR classification criteria and DAS28 evaluation.

On Day 0 (visit 2) subjects will receive Tc 99m injection and imaging procedures. Pre-injection procedures include the following: Urine pregnancy testing for all women of childbearing potential. Up to 30 minutes prior to study drug administration, an ECG will be performed, followed by assessment of vital signs, AEs, and concomitant medications. After pre-injection procedures are completed, subjects will receive a single IV dose of 150 μg of tilmanocept radiolabeled with 10 mCi of Tc 99m. Within 30 minutes after injection, an ECG will be performed, followed by assessment of vital signs and AEs. Between 60 and 75 minutes after injection, subjects will receive an AE assessment and a static gamma camera scan of bilateral hands and wrists. Blood will be drawn for clinical laboratory evaluations after the image acquisition has been completed. Subjects who are administered Tc 99m tilmanocept on Day 0 will be considered to be enrolled in the study.

On the third visit (24-72 hours post-injection), a safety follow-up telephone call will include a review of concomitant medications and an AE check.

On the fourth visit (3-7 days post-injection), subjects will be given an ultrasound assessment of synovitis and then a tissue biopsy of the selected joint in

accordance with Table 1 as described in Section 1.1. In addition, an AE check and a review of concomitant medications will be conducted.

On the fifth and final visit (5 ± 2 days post-biopsy), a safety follow-up telephone call will include a review of concomitant medications and an AE check.

For the entire study, end of study is defined as last subject last visit.

1.3 Sample Size

The sample size is expected to be approximately 12 to 24 joints. The final sample size will be determined after the completion of an interim analysis including at least 4 subjects in each pathotype (diffuse myeloid, lympho-myeloid and pauci-immune fibroid). The final sample size will be chosen based on the sponsor's business requirements regarding precision for the estimated correlation between CD206 expressing macrophage density and TUV_{joint}. The final sample size will be at least N = 12. If the rarest pathotype has 25% prevalence in the study patient pool, the expected number of subjects at the interim analysis is N = 16. These needs may be further increased because synovial biopsy fails to recover enough tissue for histological analysis in about 15% of cases.

2.0 Data Analysis Considerations

2.1 Types of Analyses

Data analyses described in this SAP will consist of analyzing efficacy and safety data.

2.2 Analysis Populations

The following analysis populations will be used in the study:

Safety Population – The safety population includes all subjects who have been enrolled in the study and injected with Tc 99m tilmanocept regardless of imaging or biopsy status.

Intent-to-Assay (ITA) Population – The ITA population includes all subjects that have been enrolled in the study, injected with Tc 99m tilmanocept, received all imaging procedures, and have been biopsied.

Per-Protocol (PP) Population: The PP population will include all ITA subjects without major protocol violations. At least 4 evaluable synovial biopsy samples must be available for a subject to be included in the PP population.

2.3 Missing Data Conventions

The analysis of the efficacy and safety variables will be carried out on the observed data (i.e., a complete case analysis). For the regression and correlation analyses, a subject must have valid values for all variables to be used in the analysis.

2.4 Interim Analyses

An interim analysis will be performed after 4 subjects in each of the 3 pathotypes (diffuse myeloid, lympho-myeloid, and pauci-immune fibroid) have been imaged. The final sample size will be recalculated after completion of the interim analysis.

2.5 Calculation of TUV

All calculations are done on a reader-specific basis. That is, there is no statistical aggregation of the reader results.

Calculating Joint TUV

For an individual joint, TUV_{joint} is defined as the intrasubject ratio of the average pixel intensity of a joint to the average pixel intensity of the reference region, such that:

$$TUV_{joint} = \frac{\bar{x}_{Joint\ ROI}}{\bar{x}_{RR}}$$

where

- $\bar{X}_{Joint\ ROI}$ is the average pixel intensity of a region of interest (ROI) of a subject at the anterior or posterior view at the time of imaging (nominally 60 minutes);
- $\bar{X}_{RR}$ is the average pixel intensity of the reference region (RR) of a subject at the anterior or posterior view at the time of imaging (nominally 60 minutes).

Calculating Global TUV

For each independent blind reader, determine the average TUV_{joint} and 95% prediction interval of both the anterior and posterior views of the wrists, MCPs, and PIPs in healthy individuals. For all following calculations, reader specific average TUV_{joint} and 95% prediction intervals will be used.

For each RA subject do the following.

Step 1: Calculate TUV_{joint} for each of the 22 DAS28 joints for which data are collected.

Step 2: Identify all imaged joints with TUV_{joint} > upper limit of normal for the anatomically similar joint and view. These will be referred to as inflamed joints (IJ). Each joint has an anterior and posterior view: a joint is considered an IJ if either view has a TUV_{joint} higher than the upper bound from the normative data set.

Step 3: Calculate the macrophage-involved contribution (MI) to Tc 99m tilmanocept localization for each IJ. This is done by expressing the TUV for the IJ as a fractional change from the mean TUV for the anatomically equivalent joint and view. That is, if TUV_{joint} and $\overline{H}_{joint}$ represent the joint and view specific TUV and the mean TUV for the anatomically equivalent joint and view from the normative data set respectively, the macrophage contribution to TUV is MI_{joint}:

$$\mathrm{MI}_{\mathrm{joint}} = \frac{\mathrm{TUV}_{\mathrm{joint}} - \overline{\mathrm{H}}_{\mathrm{joint}}}{\overline{\mathrm{H}}_{\mathrm{joint}}}.$$

Step 4: TUV_{global} is the total of the macrophage-involved contributions for the IJs. (Note that MI_k is effectively 0 if TUV_{joint} is less than or equal to the upper limit of normal from the normative data set.) That is,

$$\mathrm{TUV}_{\mathrm{global}} = \sum_{\text{All IJs}} \mathrm{MI}_{\mathrm{IJ}},$$

$$\mathrm{TUV}_{\mathrm{global}} = \sum_{k=1}^{22} \mathrm{MI}_{k}.$$

It is presumed that the presence of radiotracer uptake for a joint indicates the presence of activated macrophages. The use of the term “localization” is synonymous with radiotracer uptake.

2.6 Study Center Considerations in the Data Analysis

Up to 10 Centers which include sites in the US, UK, and EU. Analysis will be conducted on the pooled data from all study centers.

2.7 Documentation and Other Considerations

The data analyses described in this SAP will be conducted using SAS© Software, version 9.4 or later.

3.0 Analysis of Baseline Patient Characteristics

Baseline and demographic characteristics of the safety population will be summarized. Continuous variables (age, height, and weight) will be summarized via mean, standard deviation, minimum, maximum, and number of non-missing responses. Categorical variables (gender, race, and ethnicity) will be summarized via counts and percentages.

A detailed listing of baseline data for each patient in the safety population will also be provided, as shown in Appendix B.

4.0 Analysis of Efficacy

4.1 Description of Efficacy Variables

4.1.1 Primary efficacy variables

The primary efficacy variables for this study are:

- Tc 99m tilmanocept uptake values (TUV_{joint}) for the biopsied joints;
- IHC assessment of macrophage expression of the CD206 receptor.

The primary endpoint is:

- The correlation between joint-specific tilmanocept uptake value (TUV_{joint}) and the number and area fraction of CD206 expression as determined by IHC assessment.

4.1.2 Secondary efficacy variables

The secondary variables for this study are:

- IHC and immunofluorescence assessment of macrophage expression and co-expression of the CD68 and CD163 receptors.
- Pathotype classification of RA disease as lympho-myeloid, diffuse myeloid, or pauci-immune fibroid, based on TUV_{joint}.

The secondary endpoints are:

- The correlation between TUV_{joint} and the number and area fraction of CD68 and CD163 determined by IHC assessments.
- Classification of synovial anatomic pathology into Lympho-myeloid, Diffuse myeloid, and Pauci-immune fibroid types as a function of CD68, CD163, CD206, CD3, CD20, CD55, and TE7 expression determined by

IHC assessments using a multinomial logistic regression model with TUV_{joint} as a covariate.
- The correlation between the expression of CD68, CD163, and CD206.

4.1.3 Exploratory efficacy variables

The exploratory variables for this study are:

- IHC assessment of macrophage expression of the CD3, CD20, CD55, and TE7 biomarkers.
- mRNA levels in synovial tissue for the CD206, CD163, and CD68 biomarkers.
- Flow cytometry measurements of CD206, CD163, and CD68 biomarker expression and co-expression.
- Tc 99m tilmanocept global uptake values (TUV_{global}) per subject.
- IHC assessment of the expression of a biomarker (e.g., CD206, TE7) is determined from immunofluorescent microscopy, specifically:
    - The ratio of the total fluorescent stained area to the total field area under 4x and 10x power magnification.
- Pathotype classification of RA disease as lympho-myeloid, diffuse myeloid, or pauci-immune fibroid, based on TUV_{global}.

The exploratory endpoints for this study are:

- The correlation of the expression of CD3, CD20, CD55, and TE7 with CD206 as measured through IHC.
- The correlation of TUV_{joint} with the expression of CD206, CD163, and CD68 as measured through RNA-seq.
- The number and size of CD206, CD163, and CD68 expressing macrophages as measured through (optional) flow cytometry and their correlation with TUV_{joint}.
- The correlation between TUV_{global} and synovial anatomic pathology as determined by IHC assessments.
- Classification of synovial anatomic pathology into Lympho-myeloid, Diffuse myeloid, and Pauci-immune fibroid types using a multinomial logistic regression model with TUV_{global} as a covariate.

4.2 Analysis of Efficacy Variables

All efficacy analyses will be conducted on both the ITA and PP populations. The ITA population will be the primary analysis set.

4.2.1 Primary Efficacy Variables

The primary endpoint will be analyzed by computing the Pearson (product-moment) and Spearman (rank) correlation coefficient between the TUV for the biopsied joint and the final CD206 expressing macrophage count. The CD206 expressing macrophage count is derived from the IHC histopathology and ultrasound imaging:

- The fraction of CD206 expressing macrophages under 4x and 10x power magnification, defined as the ratio of the total fluorescent stained area to total field area. Specifically, area fraction (AF) is defined as

$$AF = \frac{Total\ Stained\ Area}{Total\ Field\ Area} \times 100\%.$$

- The volume of synovial tissue in the biopsied joint, defined as the ultrasound synovial thickness score (Vol). The CD206 macrophage count will be the product of these 2 variables (that is, CD206 = AF*Vol).

CD206 expressing macrophage fraction and TUV_{joint} will be summarized with descriptive statistics (number of data pairs, means, standard deviations, minima, medians, and maxima as well as the Pearson correlation between the variables). The ultrasound synovitis score will be summarized with a frequency table. Defining ρ to be the population correlation coefficient, a test of the hypotheses

$$\mathrm{H}_o: \rho \leq 0$$
$$\mathrm{H}_a: \rho > 0$$

will be performed using Fisher's Z-transformation and its Normal approximation. A 95% confidence interval for the population correlation coefficient (ρ) based on the Fisher Z-transformation (the inverse hyperbolic tangent) and its normal approximation will be provided. The joint distribution of the CD206 macrophage count and TUV_{joint} will be summarized graphically with a scatter diagram of the data pairs with the least-squares regression line superimposed on the graph. The joint distribution of the component variables of CD206 macrophage count will be graphically summarized with box plots showing the conditional distribution of TUV_{joint} for each category of synovitis score.

4.2.2 Secondary Efficacy Variables

Co-expression of the CD68, CD163, and CD206 markers will be analyzed by 2 methods. First, by providing the product-moment and Spearman rank correlation matrices of the IHC field measurements (that is, the fraction of macrophages expressing the markers will not be multiplied by the synovitis score). Descriptive statistics of the data triplets used to calculate the correlation matrices will be

provided (number of data triplets, means, standard deviations, minima, medians, and maxima). In the second method, histological sections will undergo immunofluorescent staining for the 3 markers and DAPI. For each section evaluated, up to 50 cells from the synovial sublining will be identified for each of the 3 markers. For each identified cell (up to 150/section), the rate of co-expression of the 3 markers will be determined. For sections with sparse marker expressing cells, four microscope fields will be randomly selected. Co-expression of the markers will be quantified for any cell observed expressing a marker.

The ability of TUV_{joint} to discriminate among lympho-myeloid, diffuse myeloid, and pauci-immune fibroid RA disease types will be evaluated with a multinomial logistic regression model. The model in terms of the logit (log odds) of the outcome is defined as:

$$ln\frac{\pi_j}{1-\pi_j} = \alpha_j + \beta_j X$$

where
j = category of the outcome

$\frac{\pi_j}{1-\pi_j}$ = odds
α = intercept
β = slope
X = TUV_{joint}

RA type will be the response variable and TUV_{joint} will be the explanatory variable. ROC curves will be generated using the lympho-myeloid type as the base class. The marginal distribution of disease type will be summarized with a frequency table, while the marginal distribution of TUV_{joint} will be summarized with descriptive statistics (number of data pairs, mean, standard deviation, minimum, median and maximum). The joint distribution will be graphically summarized with box plots showing the conditional distribution of TUV_{joint} for each disease type.

4.2.3 Exploratory Efficacy Endpoints

Expression of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 biomarkers and their association with TUV_{joint} will be assessed with the Pearson (product-moment) and the Spearman (rank) correlation matrices calculated for each measurement of expression (IHC, RNA_{seq}, and [optional] flow cytometry). The marginal distributions will be summarized with descriptive statistics (number of complete data points, means, standard deviations, minima, medians, and maxima). The joint distribution will be presented graphically in a windowpane plot of the scatter diagrams.

Expression of CD206, CD163, and CD68 genes in mRNA will be measured with cDNA probes. The TUV_{joint} values concentrations will be regressed on the mRNA

abundance as determined by RNA-seq values. The marginal distributions will be summarized with descriptive statistics (number of complete data points, means, standard deviations, minima, medians, and maxima). The joint distribution will be presented with a windowpane plot of the scatter diagrams. The regression coefficients will be presented with the estimated residual covariance matrix.
The number, size, and co-expression of CD68, CD163, and CD206 expressing macrophages measured by flow cytometry and their relationship with TUV_{joint} will be assessed with the Pearson (product-moment) and Spearman (rank) correlation matrices. The marginal distributions of all variables will be summarized by descriptive statistics (number of complete data points, means, standard deviations, minima, medians, and maxima). The joint distributions will be presented graphically in a windowpane plot of the scatter diagrams.

The ability of TUV_{global} to discriminate among lympho-myeloid, diffuse myeloid, and pauci-immune fibroid RA disease types will be evaluated with a multinomial logistic regression model. The model in terms of the logit of the outcome is defined as:

$$ln\frac{\pi_j}{1-\pi_j} = \alpha_j + \beta_j X$$

where
j = category of the outcome

$\frac{\pi_j}{1-\pi_j}$ = odds
α = intercept
β = slope
X = TUV_{global}

RA type will be the response variable and TUV_{global} will be the explanatory variable. ROC curves will be generated using the lympho-myeloid type as the base class. The marginal distribution of disease type will be summarized with a frequency table, while the marginal distribution of TUV_{global} will be summarized with descriptive statistics (number of data pairs, mean, standard deviation, minimum, median and maximum). The joint distribution will be graphically summarized with box plots showing the conditional distribution of TUV_{global} for each disease type.

If it is found (based on the ROC curves from the multinomial logistic regressions) that TUV_{joint} and TUV_{global} can discriminate between the three RA disease types, then no additional analyses will be performed. However, if this is not the case, then two binary logistic regression analyses, with fibroid vs. non-fibroid disease type as the response and TUV_{joint} and TUV_{global} as predictors, respectively, will also be conducted.

5.0 Analysis of Safety

5.1 Description of Safety Variables

The safety analysis variables are defined as follows:

- Adverse Events (AEs)
- Clinical Laboratory Tests (hematology, serum chemistry, urinalysis)
- ECG Parameters
- Vital Signs

All adverse events (AEs) will be observed for each subject from the time of signing of informed consent until study completion. A treatment-emergent AE (TEAE) is defined as an AE whose start date is on or after the date of the first tilmanocept injection. If the first injection date or the AE start date is missing, the AE will be considered treatment emergent.

Prior to analysis to all AEs will be coded using the MedDRA coding dictionary. Based on the coded terms, TEAEs will be summarized as follows:

- By system organ class (SOC) and preferred term (PT);
- By SOC and PT and relation to the study drug;
- By SOC and PT and severity.

5.2 Description of Safety Analysis

The following describes the safety analyses to be performed for the study. All safety analyses will be performed on the safety population.

Observed and change from baseline for vital sign parameters, ECG parameters, hematology, clinical chemistry, and urinalysis parameters will be summarized using descriptive statistics (n, mean, standard deviation, min, median, and max) at each timepoint.

A data listing will be prepared that reflects the occurrence of TEAEs associated with each concomitant medication or class of medications to examine whether a drug interaction signal is detectable.

Clinical Laboratory Tests
Clinical laboratory tests will be performed at screening and after image acquisition. Abnormal laboratory values will be assessed for clinical significance. For each quantitative laboratory test, descriptive statistics (mean, standard

deviation, median, range, n) on the raw, as well as their changes from baseline, will be presented by timepoint.

If multiple labs were performed at a given visit, then the latest results will be summarized in the analysis tables. All collected lab data will be listed.

ECG Parameters
A standard 12-lead ECG will be obtained up to 30 minutes before investigational product administration and within 30 minutes after investigational product administration. The ECG will be performed with the subject in a resting position for at least 1 minute. Continuous ECG monitoring is not required. At a minimum, the heart rate, QRS, PR, and QT intervals will be collected. QTc will be calculated using the Fridericia formula.

Vital Signs
Vital signs will be performed at screening, up to 30 minutes before, and within 30 minutes after investigational product administration. Height and weight will be measured only at screening and will be summarized as part of the baseline and demographic information. For each vital sign (respiration rate, systolic blood pressure, diastolic blood pressure, heart rate, and temperature), descriptive statistics (mean, standard deviation, minimum, maximum, n) on the raw, as well as their changes from baseline, will be presented by timepoint. The baseline value for each of the post-injection vital sign parameters will be the corresponding pre-injection time point. If there are multiple vital signs taken at any time point, then the latest set of vital signs will be used for the analysis. All vital sign data will be listed.

6.0 Other Relevant Data Analyses/Summaries

6.1 Patient Completion

A table will be constructed with counts of screen failures and enrolled subjects. Of those enrolled, counts and percentages of patients withdrawing from the study before study completion and the number completing the study will be displayed. For those subjects that withdraw before completion of the study, counts and percentages of the reasons for withdrawal will be tabulated. The table will include summary counts and percentages. A data listing of all subject completion and withdrawal data will also be constructed.

6.2 Physical Exam

Physical exams will be performed at screening. All physical exam data will be listed.

6.3 Study Drug Administration

The volume, calculated mass dose, and radioactivity of Tc 99m Tilmanocept injected will be summarized with descriptive statistics. All study drug administration data will be listed.

6.4 RA Evaluation and Screening Physical Exam

Each RA subject will undergo a DAS28 evaluation during screening. The swollen and tender joints will be identified and documented during the physical examination. Results of all DAS28 evaluations will be listed.

6.5 Concomitant Medications

All prior and concomitant medications will be listed, as shown in Appendix B. A separate data listing will be created to show only those medications that were taken for RA within the 6 months prior to Day 0 injection.

7.0 List of Analysis Tables, Figures and Listings

Table No.	Table Title	Included in Final Tables	Shown in Appendix B
1	Subject Disposition	X	X
2	Demographics and Baseline Data Descriptive Statistics - Continuous Variables (Safety Population)	X	X
3	Demographics and Baseline Data Descriptive Statistics – Categorical Variables (Safety Population)	X	X
4	Descriptive Statistics of TUV_{joint} and the CD206 Expressing Macrophage Fraction (ITA population)	X	X
5	Descriptive Statistics of TUV_{joint} and the CD206 Expressing Macrophage Fraction (PP Population)	X	
6	Number and Percent of Subject's Ultrasound Synovitis Scores (ITA Population)	X	X
7	Number and Percent of Subject's Ultrasound Synovitis Scores (PP Population)	X	
8	Pearson (Product-Moment) Correlation between CD68, CD163, and CD206 of IHC Measurements (ITA Population)	X	X
9	Pearson (Product-Moment) Correlation between CD68, CD163, and CD206 of IHC Measurements (PP Population)	X	
10	Spearman (Rank) Correlation between CD68, CD163, and CD206 of IHC Measurements (ITA Population)	X	
11	Spearman (Rank) Correlation between CD68, CD163, and CD206 of IHC Measurements (PP Population)	X	
12	Descriptive Statistics of CD68, CD163, and CD206 from IHC Measurements (ITA Population)	X	X
13	Descriptive Statistics of CD68, CD163, and CD206 from IHC Measurements (PP population)	X	
14	Number and Percent of Subjects in Each RA Disease Type - TUV_{joint} (ITA Population)	X	X
15	Number and Percent of Subjects in Each RA Disease Type - TUV_{joint} (PP Population)	X	
16	Number and Percent of Subjects in Each RA Disease Type – TUV_{global} (ITA Population)	X	
17	Number and Percent of Subjects in Each RA Disease Type – TUV_{global} (PP Population)	X	
18	Descriptive Statistics of the Marginal Distribution of TUV_{joint} (ITA Population)	X	X
19	Descriptive Statistics of the Marginal Distribution of TUV_{joint} (PP Population)	X	
20	Descriptive Statistics of the Marginal Distribution of TUV_{global} (ITA Population)	X	
21	Descriptive Statistics of the Marginal Distribution of TUV_{global} (PP Population)	X	
22	Pearson (Product-Moment) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by IHC Measurement (ITA Population)	X	X

Table No.	Table Title	Included in Final Tables	Shown in Appendix B
23	Pearson (Product-Moment) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by IHC Measurement (PP Population)	X	
24	Pearson (Product-Moment) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by RNA_{seq} (ITA Population)	X	
25	Pearson (Product-Moment) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by RNA_{seq} (PP Population)	X	
26	Pearson (Product-Moment) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by Flow Cytometry (ITA Population)	X	
27	Pearson (Product-Moment) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by Flow Cytometry (PP Population)	X	
28	Spearman (Rank) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by IHC Measurement (ITA Population)	X	X
29	Spearman (Rank) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by IHC Measurement (PP Population)	X	
30	Spearman (Rank) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by RNA_{seq} (ITA Population)	X	
31	Spearman (Rank) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by RNA_{seq} (PP Population)	X	
32	Spearman (Rank) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by Flow Cytometry (ITA Population)	X	
33	Spearman (Rank) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by Flow Cytometry (PP Population)	X	
34	Descriptive Statistics of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by IHC Measurement (ITA Population)	X	X
35	Descriptive Statistics of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with	X	

Table No.	Table Title	Included in Final Tables	Shown in Appendix B
	TUV_{joint} Measured by IHC Measurement (PP Population)		
36	Descriptive Statistics of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by RNA_{seq} (ITA Population)	X	
37	Descriptive Statistics of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by RNA_{seq} (PP Population)	X	
38	Descriptive Statistics of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by Flow Cytometry (ITA Population)	X	
39	Descriptive Statistics of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by Flow Cytometry (PP Population)	X	
40	Descriptive Statistics of CD68, CD163, and CD206 Genes in mRNA (ITA Population)	X	X
41	Descriptive Statistics of CD68, CD163, and CD206 Genes in mRNA (PP Population)	X	
42	Estimated Residual Covariance with the Regression Coefficients of the CD68, CD163, and CD206 Genes in mRNA (ITA Population)	X	X
43	Estimated Residual Covariance with the Regression Coefficients of the CD68, CD163, and CD206 Genes in mRNA (PP Population)	X	
44	Pearson (Product-Moment) Correlation of CD68, CD163, CD206 Expressing Macrophages Measured by Flow Cytometry and Their Relationship to TUV_{joint} (ITA Population)	X	X
45	Pearson (Product-Moment) Correlation of CD68, CD163, CD206 Expressing Macrophages Measured by Flow Cytometry and Their Relationship to TUV_{joint} (PP Population)	X	
46	Spearman (Rank) Correlation of CD68, CD163, CD206 Expressing Macrophages Measured by Flow Cytometry and Their Relationship to TUV_{joint} (ITA Population)	X	
47	Spearman (Rank) Correlation of CD68, CD163, CD206 Expressing Macrophages Measured by Flow Cytometry and Their Relationship to TUV_{joint} (PP Population)	X	
48	Descriptive Statistics of CD68, CD163, and CD206 Expressing Macrophages Measured by Flow Cytometry (ITA Population)	X	X
49	Descriptive Statistics of CD68, CD163, and CD206 Expressing Macrophages Measured by Flow Cytometry (PP Population)	X	
50	Descriptive Statistics of TUV_{global} by Pathology Type (ITA Population)	X	X
51	Descriptive Statistics of TUV_{global} by Pathology Type (PP Population)	X	
52	Vital Signs Descriptive Statistics (Safety Population)	X	X
53	Clinical Laboratory Tests Descriptive Statistics (Safety Population)	X	X

Table No.	Table Title	Included in Final Tables	Shown in Appendix B
54	ECG Parameters Descriptive Statistics (Safety Population)	X	X
55	Summary of Treatment Emergent Adverse Events (Safety Population)	X	X
56	Number and Percent of Subjects with TEAEs (Safety Population)	X	X
57	Descriptive Statistics of TUV_{joint} by Fibroid vs. Non-Fibroid Type (ITA Population)	X	X
58	Descriptive Statistics of TUV_{joint} by Fibroid vs. Non-Fibroid Type (PP Population)	X	
59	Descriptive Statistics of TUV_{global} by Fibroid vs. Non-Fibroid Type (ITA Population)	X	
60	Descriptive Statistics of TUV_{global} by Fibroid vs. Non-Fibroid Type (PP Population)	X	

Figure No.	Figure Title	Included in Final Figures	Shown in Appendix B
Fig1	Scatterplot of the Joint Distribution of CD206 Macrophage Count and TUV_{joint}	X	X
Fig2	Boxplots of the Conditional Distribution of TUV_{joint} for Each Category of Synovitis Score	X	X
Fig3	Boxplots of the Conditional Distribution of TUV_{global} for Each Category of Synovitis Score	X	
Fig4	ROC Curves by RA Disease Type, Logistic Regression with TUV_{joint}	X	X
Fig5	ROC Curves by RA Disease Type, Logistic Regression with TUV_{global}	X	
Fig6	Conditional Distribution of TUV_{joint} by RA Disease Type	X	X
Fig7	Joint Distribution of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint}	X	X
Fig8	Joint Distribution of CD68, CD163, and CD206 in mRNA	X	X
Fig9	Joint Distribution of CD68, CD163, and CD206 Measured by Flow Cytometry	X	X

Data Listing No.	Data Listing Title	Included in Final Listings	Shown in Appendix B
DL1	Subject Disposition Data Listing	X	X
DL2	Inclusion/Exclusion Data Listing	X	X
DL3	Protocol Deviations Data Listing	X	X
DL4	Demographics Data Listing	X	X
DL5	Subjects Excluded from ITA Population Data Listing	X	X
DL6	Subjects Excluded from PP Population Data Listing	X	X
DL7	Subjects Excluded from Safety Population Data Listing	X	X
DL8	Medical History Data Listing	X	X
DL9	Prior and Concomitant Medications Data Listing	X	X
DL10	Prior and Concomitant RA Medications Data Listing	X	X
DL11	Adverse Events Data Listing	X	X
DL12	Occurrence of TEAEs Associated with Concomitant Medications or Class of Medications	X	X
DL13	Subject Laboratory Profiles – Hematology Data Listing	X	X
DL14	Subject Laboratory Profiles – Serum Chemistry Data Listing	X	
DL15	Subject Laboratory Profiles – Urinalysis Data Listing	X	
DL16	Subject Laboratory Profiles – Rheumatology Panel Data Listing	X	
DL17	Physical Exam Data Listing	X	X
DL18	ACR/EULAR 2010 Classification Data Listing	X	X
DL19	DAS-28 by Joint Data Listing	X	X
DL20	DAS-28 by Subject Data Listing	X	X
DL21	Vital Signs Data Listing	X	X
DL22	ECG Parameters Data Listing	X	X
DL23	Study Drug Administration Data Listing	X	X
DL24	Post-Injection Imaging Data Listing	X	X
DL25	TUV Data Listing	X	X
DL26	TUV by Pathology Type	X	X
DL27	Biomarkers Data Listing	X	X

8.0 References

N/A

Appendix A – Tables, Figures and Listing Specifications

Orientation

Tables and figures will be displayed in landscape.

Margins

Margins will be 1 inch on all sides. Table and listing boundaries will not extend into the margins.

Font

Courier New, 8 point.

Headers

The table number will be on the first line of the title. The title area will contain the Sponsor name, the study number, and the name of the table. The title area will contain the page number (Page x of y) on the far right, 1 line above the name of the table.

Footers

- The first line will be a solid line.
- Next will be any footnotes regarding information displayed in the table.
- Below these footnotes will be displayed “STATKING Clinical Services (DD-MMM-YYYY)” on the far left.
- The last line will display the name of the SAS program that generated the table and (if applicable) the source data reference.

Table Disclaimer

The format of the mock tables shown in the appendix of this SAP will be the format of the deliverable tables to the extent that Word document constructed tables can match production tables produced by SAS. This formatting includes the content and format of the header and footer areas of the tables. The Sponsor agrees to the format of the tables as shown in the appendix.

Further programming charges will be applicable for changes in the format of tables (including title statements, notes, data dependent footnotes, etc.) made after the approval of the SAP.

Appendix B – Table Shells

Page x of y

Table 1. Subject Disposition
Navidea Biopharmaceuticals - Study No. NAV3-32

		Overall
Screen Failures		xx
Enrolled		xx
Completed		xx (xxx%)
Withdrawn		xx (xxx%)
Reason for Withdrawal	Adverse Event	xx (xxx%)
	Protocol Violation	xx (xxx%)
	Lost to Follow-Up	xx (xxx%)
	Withdrawal of Consent	xx (xxx%)
	Sponsor Discretion	xx (xxx%)
	Investigator Discretion	xx (xxx%)
	Death	xx (xxx%)
	Other	xx (xxx%)

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Table 2. Demographics and Baseline Data Descriptive Statistics – Continuous Variables
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

	Mean	Std Dev	n	Min	Max	Median
Age (years)	xxx	xxx	xxx	xxx	xxx	xxx
Height (inches)	xxx	xxx	xxx	xxx	xxx	xxx
Weight (pounds)	xxx	xxx	xxx	xxx	xxx	xxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Table 3. Demographics and Baseline Data Descriptive Statistics – Categorical Variables
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Variable	Category	Overall
Gender	Male	xx (xxx%)
	Female	xx (xxx%)
Race	American Indian or Alaska Native	xx (xxx%)
	Asian	xx (xxx%)
	Black or African American	xx (xxx%)
	Native Hawaiian or Other Pacific Islander	xx (xxx%)
	White	xx (xxx%)
	Other	xx (xxx%)
Ethnicity	Hispanic or Latino	xx (xxx%)
	Not Hispanic or Latino	xx (xxx%)

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 4. Descriptive Statistics of TUV_{joint} and the CD206 Expressing Macrophage Fraction
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Measure /Biomarker	Mean	Std Dev	n	Min	Max	Median	Pearson (Product-Moment) Correlation Coefficient	95% Confidence Limits[a]	Spearman (Rank) Correlation Coefficient	95% Confidence Limits[b]
CD206	xxx	xxx	xxx	xxx	xxx	xxx	x.xxx	(x.xxx, x.xxx)	x.xxx	(x.xxx, x.xxx)
TUV_{joint}	xxx	xxx	xxx	xxx	xxx	xxx				

[a] 95% Confidence limits for the Pearson (Product-Moment) Correlation Coefficient are based on the Fisher Z-Transformation (the inverse hyperbolic tangent) and its normal approximation.
[b] 95% Confidence limits for the Spearman (Rank) Correlation Coefficient are based on the Fisher Z-Transformation (the inverse hyperbolic tangent) and its normal approximation.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the PP Population (Table 5)

Table 6. Number and Percent of Subject's Ultrasound Synovitis Scores
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Ultrasound Synovitis Score	Visit	Number (Percentage)
2	1	xxx(xxx%)
2	4	xxx(xxx%)
3	1	xxx(xxx%)
3	4	xxx(xxx%)

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the PP Population (Table 7)

Table 8. Pearson (Product-Moment) Correlation between CD68, CD163, and CD206 of IHC Measurements
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Biomarker 1	Biomarker 2	Pearson (Product-Moment) Correlation Coefficient	95% Confidence Limits	n[a]
CD68	CD163	x.xxx	x.xxx	xxx
CD163	CD206	x.xxx	x.xxx	xxx
CD206	CD68	x.xxx	x.xxx	xxx

[a] Number of data pairs
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table will be repeated for the Spearman (Rank) Correlation Matrix (Table 10). Tables are repeated for the PP Population (Tables 9, 11).

Table 12. Descriptive Statistics of CD68, CD163, and CD206 from IHC Measurements
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Biomarker	Mean	Std Dev	n[a]	Min	Max	Median
CD68	xxx	xxx	xxx	xxx	xxx	xxx
CD163	xxx	xxx	xxx	xxx	xxx	xxx
CD206	xxx	xxx	xxx	xxx	xxx	xxx

[a] Number of data triplets
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the PP Population (Table 13)

Table 14. Number and Percent of Subjects in Each RA Disease Type - TUV_{joint}
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

RA Disease Type	Number (Percent) of Subjects
Lympho-Myeloid	xxx(xxx)
Diffuse Myeloid	xxx(xxx)
Pauci-immune Fibroid	xxx(xxx)

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table will be repeated for TUV_{global} (Table 16). Tables are repeated for the PP Population (Tables 15, 17).

Table 18. Descriptive Statistics of the Marginal Distribution of TUV_{joint}
Navidea Biopharmaceuticals – Study No. NAV3-32
ITA Population (N=xxx)

	Mean	Std Dev	n[a]	Min	Max	Median
TUV_{joint}	xxx	xxx	xxx	xxx	xxx	xxx

[a] Number of complete data points
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas
Table will be repeated for TUV_{global} (Table 20). Tables are repeated for the PP Population (Tables 19, 21).

Table 22. Pearson (Product-Moment) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by IHC Measurement
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Measure /Biomarker	Pearson (Product-Moment) Correlation[a]	95% Confidence Limits[b]	n[c]
TUV_{joint}	--	--	xxx
CD3	x.xxx	(x.xxx, x.xxx)	xxx
CD20	x.xxx	(x.xxx, x.xxx)	xxx
xxx	x.xxx	(x.xxx, x.xxx)	xxx
CD206	x.xxx	(x.xxx, x.xxx)	xxx
TE7	x.xxx	(x.xxx, x.xxx)	xxx

[a] Pearson (Product-Moment) correlation between TUV_{joint} and the indicated measurement/biomarker.
[b] Confidence limits calculated using the Fisher Z-transformation.
[c] Number of complete data points.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for RNA_{seq} and Flow Cytometry (Tables 24, 26). Each table will be repeated for the PP Population (Tables 23, 25, 27).

Table 28. Spearman (Rank) Correlation of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Association with TUV_{joint} Measured by IHC Measurement
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Measure /Biomarker	Spearman (Rank) Correlation[a]	95% Confidence Limits[b]	n[c]
TUV_{joint}	--	--	xxx
CD3	x.xxx	(x.xxx, x.xxx)	xxx
CD20	x.xxx	(x.xxx, x.xxx)	xxx
xxx	x.xxx	(x.xxx, x.xxx)	xxx
CD206	x.xxx	(x.xxx, x.xxx)	xxx
TE7	x.xxx	(x.xxx, x.xxx)	xxx

[a] Spearman (Rank) correlation between TUV_{joint} and the indicated measurement/biomarker.
[b] Confidence limits calculated using the Fisher Z-transformation.
[c] Number of complete data points.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for RNA_{seq} and Flow Cytometry (Tables 30, 32). Each table will be repeated for the PP Population (Tables 29, 31, 33).

Table 34. Descriptive Statistics of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers Association with TUV_{joint} Measured by IHC Measurement
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Measure /Biomarker	n[a]	Mean	Std Dev	Min	Max	Median
TUV_{joint}	xxx	xxx	xxx	xxx	xxx	xxx
CD3	xxx	xxx	xxx	xxx	xxx	xxx
CD20	xxx	xxx	xxx	xxx	xxx	xxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx
CD206	xxx	xxx	xxx	xxx	xxx	xxx
TE7	xxx	xxx	xxx	xxx	xxx	xxx

[a] Number of complete data points.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for RNA_{seq} and Flow Cytometry (Tables 36, 38). Each table will be repeated for the PP Population (Tables 35, 37, 39).

Table 40. Descriptive Statistics of CD68, CD163, and CD206 Genes in mRNA
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Biomarker	n[a]	Mean	Std Dev	Min	Max	Median
CD68	xxx	xxx	xxx	xxx	xxx	xxx
CD163	xxx	xxx	xxx	xxx	xxx	xxx
CD206	xxx	xxx	xxx	xxx	xxx	xxx

[a] Number of complete data points
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the PP Population (Table 41)

Table 42. Estimated Residual Covariance with the Regression Coefficients of the CD68, CD163, and CD206 Genes in mRNA
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Covariance Parameter[a]	Covariance Parameter Estimates	Regression Coefficient
COV(CD68,CD68)	x.xxx	x.xxx
COV(CD163,CD68)	x.xxx	
COV(CD163,CD163)	x.xxx	x.xxx
COV(CD206,CD68)	x.xxx	
COV(CD206,CD163)	x.xxx	
COV(CD206,CD206)	x.xxx	x.xxx

A least-squares regression model will be implemented with TUV_{joint} values concentrations as the independent variable and the mRNA abundance as determined by RNA_{seq} values as the dependent variables.
[a] COV = Covariance (i.e. COV(CD163,CD68) = Covariance of CD163 and CD68)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the PP Population (Table 43)

Table 44. Pearson (Product-Moment) Correlation of CD68, CD163, CD206 Expressing Macrophages Measured by Flow Cytometry and Their Relationship to TUV_{joint}
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Measure /Biomarker	Pearson (Product-Moment) Correlation[a]	95% Confidence Limits[b]	n[c]
TUV_{joint}	--	--	xxx
CD68	x.xxx	(x.xxx, x.xxx)	xxx
CD163	x.xxx	(x.xxx, x.xxx)	xxx
CD206	x.xxx	(x.xxx, x.xxx)	xxx

[a] Pearson (Product-Moment) correlation between TUV_{joint} and the indicated measurement/biomarker.
[b] Confidence limits calculated using the Fisher Z-transformation.
[c] Number of complete data points.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the Spearman (Rank) Correlation Matrix (Table 46). Tables will be repeated for the PP Population (Tables 45, 47).

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Table 48. Descriptive Statistics of CD68, CD163, and CD206 Expressing Macrophages Measured by Flow Cytometry
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Biomarker	n	Mean	Std Dev	Min	Max	Median
CD68	xxx	xxx	xxx	xxx	xxx	xxx
CD163	xxx	xxx	xxx	xxx	xxx	xxx
CD206	xxx	xxx	xxx	xxx	xxx	xxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the PP Population (Table 49)

Table 50. Descriptive Statistics of TUV_{global} by Pathology Type
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Pathology Type	n[a]	Mean	Std Dev	Min	Max	Median
Lympho-myeloid	xxx	xxx	xxx	xxx	xxx	xxx
Diffuse myeloid	xxx	xxx	xxx	xxx	xxx	xxx
Pauci-immune fibroid	xxx	xxx	xxx	xxx	xxx	xxx

[a] Number of complete data points
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for the PP Population (Table 51)

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Table 52. Vital Signs Descriptive Statistics
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Vital Sign Parameter (units)	Visit	Data Type[a]	n	Std Dev	Mean	Min	Max	Median
xxxxxxxxxxxxxxxxx (xxx)	Screening	Raw	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Pre Admin	Raw	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Post Admin	Raw	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxxxxxxxxxxx (xxx)	Screening	Raw	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Pre Admin	Raw	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Post Admin	Raw	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxxxxxxxxxxx (xxx)	Screening	Raw	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Pre Admin	Raw	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Post Admin	Raw	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx

[a] RAW = data recorded in database; CFB = change from baseline = (parameter value at the current time point)-(Baseline parameter value).
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Table 53. Clinical Laboratory Tests Descriptive Statistics
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Laboratory Test	Visit	Data Type[a]	n	Std Dev	Mean	Min	Max	Median
xxxxxxxxxxxxxxxxx	Screening	RAW	xxx	xxx	xxx	xxx	xxx	xxx
	Day 0 – 60 to 75 Minutes Post Admin	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxxxxxxxxxxx	Screening	RAW	xxx	xxx	xxx	xxx	xxx	xxx
	Day 0 – 60 to 75 Minutes Post Admin	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxxxxxxxxxxx	Screening	RAW	xxx	xxx	xxx	xxx	xxx	xxx
	Day 0 – 60 to 75 Minutes Post Admin	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx

[a] RAW = data recorded in database; CFB = change from baseline = (parameter value at the current time point)-(Baseline parameter value).
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Table 54. ECG Parameters Descriptive Statistics
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

ECG Parameter (units)	Visit	Data Type[a]	n	Std Dev	Mean	Min	Max	Median
xxxxxxxxxxxxxxxxx (xxx)	Baseline	RAW	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Post Admin	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxxxxxxxxxxx (xxx)	Baseline	RAW	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Post Admin	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxxxxxxxxxxx (xxx)	Baseline	RAW	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Post Admin	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxxxxxxxxxxx (xxx)	Baseline	RAW	xxx	xxx	xxx	xxx	xxx	xxx
	30 Minute Post Admin	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		CFB	xxx	xxx	xxx	xxx	xxx	xxx

[a] RAW = data recorded in database; CFB = change from baseline = (parameter value at the current time point)-(Baseline parameter value).
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 55. Summary of Treatment Emergent Adverse Events
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

	Overall
Subjects with at Least One Treatment Emergent Adverse Event (TEAE)	xxx (xxx%)
Maximum TEAE Severity Grade	
Mild	xxx (xxx%)
Moderate	xxx (xxx%)
Severe	xxx (xxx%)
Highest Relationship of TEAE to Study Drug	
Definitely Not [n(%)]	xxx (xxx%)
Probably Not [n(%)]	xxx (xxx%)
Possibly [n(%)]	xxx (xxx%)
Probably [n(%)]	xxx (xxx%)
Definitely [n(%)]	xxx (xxx%)
Highest Relationship of TEAE to Study Procedure	
Definitely Not [n(%)]	xxx (xxx%)
Probably Not [n(%)]	xxx (xxx%)
Possibly [n(%)]	xxx (xxx%)
Probably [n(%)]	xxx (xxx%)
Definitely [n(%)]	xxx (xxx%)

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 56. Number and Percent of Subjects with TEAEs
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Adverse Event Category[a]:	Overall
Total Number of Treatment Emergent Adverse Events (TEAEs)	xxx
Subjects with at Least One TEAE	xxx (xxx%)
System Organ Class 1	xxx (xxx%)
Preferred Term 1	xxx (xxx%)
Preferred Term 2	xxx (xxx%)
System Organ Class 2	xxx (xxx%)
Preferred Term 1	xxx (xxx%)
Preferred Term 2	xxx (xxx%)

[a] Adverse events coded with MedDRA Coding Dictionary Version XXX.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

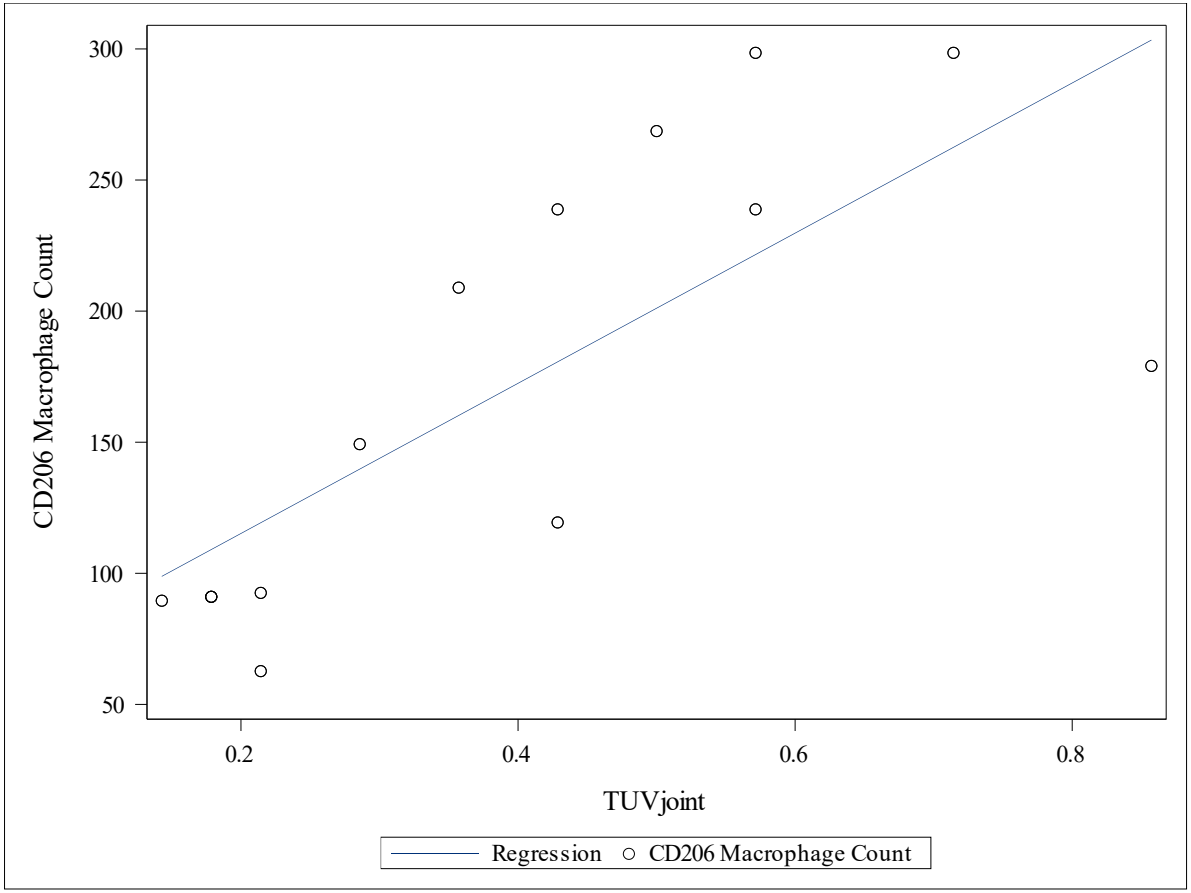
Table 57. Descriptive Statistics of TUV_{joint} by Fibroid vs. Non-Fibroid Type
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)

Type	n[a]	Mean	Std Dev	Min	Max	Median
Fibroid	xxx	xxx	xxx	xxx	xxx	xxx
non-Fibroid	xxx	xxx	xxx	xxx	xxx	xxx

[a] Number of complete data points
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

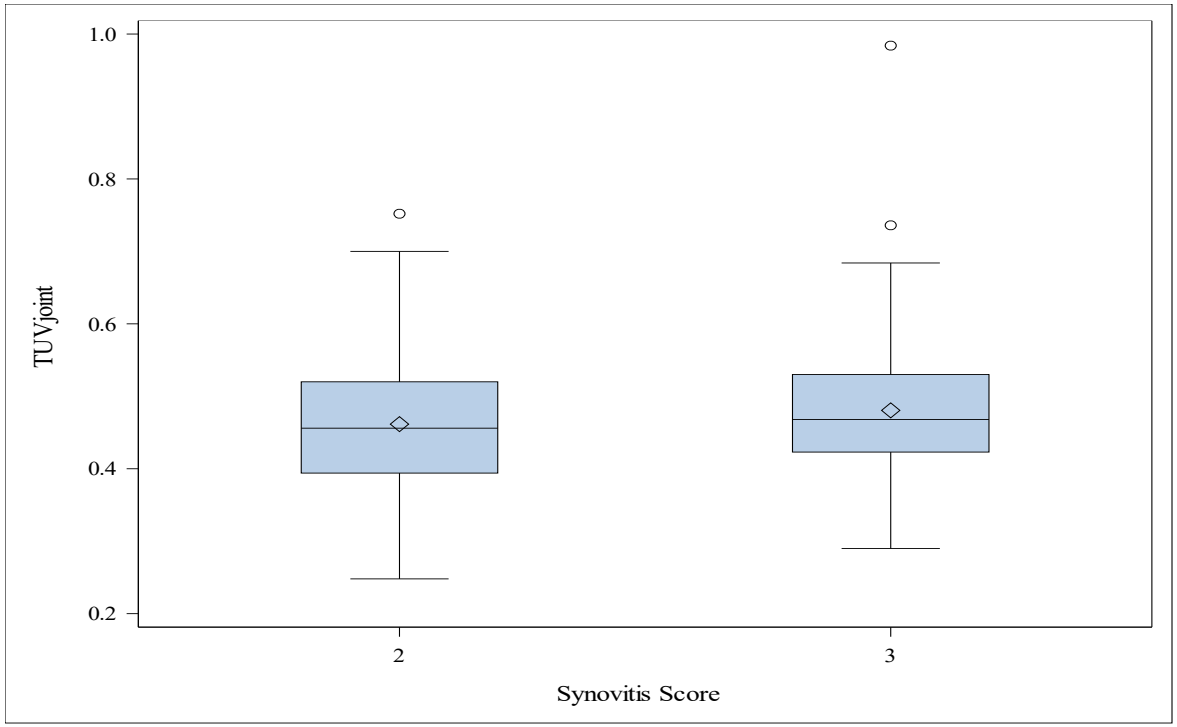
Table Format is Repeated for TUV_{global} (Table 59). Tables will be repeated for the PP Population (Tables 58, 60).

Figure 1. Scatterplot of the Joint Distribution of CD206 Macrophage Count and TUV_{joint}
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)



STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

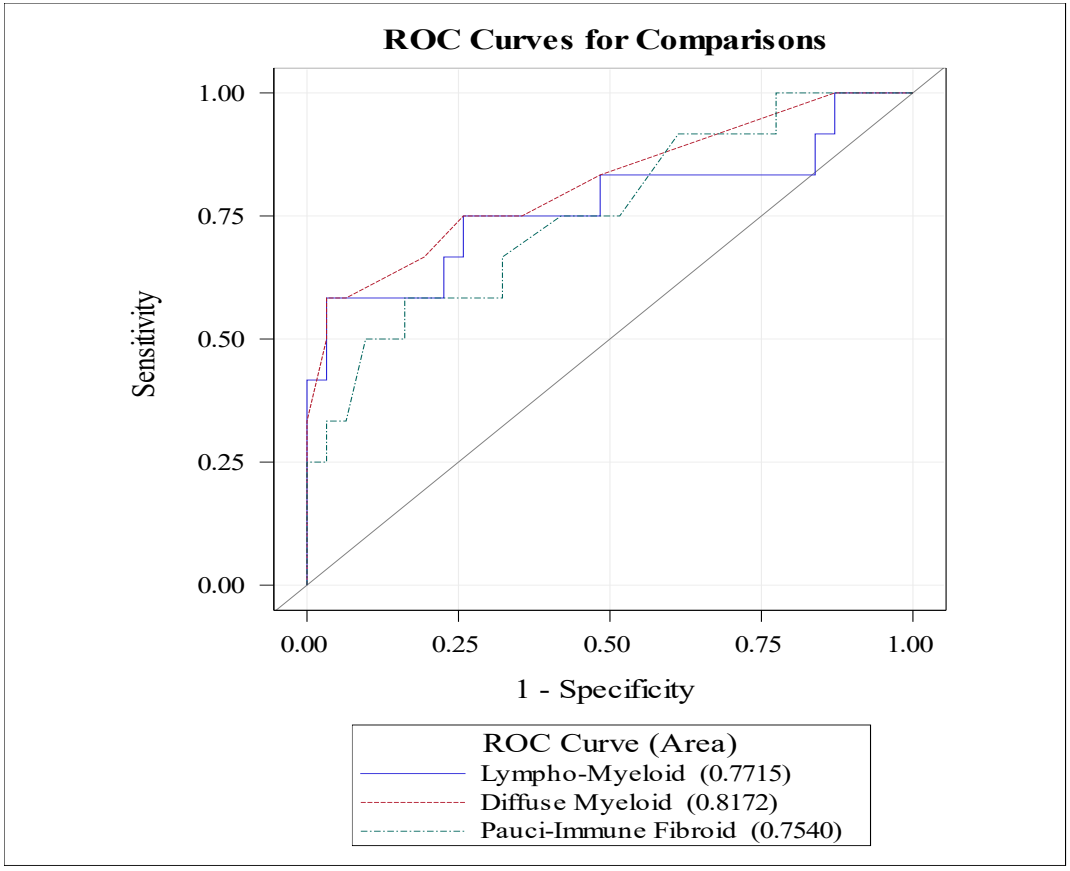
Figure 2. Boxplots of the Conditional Distribution of TUV_{joint} by Synovitis Score
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)



STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for TUV_{global} (Figure 3).

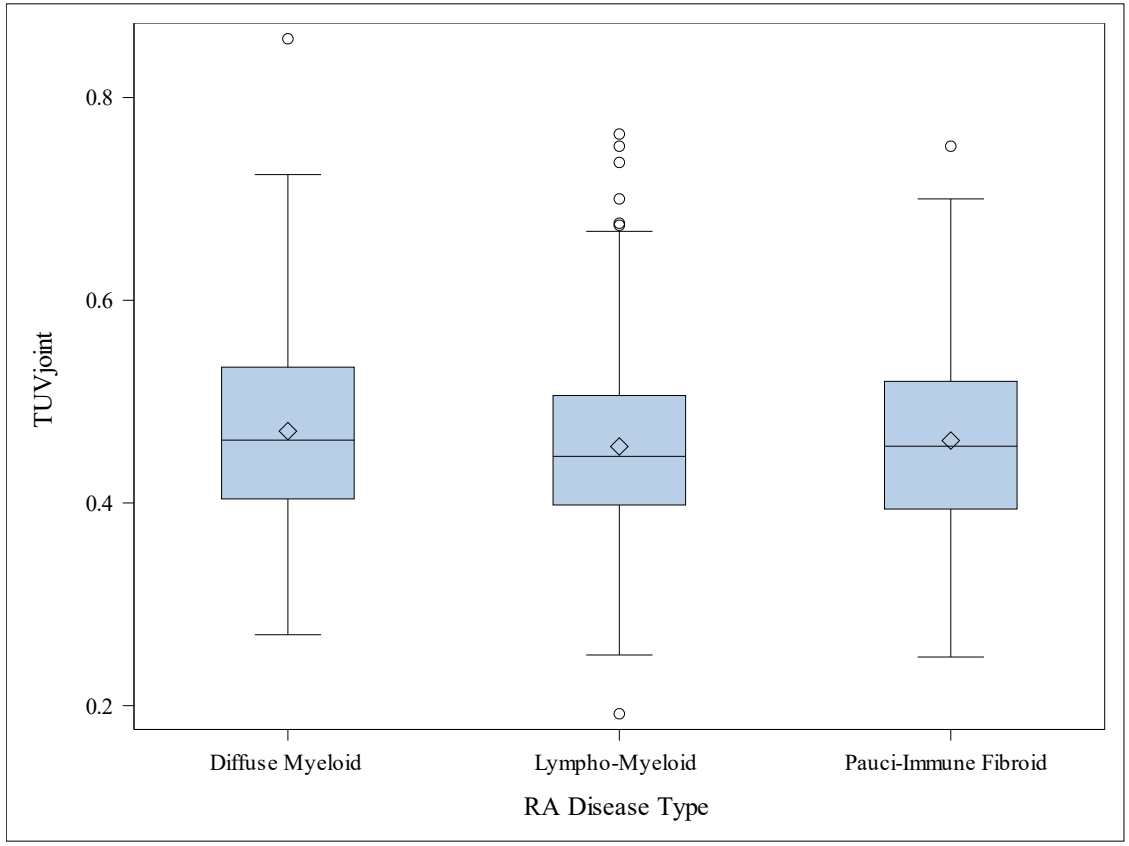
Figure 4. ROC Curves by RA Disease Type, Logistic Regression with TUV_{joint}
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)



STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table Format is Repeated for TUV_{global} (Figure 5).

Figure 6. Conditional Distribution of TUV_{joint} by RA Disease Type
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)



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Source Program: xxxxxxx.sas

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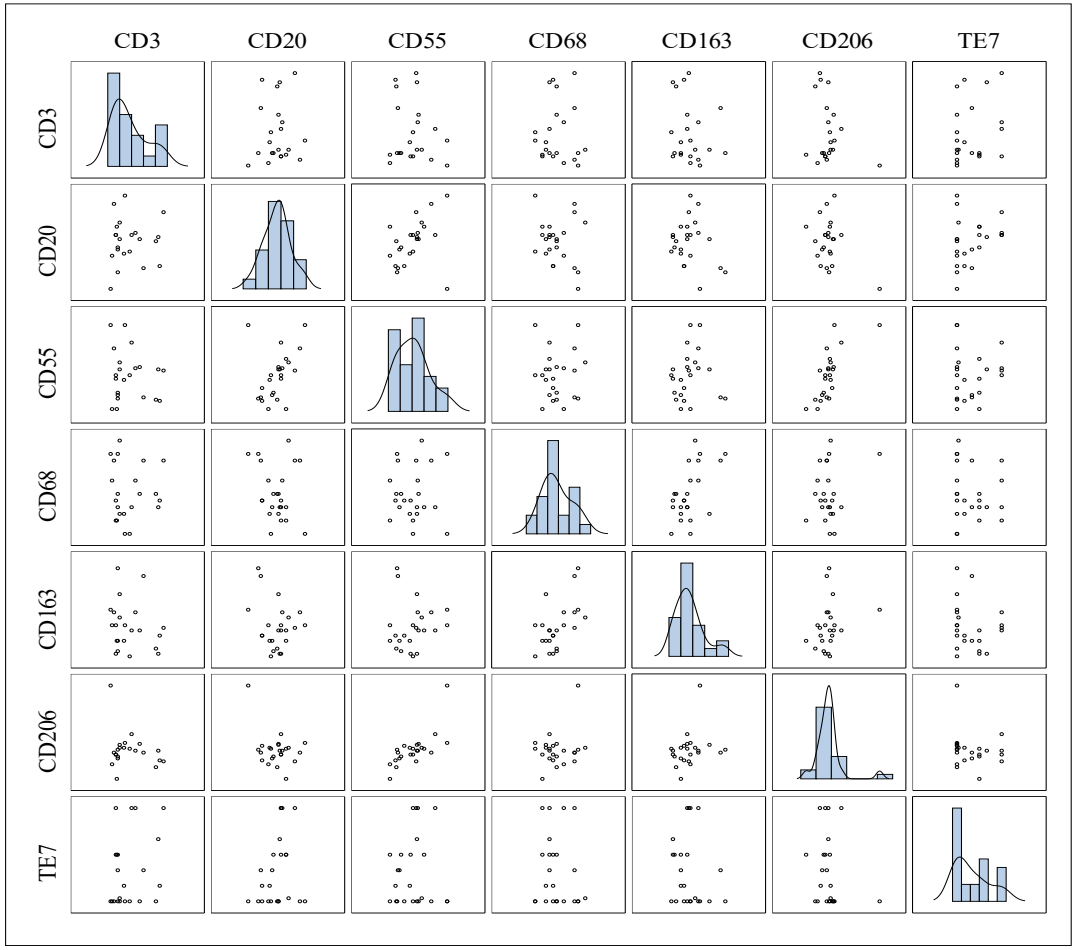
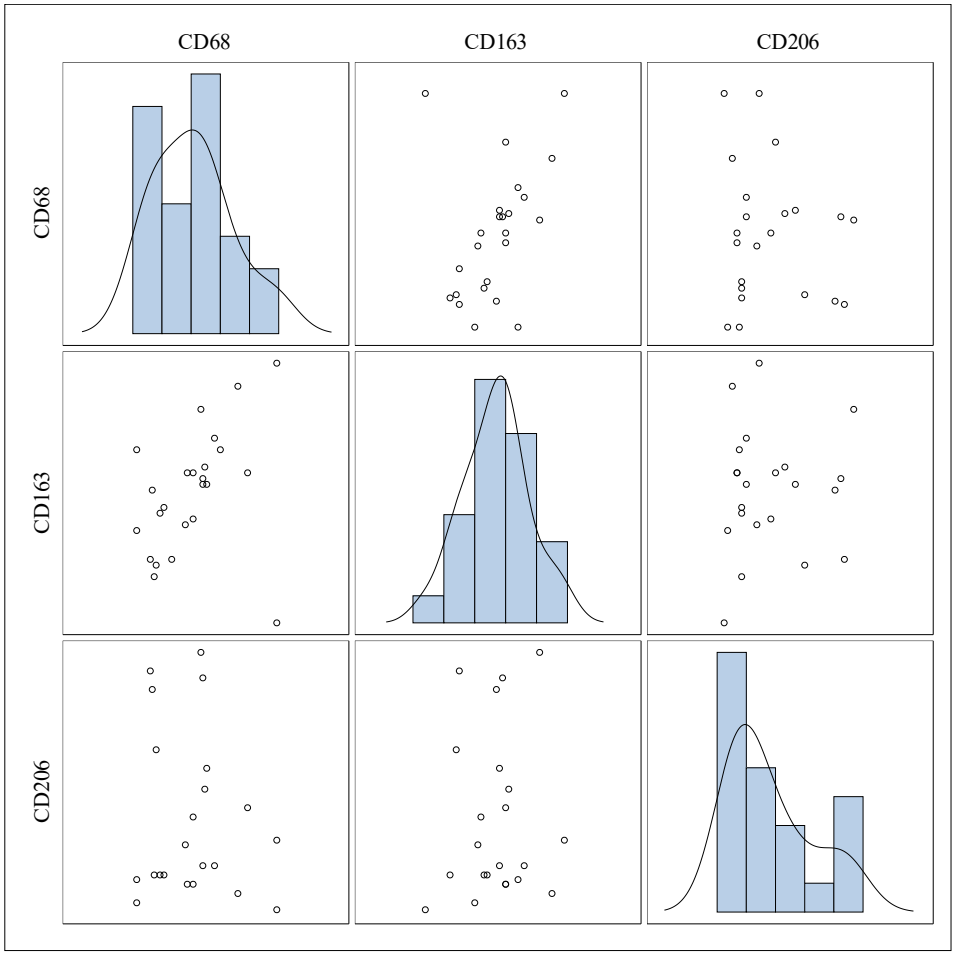
Figure 7. Joint Distribution of CD3, CD20, CD55, CD68, CD163, CD206, and TE7 Biomarkers
Association with TUV_{joint}
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)



STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Figure 8. Joint Distribution of CD68, CD163, and CD206 in mRNA
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)



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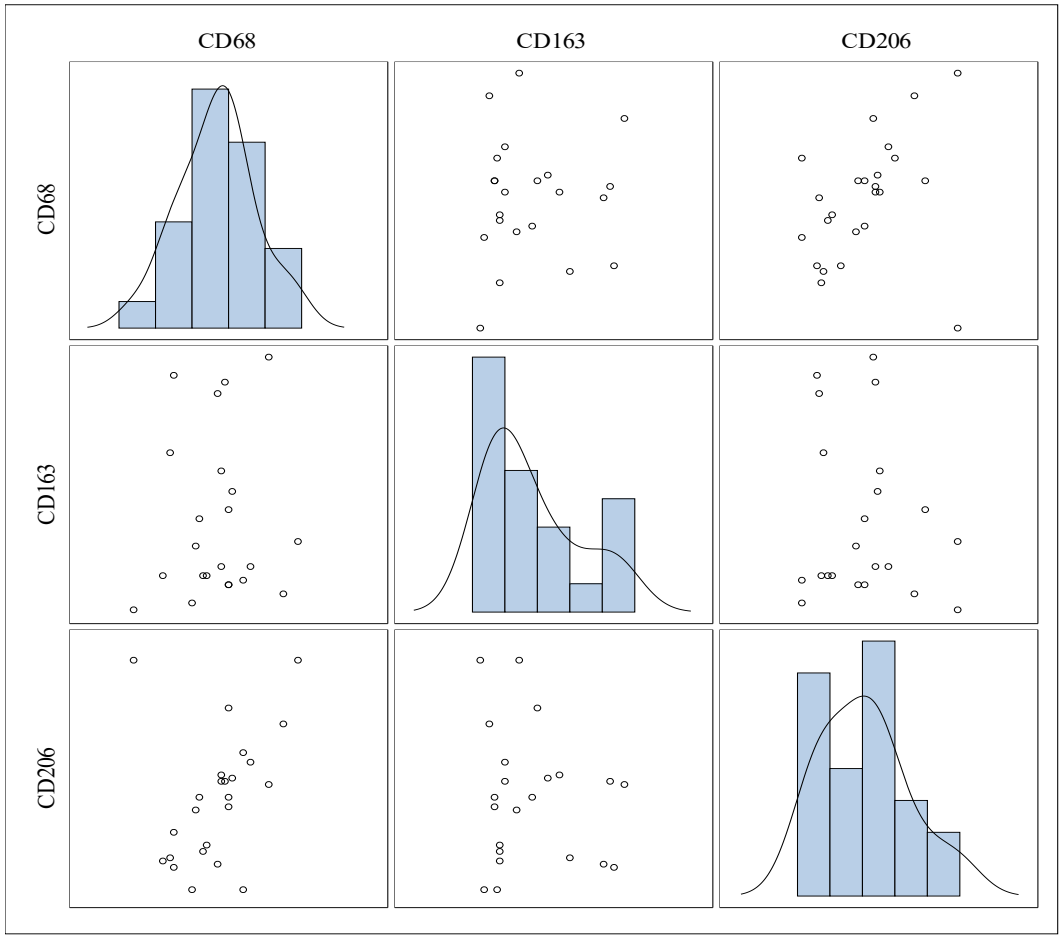
Source Program: xxxxxxx.sas

Figure 9. Joint Distribution of CD68, CD163, and CD206 Measured by Flow Cytometry
Navidea Biopharmaceuticals - Study No. NAV3-32
ITA Population (N=xxx)



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Source Program: xxxxxxx.sas

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Data Listing 1. Subject Disposition Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32

Subject No.	Disposition Status	Date of Completion/ Withdrawal/Screen Fail	Withdrawal Reason
xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 2. Inclusion/Exclusion Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32

Subject No.	Did Subject Meet All Eligibility Criteria?	Criterion Category	Criterion	Was a Waiver Granted?	Is Subject a Screen Failure?
xxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx	xxxx	xxxx
xxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx	xxxx	xxxx
xxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx	xxxx	xxxx
xxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx	xxxx	xxxx

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Source Program: xxxxxxx.sas

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Data Listing 3. Protocol Deviations Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32

Subject No.	Date of Deviation	Deviation Description	Deviation Category (Major/Minor)
xxxx	xxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx
xxxx	xxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx
xxxx	xxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx
xxxx	xxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxxxxx

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Source Program: xxxxxxx.sas

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Data Listing 4. Demographics Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Informed Consent Date/Time	Date of Birth	Height (inches)	Weight (pounds)	Age (yrs)	Gender	Race	Ethnicity
xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx
xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx
xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx
xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 5. Subjects Excluded from ITA Population Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
All Enrolled Subjects (N=xxx)

Subject No.	Reason for Exclusion
xxxx	xxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 6. Subjects Excluded from PP Population Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
All Enrolled Subjects (N=xxx)

Subject No.	Reason for Exclusion
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 7. Subjects Excluded from Safety Population Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
All Enrolled Subjects (N=xxx)

Subject No.	Reason for Exclusion
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 8. Medical History Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	MedDRA System Organ Class[a]/ MedDRA Preferred Term/ CRF Verbatim Term	Start Date	Resolution/Stop Date	Ongoing?
xxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxx	xxxxxxx	xxx
	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxx	xxxxxxx	xxx
	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxx	xxxxxxx	xxx

[a] Medical history terms coded with MedDRA Coding Dictionary Version xxx.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 9. Prior and Concomitant Medications Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Drug Preferred Term[a]/ Verbatim/ ATC Level 1 Text/ ATC Level 4 Text	Indication	Frequency	Start Date	Stop Date	Route	Ongoing?
xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxx	xxxxx
xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxx	xxxxx

[a] Medications coded with WHO Coding Dictionary xxxxxxxxx
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

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Data Listing 10. Prior and Concomitant RA Medications Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Drug Preferred Term[a]/ Verbatim/ Indication/ ATC Level 1 Text/ ATC Level 4 Text	Frequency	Start Date	Stop Date	Route	Ongoing?
xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxx	xxxxx
xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxx	xxxxx

[a] Medications coded with WHO Coding Dictionary xxxxxxxxx
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 11. Adverse Events Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Start Date and Time/ End Date and Time	Start Date and Time of Nearest Previous tilmanocept Injection	MedDRA System Organ Class[a]/ MedDRA Preferred Term/ CRF Verbatim Term	Severity	Relation to Tc-99m tilmanocept/ Procedure	Serious?	Outcome
xxxxxxxxx	xxxxxxx xxxxxxx/ xxxxxxx xxxxxxx	xxxxxxx xxxxxxx	xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx	xxxxxxxx	xxxxxxxx/ xxxxxxxx	xxx	xxxxxxxx
xxxxxxxxx	xxxxxxx xxxxxxx/ xxxxxxx xxxxxxx	xxxxxxx xxxxxxx	xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx	xxxxxxxx	xxxxxxxx/ xxxxxxxx	xxx	xxxxxxxx

[a] Adverse events coded with MedDRA Coding Dictionary Version xxx.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

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Data Listing 12. Occurrence of TEAEs Associated with Concomitant Medication or Class of Medications
Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Start Date and Time/ End Date and Time	Start Date and Time of Nearest Previous tilmanocept Injection	MedDRA System Organ Class[a]/ MedDRA Preferred Term/ CRF Verbatim Term	Concomitant Medication or Class of Medications Associated with AE
xxxxxxxxx	xxxxxxx xxxxxxx/ xxxxxxx xxxxxxx	xxxxxxx xxxxxxx	xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx	xxxxxxxx
xxxxxxxxx	xxxxxxx xxxxxxx/ xxxxxxx xxxxxxx	xxxxxxx xxxxxxx	xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxx	xxxxxxxx

[a] Adverse events coded with MedDRA Coding Dictionary Version xxx.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

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Data Listing 13. Subject Laboratory Profiles - Hematology Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Sample Date and Time	Lab Parameter (Units)	Result	Normal Range		Clin. Sig?
					Lab Low	Lab High	
xxxx	xxxxxxxx	xxxxxxxx / xx:xx	xxxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
			xxxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
			xxxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
			xxxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
			xxxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
			xxxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx

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Source Program: xxxxxxx.sas

Table format is repeated for Serum Chemistry, Urinalysis, and Rheumatology Panel Listings (Listings 14, 15, 16).

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Data Listing 17. Physical Exam Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Date Conducted	Body System	Result	Abnormality
xxxx	xxxxxxx	xxxxxxx	General Appearance	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Skin	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Eyes, Ears, Nose, Throat	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Head and Neck	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Lungs	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Heart	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Abdomen	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Lymph Nodes	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Musculoskeletal	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Nervous System	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
			Other: XXXXXX	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 18. ACR/EULAR 2010 Classification Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

			ACR/EULAR 2010				
Subject No.	Visit	Date	Joint Involvement	Serology	Acute-Phase Reactants	Duration of Symptoms	Total Score
xxxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx	xxx	xxx
xxxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx	xxx	xxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 19. DAS-28 By Joint Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

				DAS28 Joint Classification	
Subject No.	Visit	Date	Joint	Result (Right Body)	Result (Left Body)
xxxx	xxxxxxx	xxxxxxx	xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx
xxxx	xxxxxxx	xxxxxxx	xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx
			xxxxxxxxx	xxx	xxx

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Source Program: xxxxxxx.sas

Data Listing 20. DAS-28 By Subject Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

			DAS28				
Subject No.	Visit	Date	Tender Joint Count	Swollen Joint Count	Patient VAS Global (mm)	C-reactive Protein (CRP; mg/L)	DAS28 Score
xxxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx	xxx	xxx
xxxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx	xxx	xxx

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Source Program: xxxxxxx.sas

Data Listing 21. Vital Signs Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Date	Time	Temp. (°F)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (bpm)	Respirations per Minute
xxxx	xxxxxxx	xxxxxxx	xxxxx	xxx	xxx	xxx	xxx	xxx
			xxxxx	xxx	xxx	xxx	xxx	xxx
			xxxxx	xxx	xxx	xxx	xxx	xxx
xxxx	xxxxxxx	xxxxxxx	xxxxx	xxx	xxx	xxx	xxx	xxx
			xxxxx	xxx	xxx	xxx	xxx	xxx
			xxxxx	xxx	xxx	xxx	xxx	xxx

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Source Program: xxxxxxx.sas

Data Listing 22. ECG Parameters Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Date	Time	Heart Rate	PR Interval	QRS Interval	QT Interval	QTcF Interval	Overall Interpretation
xxxx	xxxxxx	xxxxx	xxxxxx	xxxxxx	xxxxxxxx	xxxxxxx	xxxxxx	xxxx	xxxxxxxxxxxxxxxx

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Source Program: xxxxxxx.sas

Data Listing 23. Study Drug Administration Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Date/ Time of Injection	Anatomic Location of Injection	Pre-Injection Radioactivity (mCi)/Time of Measurement	Post-Injection Radioactivity (mCi)/Time of Measurement	Calculated Amount of Administered Radioactivity (mCi)	Calculated Mass Dose (µg)	Volume Injected (mL)	Lot Number
xxxx	xxxxxxxx/ xxxx	xxxxxxxx	xxx/ xxxx	xxx/ xxxx	xxx	xxx	xxx	xxx
xxxx	xxxxxxxx/ xxxx	xxxxxxxx	xxx/ xxxx	xxx/ xxxx	xxx	xxx	xxx	xxx
	xxxxxxxx/ xxxx	xxxxxxxx	xxx/ xxxx	xxx/ xxxx	xxx	xxx	xxx	xxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

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Data Listing 24. Post-Injection Imaging Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Date of Imaging	Start Time of Imaging	Planar Imaging Performed?
xxxx	xxxxxxxx	xxxxxx	xx:xx	xxx
xxxx	xxxxxxxx	xxxxxx	xx:xx	xxx

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Source Program: xxxxxxx.sas

Data Listing 25. TUV Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Date / Time	Region of Interest[a]	TUV	Upper Limit of Normal	Mean of Normal
xxxx	xxxxxxx	xxxxxxxx / xx:xx	xxxxxx	xxxxx	xxx	xxx
xxxx	xxxxxxx	xxxxxxxx / xx:xx	xxxxxx	xxxxx	xxx	xxx

[a] Region of Interest is joint or global.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

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Data Listing 26. TUV_{global} by Pathology Type Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Date / Time	Pathology Type	TUV_{global}	Upper Limit of Normal	Mean of Normal
xxxx	xxxxxxx	xxxxxxxx / xx:xx	xxxxxx	xxxxx	xxx	xxx
xxxx	xxxxxxx	xxxxxxxx / xx:xx	xxxxxx	xxxxx	xxx	xxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 27. Biomarkers Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-32
Safety Population (N=xxx)

Subject No.	Visit	Date / Time	Biomarker	Anatomic Pathology Evaluation	Result
xxxx	xxxxxxx	xxxxxxxx / xx:xx	xxxxx	xxxxx	xxxxx
xxxx	xxxxxxx	xxxxxxxx / xx:xx	xxxxx	xxxxx	xxxxx

STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas