Statistical Analysis Plan (SAP)

Development of a Normative Database for Rheumatoid Arthritis (RA) Imaging with Tc 99m Tilmanocept

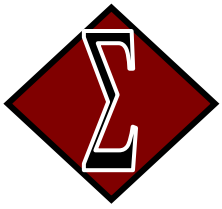
Study No: NAV3-35

Version 1.0

July 14, 2022

Prepared for
Navidea Biopharmaceuticals, Inc.
4995 Bradenton Avenue, Suite 240
Dublin, OH 43017

Prepared by
STATKING Clinical Services
759 Wessel Drive
Fairfield, OH 45014
513-858-2989
www.statkingclinical.com



STATKING Clinical Services

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.

Approved by:

Michael Rosol, PhD
Chief Medical Officer
Navidea Biopharmaceuticals
4995 Bradenton Avenue, Suite 240
Dublin, Ohio 43017
MRosol@navidea.com

20 July 2022
Date

Rachael Hershey, MS, CCRP
Associate Director, Clinical Research & Operations
Navidea Biopharmaceuticals
4995 Bradenton Avenue, Suite 240
Dublin, Ohio 43017
RHershey@navidea.com

20 July 2022
Date

Authored by:

Ian Lees, MS
Statistician
STATKING Clinical Services
759 Wessel Drive
Fairfield, OH 45014
513-858-2989 ext. 327
ian@statkingclinical.com

07/21/2022
Date

Approved by (internal review):

07/21/2022

Lori Christman, PhD
Director of Biostatistics
STATKING Clinical Services
759 Wessel Drive
Fairfield, OH 45014
513-858-2989 ext. 330
lori@statkingclinical.com

Date

Approved by:

7-20-2022

Clare Geiger, RN
Project Manager
STATKING Clinical Services
759 Wessel Drive
Fairfield, OH 45014
513-858-2989 ext. 304
clare@statkingclinical.com

Date

Revision History

Not Applicable.

List of Abbreviations and Definitions of Terms

Term	Definition
Δ	Greek letter delta, used to represent the change in a particular variable
μg	microgram
ACPA	anti-citrullinated protein/peptide antibody
ACR/EULAR	American College of Rheumatology/ European League Against Rheumatism
AE	adverse event
Anti-TNF-α bDMARD	Anti-Tumor Necrosis Factor α biological Disease Modifying Anti-Rheumatic Drug
CDAI	Clinical Disease Activity Index
CFB	change from baseline
CI	confidence interval
CRF	case report form
CSR	clinical study report
CT	X-ray computed tomography
CV	coefficient of variation
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(s)	healthy control(s)
ICH	International Conference on Harmonization
ITD	intent-to-diagnose
IV	intravenous
mCi	milliCurie ($37x10^6$ becquerels; 37megabecquerels)
MCP	metacarpophalange
MedDRA	Medical Dictionary for Regulatory Activities
NPV	Negative Predictive Value
OA	Osteoarthritis or Overall Accuracy, depending on context
PIP	proximal interphalange
PP	per protocol
PPV	Positive Predictive Value
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

Term	Definition
Tc 99m	technetium-99m metastable isotope; γ-emitting (half-life 6.02 h)
TEAE	treatment-emergent adverse event
TESAE	treatment-emergent serious adverse event
tilmanocept	DTPA Mannosyl Dextran (the US Adopted Name for the drug substance of Lymphoseek)
TUV	Tilmanocept uptake value
US	United States
$\bar{X}_{BRAIN}$	the decay-corrected average voxel intensity of the brain RR of a subject at the anterior view at 1 or 3-hours post-injection
$\bar{X}_{ROI}$	the decay-corrected average voxel intensity of a region of interest

Table of Contents

INTRODUCTION

Description

This Statistical Analysis Plan (SAP) is consistent with the final study protocol (dated 17 March 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 was done in accordance with STATKING Clinical Services SOP SCI 02-54, Statistical Analysis Plans.

1.0 Synopsis of Study Design/Procedures

This is a prospective, open-label, multicenter, single-dose study designed to develop a normative database of joint-specific Tilmanocept Uptake Values (TUV_{joint}) in healthy controls (HCs) and to assess the feasibility of qualitative and quantitative single photon emission computed tomography/ computed tomography (SPECT/CT) assessments in HCs and subjects with active rheumatoid arthritis RA following Tc 99m tilmanocept administration.

Tilmanocept Uptake Value (TUV) is a quantitative imaging metric used to characterize Tc 99m tilmanocept uptake on planar imaging. A per-joint TUV (TUV_{joint}) relative ratio will be calculated for the each of the 22 DAS28 joints located in the hands and wrists. A subject-level global TUV (TUV_{global}) assessed across the 22 joints will be used as an indication of overall disease burden in RA patients.

The study is stratified into two arms. Arm 1 consists of HC subjects. Arm 2 consists of HCs and clinically diagnosed RA patients on stable therapy.

The objectives of the study are:

Primary Objectives:

- To establish mean and variance of TUV_{joint} in HCs age-matched to RA population.
- To assess the feasibility of detecting Tc 99m tilmanocept anatomic localization using SPECT/CT imaging of hands and wrists in HCs and subjects with active RA.

Secondary Objectives:

- To quantitate Tc 99m tilmanocept anatomic localization based on SPECT/CT imaging of hands and wrists in HCs and joints with RA-involved inflammation.

Safety Objective:

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

1.1 Design and Treatment

Subjects will receive the administration of Tc 99m tilmanocept through an IV route of administration. All subjects will receive a 150 μg mass dose of tilmanocept labeled with 10 mCi of Tc 99m in a 3 ml volume. 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.

Table 1 Study arms

Arm	Subjects	Evaluations
1	HC subjects clinically free of any inflammatory disease and/or joint pain.	Planar image of bilateral hands/wrists.
2	HC subjects clinically free of any inflammatory disease and/or joint pain. Subjects with clinically diagnosed RA who have been on stable anti-rheumatic therapy.	Planar image of bilateral hands/wrists followed by SPECT/CT of bilateral hands/wrists.

1.2 Study Procedures

Subjects will visit the study site (Visit 1) for screening procedures up to 30 days (Day -30 to Day -1) before enrollment into the study. Screening procedures (demographics, vital signs, medical history, blood and urine samples for clinical labs, RA specific labs, urine pregnancy testing for subjects of childbearing potential, and physical exam) will be completed along with the 2010 ACR/EULAR score. RA subjects will also undergo a DAS28 evaluation and a review of RA history including previous treatments, date of symptom onset, and date of diagnosis.

Subjects arriving for Study Day 0 (Visit 2) will be considered enrolled in the study. On Day 0 subjects will receive Tc 99m injection and imaging procedures. A urine pregnancy test will be administered (pre-injection) to all subjects with childbearing potential. Up to 30 minutes prior to drug administration assessment of vital signs and AEs will be performed. After pre-injection procedures are completed subjects will receive a single IV dose with 150 μg of tilmanocept radiolabeled with 10 mCi of Tc 99m. Within 30 minutes of injection, subjects will receive vital sign and AE check. For all subjects, planar images of the bilateral hands and wrists will be taken at 60 - 75 minutes for 10 – 13 minutes. After preparation up to 10 minutes, for Arm 2, SPECT/CT of the bilateral hands and wrists will be acquired for 25-30 minutes.

On Study Day 5 (± 3 days) (Visit 3) a safety follow-up telephone call will include a review of concomitant medications and assessment of adverse events. Subjects have completed the study at this point.

For all subjects, delegated trained imaging scientists blinded to all clinical subject information will perform semi-automated region-of-interest ROI drawing on planar images of the bilateral hands and wrists to derive relevant count statistics, which are input parameters for TUV_{joint} and TUV_{global}.

1.3 Sample Size

The study will enroll up to 135 evaluable subjects in Arms 1 and 2 allocated below, imaged at up to 8 study centers.

Arm 1 will have up to N = 120 evaluable HC subjects, Arm 2 will have up to N = 15 evaluable subjects; 5 HCs and 10 RA subjects.

A subject is considered evaluable if he/she meets the criteria for the analysis population and has the data necessary for computing the primary endpoint(s) relevant to his/her study Arm.

The sample will be stratified 3:1, females to males ratio to reflect RA incidence in the United States. The sex-specific samples will be further stratified by age to reflect the Census estimated US population in 2019.

The target sample sizes are given below.

Age Range	Male	Female	Total
30 to 39 years	8	23	31
40 to 49 years	7	21	28
50 to 59 years	8	22	30
60 to 69 years	7	21	28
70 years and older	6	21	27
Total	36	108	144

An effort will be made to target enrollment in this group to include 2 men and 8 women 80 years old and over.

The existing data for HC subjects was used in a bootstrap procedure to evaluate the width of 95% confidence intervals for the 95 percentiles for various sample sizes. The sponsor has decided for its business purposes that knowing the percentile to within 0.05 of its true value is sufficient. A sample of size N = 144 HC results (this includes the subjects from Arm 1 of NAV3-31) in 95% confidence intervals with half-widths less than 0.05.

The sample size for Arm 2 was determined to be sufficient for the business purposes of the sponsor. The sample size for Arm 2 will be 5 HCs and 10 RA subjects.

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 patients that have been enrolled in the study and injected with Tc 99m tilmanocept.

Intent-to-Diagnose (ITD) Population – The ITD population includes all subjects that have been enrolled in the study, injected with Tc 99m tilmanocept, and

received all imaging and evaluations necessary for the primary endpoint(s) appropriate to their respective arm.

Per Protocol (PP) Population: The PP population will include all ITD subjects without major protocol violations. All protocol violations will be classified as major or minor prior to database lock.

All efficacy analyses will be carried out on the ITD and PP populations with the ITD population being the primary analysis set. All analyses of safety data and baseline subject characteristics will be carried out on the safety population. A data listing displaying the patients excluded from each population will be created, as shown in Appendix B.

2.3 Missing Data Conventions

No missing value imputation will be used in this analysis. All analyses will be based on the observed data.

2.4 Interim Analyses

There are no interim analyses planned for this study.

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 average pixel intensity of the joint (ROI) divided by the average pixel intensity of the whole hand and part of the forearm on the same view and side as the joint ROI.

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,

$$\mathrm{TUV}_{\mathrm{global}} = \sum_{\text{All IJs}} \mathrm{MI}_{\mathrm{IJ}} = \sum_{k=1}^{22} \mathrm{MI}_k.$$

Arms 1 and 2:

Precision endpoints for both arms will be assessed estimating the mean, standard deviation, n, minimum, median, and maximum of TUV for each evaluated DAS28 joint.

2.6 Study Center Considerations in the Data Analysis

A study center is defined as a treatment administration site or group of treatment administration sites under the control and supervision of the same Principal Investigator (PI). There will be no selective pooling of 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 by subject arm and overall. 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 Endpoints

The efficacy variables for this study are as follows:

- Quantitative determination of TUV_{joint} and TUV_{global}.
- Qualitative determination of tilmanocept localization in planar images and SPECT/CT images of the bilateral hands and wrists.
- Quantitative determination of tilmanocept localization in planar and SPECT/ CT images of the bilateral hands and wrists

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

TUV is defined as:

$$\mathrm{TUV}_{\mathrm{joint}} = \frac{\bar{X}_{joint}}{\bar{X}_{\mathrm{RR}}};$$

where

- $\bar{X}_{\mathrm{joint}}$ is the average voxel intensity of a particular joint of a subject at the anterior or posterior views at 1 hour post-injection.
- $\bar{X}_{\mathrm{RR}}$ is the average voxel intensity of the reference region (RR) of a subject at the anterior or posterior views at 1 hour post-injection.

4.1.1 Primary Efficacy Endpoints

The primary efficacy endpoints of this study are:

Arm 1:

The normal limits of TUV_{joint} per joint basis in HC subjects, which are defined as the 5 and 95 percentiles of TUV_{joint} of bilateral joints (i.e., bilateral wrists, metacarpophalangeal joint [MCPs], proximal interphalangeal [PIPs]). The normal range will be determined separately for each of the three blinded readers.

Arm 2:

The qualitative evaluations of planar and SPECT/CT in detecting localization within synovial spaces of the bilateral hands and wrists in HCs and RA subjects.

4.1.2 Secondary efficacy Endpoints

The Secondary efficacy endpoints of this study are:

Healthy Controls in Both Arms 1 and 2:

- Applicability of the Normal (Gaussian) distribution to TUV_{joint} data.
- Relationship between TUV_{joint} and age by joint.
- Relationship between the variance of TUV_{joint} and age.
- Relationship between TUV_{joint} and sex (male vs female).
- Relationship between TUV_{joint} and BMI.

Arm 2:

- Quantitative evaluations of Tc 99m tilmanocept localization from SPECT/CT within synovial spaces of the bilateral hands and wrists in HCs and RA subjects.
- Normative joint-specific standardized uptake value (SUV).
- Predictive value of planar scans for SPECT/CT scans.

4.2 Analysis of Efficacy Variables

4.2.1 Analysis of Primary Efficacy Variables

Arm 1:

All TUV_{joint} data will be analyzed with summary statistics (mean, standard deviation, n, minimum, median, maximum) by reader, joint and view.

The 5 and 95 percentiles will be estimated with quantile regression fitting an intercept as a fixed term. The lower and upper limits of normal TUV_{joint} will be determined using non-parametric confidence intervals and kernel density-based confidence intervals.

Arm 2:

Localization of tilmanocept in the hands and wrists will be summarized with frequency counts and percentages by reader and joint.

4.2.2 Analysis of Secondary Efficacy Variables

Healthy Controls in Both Arms 1 and 2:

Normal quantile plots will be provided per-joint and reader, along with the p-value for the Shapiro-Wilk test of Normality.

Scatter plots of TUV_{joint} by age per-joint will be provided, along with the correlation coefficients and p-values. The hypotheses for the p-value to test the correlation coefficient are: H_0: $\rho = 0$ vs H_1: $\rho \neq 0$, where ρ is the correlation coefficient. The p-value evaluating age in the regression model will be provided in the figure.

Scatter plots of TUV_{joint} by BMI will be provided, along with the correlation coefficients and p-values. The hypotheses for the p-value to test the correlation coefficient are: H_0: $\rho = 0$ vs H_1: $\rho \neq 0$, where ρ is the correlation coefficient. The p-value evaluating BMI in the regression model will be provided in the figure.

Scatter plots of TUV_{joint} by sex will be provided.

To check the relationship between the variance of TUV_{joint} and age, a quantile regression model will be fitted with an intercept as a fixed term.The plot of the residuals on the y-axis and age on the x-axis will be provided.

Arm 2:

SUV will be calculated and summarized on both a per-joint and a total of all joints with summary statistics: mean, standard deviation, n, minimum, maximum, and median. The formula for SUV is:

$$SUV = \frac{r}{(a'/w)};$$

where:
r: The radioactivity activity concentration [kBq/mL]
a': The decay-corrected amount of injected radiolabeled FDG [kBq]
w: The weight of the patient [g]
The predictive value of planar scans for SPECT/CT qualitative findings will be summarized per joint and reader with a crosstabulation and the uncertainty coefficients for row | column, column | row, and symmetric. The planar result will be deemed "positive" (i.e., inflamed) if TUV_{joint} > 95 percentile of the reader.

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, RA panel)
- Vital Signs

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. Follow up timing will vary by arm as noted above.

Adverse Events
Adverse events will be observed for each subject from signing of informed consent until termination from the study. AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®). A treatment-emergent AE (TEAE) is defined as an AE whose start date is on or after the initial procedure date. Based on the coded terms, frequencies of each TEAE will be summarized by MedDRA® preferred term within system organ class (SOC), by severity grade, and by relationship to Tc 99m Tilmanocept for each arm and overall.

A summary of TEAEs will be constructed showing the following by arm and overall:

- Number of subjects with at least one TEAE
- TEAEs by arm and severity grade
- TEAE by arm and relationship to Tc 99m tilmanocept
- TEAEs by arm and relationship of TEAE to study procedure
- Number of subjects with at least one treatment emergent serious adverse event

Treatment-emergent serious adverse events (TESAEs) will be tabulated by MedDRA® preferred term within SOC by arm and overall.

A by-patient AE data listing of all AEs including verbatim term, coded term, grade, and relation to study drug will be provided.

Clinical Laboratory Tests

Clinical laboratory tests will be performed at screening (baseline) and after the final image acquisition on the imaging day. Only abnormal laboratory values and RA lab values will be assessed for clinical significance as applicable. For each quantitative laboratory test, summary statistics (mean, standard deviation, median, range, n) on the raw as well as their changes from baseline will be presented by timepoint, by arm, and overall. A shift table will also be produced to show the changes in lab values over time relative to the normal ranges.

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.

Vital Signs

Vital signs will be performed at screening, just prior to and just after injection. 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), summary statistics (mean, standard deviation, minimum, maximum, n) on the raw as well as their changes from baseline will be presented by timepoint, by arm, and overall. 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 by study arm and overall. 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, the calculated mass dose, and radioactivity of Tc 99m tilmanocept injected will be summarized by arm and overall. All study drug administration data will be listed.

6.4 RA Evaluation

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

Prior and concomitant medications will be collected for 30 days prior to Day 0, and all RA medications will be collected for 6 months prior to Day 0. 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 by Study Arm	X	X
2	Demographics and Baseline Data Summary Statistics by Arm – Continuous Variables (Safety Population)	X	X
3	Demographics and Baseline Data Summary Statistics by Arm – Categorical Variables (Safety Population)	X	X
4	Summary of Study Drug Administration by Arm (Safety Population)	X	X
5	Summary of TUV_{joint} on both Arms Per Reader, Joint, and View (ITD population)	X	X
6	Summary of TUV_{joint} on both Arms Per Reader, Joint, and View (PP Population)	X	
7	Summary of SUV on Arm 2 per Joint and a Total of All Joints (ITD population)	X	X
8	Summary of SUV on Arm 2 per Joint and a Total of All Joints (PP Population)	X	
9	Normal Range of TUV_{joint} for the Three Blinded Readers in All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
10	Normal Range of TUV_{joint} for the Three Blinded Readers in All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
11	Correlation Between TUV_{joint} and Age and BMI – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
12	Correlation Between TUV_{joint} and Age and BMI – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
13	Frequency Counts and Percentage of Localization in SPECT/ CT Imaging in RA Subjects (ITD Population)	X	X
14	Frequency Counts and Percentage of Localization in SPECT/ CT Imaging in RA Subjects (PP Population)	X	
15	Shapiro-Wilk P-Value for Normality Test for TUV_{joint} Data – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
16	Shapiro-Wilk P-Value for Normality Test for TUV_{joint} Data – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
17	Predictive Value of Planar Scans for SPECT/CT Per Joint and Reader (ITD Population)	X	X
18	Predictive Value of Planar Scans for SPECT/CT Per Joint and Reader (PP Population)	X	
19	Number and Percentage of Subjects with TEAEs (Safety Population)	X	X
20	Summary of TEAEs (Safety Population)	X	X
21	Number and Percentage of Subjects with TESAEs (Safety Population)	X	X
22	Number and Percentage of Subjects With TEAEs by Severity Grade (Safety Population)	X	X
23	Number and Percentage of Subjects With TEAEs by Level of Relationship to Tc 99m Tilmanocept (Safety Population)	X	X
24	Number and Percentage of Subjects With TEAEs by Level of Relationship to Procedure (Safety Population)	X	

Table No.	Table Title	Included in Final Tables	Shown in Appendix B
25	Serum Chemistry Clinical Laboratory Parameters Summary Statistics by Arm (Safety Population)	X	X
26	Hematology Clinical Laboratory Parameters Summary Statistics by Arm (Safety Population)	X	
27	Urinalysis Clinical Laboratory Parameters Summary Statistics by Arm (Safety Population)	X	
28	Serum Chemistry Clinical Laboratory Parameters Shift Table by Arm (Safety Population)	X	X
29	Hematology Clinical Laboratory Parameters Shift Table by Arm (Safety Population)	X	
30	Urinalysis Clinical Laboratory Parameters Shift Table by Arm (Safety Population)	X	
31	Vital Signs Summary Statistics by Arm (Safety Population)	X	X

Figure No.	Figure Title	Included in Final Figures	Shown in Appendix B
Fig1	Normal QQ plot for TUV_{joint} Data – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
Fig2	Normal QQ plot for TUV_{joint} Data – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig3	Scatter Plot of TUV_{joint} Distribution of the Right Hand – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
Fig4	Scatter Plot of TUV_{joint} Distribution of the Right Hand – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig5	Scatter Plot of TUV_{joint} Distribution of the Left Hand – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
Fig6	Scatter Plot of TUV_{joint} Distribution of the Left Hand – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig7	Scatter Plot of TUV_{joint} Distribution for MCP1 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
Fig8	Scatter Plot of TUV_{joint} Distribution for MCP1 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig9	Scatter Plot of TUV_{joint} Distribution for MCP2 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig10	Scatter Plot of TUV_{joint} Distribution for MCP2 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig11	Scatter Plot of TUV_{joint} Distribution for MCP3 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig12	Scatter Plot of TUV_{joint} Distribution for MCP3 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig13	Scatter Plot of TUV_{joint} Distribution for MCP4 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig14	Scatter Plot of TUV_{joint} Distribution for MCP4 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig15	Scatter Plot of TUV_{joint} Distribution for MCP5 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	

Figure No.	Figure Title	Included in Final Figures	Shown in Appendix B
Fig16	Scatter Plot of TUV_{joint} Distribution for MCP5 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig17	Scatter Plot of TUV_{joint} Distribution for PIP1 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig18	Scatter Plot of TUV_{joint} Distribution for PIP1 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig19	Scatter Plot of TUV_{joint} Distribution for PIP2 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig20	Scatter Plot of TUV_{joint} Distribution for PIP2 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig21	Scatter Plot of TUV_{joint} Distribution for PIP3 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig22	Scatter Plot of TUV_{joint} Distribution for PIP3 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig23	Scatter Plot of TUV_{joint} Distribution for PIP4 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig24	Scatter Plot of TUV_{joint} Distribution for PIP4 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig25	Scatter Plot of TUV_{joint} Distribution for PIP5 by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig26	Scatter Plot of TUV_{joint} Distribution for PIP5 by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig27	Scatter Plot of TUV_{joint} Distribution for Wrist by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig28	Scatter Plot of TUV_{joint} Distribution for Wrist by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig29	Scatter Plot of TUV_{joint} Distribution by Sex – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig30	Scatter Plot of TUV_{joint} Distribution by Sex – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig31	Scatter Plot of TUV_{joint} Distribution by BMI – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	
Fig32	Scatter Plot of TUV_{joint} Distribution by BMI – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	
Fig33	Scatter Plot of Residuals by Age – All Arm 1 and 2 Healthy Control Subjects (ITD Population)	X	X
Fig34	Scatter Plot of Residuals by Age – All Arm 1 and 2 Healthy Control Subjects (PP Population)	X	

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

Listing No.	Data Listing Title	Included in Final Listings	Shown in Appendix B
DL5	Subjects Excluded from ITD 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	Subject Laboratory Profiles – Hematology Data Listing	X	X
DL13	Subject Laboratory Profiles – Serum Chemistry Data Listing	X	
DL14	Subject Laboratory Profiles – Urinalysis Data Listing	X	
DL15	Subject Laboratory Profiles – Rheumatology Panel Data Listing	X	
DL16	Physical Exam Data Listing	X	X
DL17	ACR/EULAR 2010 Classification Data Listing	X	X
DL18	DAS-28 by Joint Data Listing – Arm 2 RA Subjects	X	X
DL19	DAS-28 by Subject Data Listing – Arm 2 RA Subjects	X	X
DL20	Vital Signs Data Listing	X	X
DL21	Study Drug Administration Data Listing	X	X
DL22	Post-Injection Imaging Data Listing	X	X
DL23	SPECT/CT Reader Results Data Listing – Hands and Wrists	X	X
DL24	TUV Data Listing	X	X

8.0 References

Food & Drug Administration Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research (September 1998). Guidance for Industry: ICH E9 Statistical Principles for Clinical Trials.

Forkman, J. (2009) Estimator and Tests for Common Coefficients of Variation in Normal Distributions. *Communications in Statistics: Theory and Methods*. 38:2, pp233- 251.

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.

Missing Values

All missing values will be displayed on the output tables/listings as blanks.

Display of Study Dates

The date format to be used is dd-mmm-yyyy. Missing parts of dates are not shown (i.e., for a missing day value, the value displayed is in yyyy-mm format).

Appendix B – Table Shells

Table 1. Subject Disposition by Study Arm
Navidea Biopharmaceuticals - Study No. NAV3-35

		Arm[a]			
		HC-1 (N = xxx)	HC-2 (N = xxx)	RA (N = xxx)	Overall (N = xxx)
Screen Failures					xx
Enrolled		xxx	xxx	xxx	xxx
Completed		xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
Withdrawn		xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
Withdrawal Reason	Adverse Event	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
	Protocol Violation	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
	Lost to Follow Up	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
	Withdrawal of Consent	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
	Sponsor Discretion	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
	Investigator Discretion	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
	Death	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)
	Other	xx (xxx%)	xx (xxx%)	xx (xxx%)	xx (xxx%)

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
The denominator for all percentages in the table is the number of enrolled subjects in the respective arm and overall.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 2. Demographics and Baseline Data Summary Statistics by Arm – Continuous Variables
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Variable	Arm[a]	Mean	Std Dev	n	Min	Max	Median
Age (years)	HC-1	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	xxx	xxx	xxx	xxx	xxx	xxx
	RA	xxx	xxx	xxx	xxx	xxx	xxx
Height (inches)	HC-1	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	xxx	xxx	xxx	xxx	xxx	xxx
	RA	xxx	xxx	xxx	xxx	xxx	xxx
Weight (pounds)	HC-1	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	xxx	xxx	xxx	xxx	xxx	xxx
	RA	xxx	xxx	xxx	xxx	xxx	xxx
BMI (kg/m^2)	HC-1	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	xxx	xxx	xxx	xxx	xxx	xxx
	RA	xxx	xxx	xxx	xxx	xxx	xxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 3. Demographics and Baseline Data Summary Statistics by Arm – Categorical Variables
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N= xxx)

		Arm[a]		
		HC-1	HC -2	RA
Variable	Category	(N= xxx)	(N= xxx)	(N= xxx)
Gender	Male	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Female With Childbearing Potential	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Female With No Childbearing Potential	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Race	American Indian or Alaska Native	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Asian	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Black or African American	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Native Hawaiian or Other Pacific Islander	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	White	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Other			
Ethnicity	Hispanic or Latino	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Not Hispanic or Latino	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Handedness	Right Handed	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Left Handed	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
	Ambidextrous	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 4. Summary of Study Drug Administration by Arm
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N= xxx)

	Arm[a]	Mean	Std Dev	n	Min	Max	Median
Tc 99m Dose (mCi)	HC-1	xxxx	xxxx	xx	xxxx	xxxx	xxxx
	HC-2	xxxx	xxxx	xx	xxxx	xxxx	xxxx
	RA	xxxx	xxxx	xx	xxxx	xxxx	xxxx
Mass Dose (µg)	HC-1	xxxx	xxxx	xx	xxxx	xxxx	xxxx
	HC-2	xxxx	xxxx	xx	xxxx	xxxx	xxxx
	RA	xxxx	xxxx	xx	xxxx	xxxx	xxxx
Total Volume of Tc 99m Tilmanocept Injected (mL)	HC-1	xxxx	xxxx	xx	xxxx	xxxx	xxxx
	HC-2	xxxx	xxxx	xx	xxxx	xxxx	xxxx
	RA	xxxx	xxxx	xx	xxxx	xxxx	xxxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 5. Summary of TUV_{joint} on both Arms Per Reader, Joint, and View
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

Arm[a]	Reader	View	Joint	Mean	Std Dev	n	Min	Max	Median
xxxx	xxxxxxxxxxxxxxx	xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xxxxxxxxxxxxxxx	xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
xxxx	xxxxxxxxxxxxxxx	xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xxxxxxxxxxxxxxx	xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
		xxxxxxxxx	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format is repeated for the PP population.

Page x of y

Table 7. Summary of SUV on Arm 2 per Joint and Total of All Joints
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

Arm 2[a]	Joint	Mean	Std Dev	n	Min	Max	Median
HC-2	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	Total of All Joints	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
RA	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	xx	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x
	Total of All Joints	xxxx.x	xxxx.x	xxx	xxxx.x	xxxx.x	xxxx.x

[a] HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format is repeated for the PP population.

Table 9. Normal Range of TUV_{joint} for the Three Blinded Readers in All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

Joint	View	Reader	Number of Joints	Mean	Standard Deviation	Estimated 5 %tile	Estimated 95 %tile
xxxxxxxxxxxx	xx	xx	xxx	xxx.xx	xx.xxx	xx.xxx	xx.xxx
		xx	xxx	xxx.xx	xx.xxx	xx.xxx	xx.xxx
		xx	xxx	xxx.xx	xx.xxx	xx.xxx	xx.xxx
	xx	xx	xxx	xxx.xx	xx.xxx	xx.xxx	xx.xxx
		xx	xxx	xxx.xx	xx.xxx	xx.xxx	xx.xxx
		xx	xxx	xxx.xx	xx.xxx	xx.xxx	xx.xxx

If there are no major protocol deviations, then analysis tables for the ITD and PP populations will contain identical results.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format is repeated for the PP population

Table 11. Correlation Between TUV_{joint} and Age and BMI – All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

Variable	TUV	P-value[a]
AGE	xx.xxx	x.xxxx
BMI	xx.xxx	x.xxxx

[a] P-value testing H0: Correlation Coefficient = 0 vs H1: Correlation Coefficient ≠ 0.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format is repeated for the PP population

Table 13. Frequency Counts and Percentage of Localization in SPECT/CT Imaging in RA Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

		Localized on SPECT/CT		
Joint	Reader	No	Yes	Total
xxxxxxxxxxxx	xx	xxx xx.x%	xxx xx.x%	xxx
	xx	xxx xx.x%	xxx xx.x%	xxx
	xx	xxx xx.x%	xxx xx.x%	xxx

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

Table format is repeated for the PP population.

Table 15. Shapiro-Wilk P-Value for Normality Test for TUV_{joint} Data - All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

Test for Normality		
Test	Statistic	P-Value
Shapiro-Wilk	xxx	xxx

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

All Table format is repeated for the PP population

Page x of y

Table 17. Predictive Value of Planar Scans for SPECT/CT Per Joint and Reader
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

			SPECT/CT (Standard of Truth)				
Reader	Joint	Planar Scans	Positive	Negative	Total	Uncertainty Coefficients	Estimated 95 %tile
xx	xxx	TUVjoint > 95 (Positive)	xxx	xxx	xxx	xxx	xxx
		Negative	xxx	xxx	xxx		
		Total	xxx	xxx	xxx		
	xxx	TUVjoint > 95 (Positive)	xxx	xxx	xxx	xxx	xxx
		Negative	xxx	xxx	xxx		
		Total	xxx	xxx	xxx		
xx	xxx	TUVjoint > 95 (Positive)	xxx	xxx	xxx	xxx	xxx
		Negative	xxx	xxx	xxx		
		Total	xxx	xxx	xxx		
	xxx	TUVjoint > 95 (Positive)	xxx	xxx	xxx	xxx	xxx
		Negative	xxx	xxx	xxx		
		Total	xxx	xxx	xxx		
xx	xxx	TUVjoint > 95 (Positive)	xxx	xxx	xxx	xxx	xxx
		Negative	xxx	xxx	xxx		
		Total	xxx	xxx	xxx		
	xxx	TUVjoint > 95 (Positive)	xxx	xxx	xxx	xxx	xxx
		Negative	xxx	xxx	xxx		
		Total	xxx	xxx	xxx		

If there are no major protocol deviations, then analysis tables for the ITD and PP populations will contain identical results.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

All Table format is repeated for the PP population

Table 19. Number and Percentage of Subjects with TEAEs
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N= xxx)

	Arm[a]			
Adverse Event Category[b]:	HC-1	HC-2	RA	Overall
Total Number of TEAEs	xxx	xxx	xxx	xxx
Subjects with at Least One TEAE	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Adverse events coded with MedDRA Coding Dictionary Version XXX
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 20. Summary of TEAEs
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

	Arm[a]			
	HC-1	HC-2	RA	Overall
Subjects With at Least One TEAE	xxx	xxx	xxx	xxx
Maximum TEAE Severity Grade				
Mild	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Moderate	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Severe	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Highest Relationship of TEAE to Tc 99m tilmanocept				
Definitely Not [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Probably Not [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Possibly [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Probably [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Definitely [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Highest Relationship of TEAE to Study Procedure				
Definitely Not [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Probably Not [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Possibly [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Probably [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Definitely [n(%)]	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Subjects with at Least One TESAE	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 21. Number and Percentage of Subjects with TESAEs
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

	Arm[a]			
Adverse Event Category[b]:	HC-1	HC-2	RA	Overall
Total Number of TESAEs	xxx	xxx	xxx	xxx
Subjects with at Least One TESAE	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Adverse events coded with MedDRA Coding Dictionary Version XXX
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table 22. Number and Percentage of Subjects With TEAEs by Severity Grade
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Part 1 of 4 – HC-1[a]

Adverse Event Category[b]:	Severity Grade		
	Mild	Moderate	Severe
Total Number of TEAEs	xxx	xxx	xxx
Subjects with at Least One TEAE	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Adverse events coded with MedDRA Coding Dictionary Version XXX
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format repeats for HA-2, RA (Parts 2 and 3) and overall (Part 4).

Table 23. Number and Percentage of Subjects With TEAEs by Level of Relationship
to Tc 99m Tilmanocept
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Part 1 of 4 : HC-1[a]

	Level of Relationship				
Adverse Event Category[b]:	Definitely Not	Probably Not	Possibly Related	Probably Related	Definitely Related
Total Number of TEAEs	xxx	xxx	xxx	xxx	xxx
Subjects with at Least One TEAE	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
System Organ Class 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 1	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
Preferred Term 2	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Adverse events coded with MedDRA Coding Dictionary Version XXX
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format repeats for HC-2, RA (Parts 2 and 3) and overall (Part 4). Full Table (all parts) repeats for Table 24.

Page x of y

Table 25. Serum Chemistry Clinical Laboratory Parameters Summary Statistics by Arm
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Parameter(units)	Arm[a]	Visit	Data Type[b]	Mean	Std Dev	n	Min	Max	Median
xxxxxxxx(xxx)	HC-1	Screening (Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 (Visit 2)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	Screening (Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 (Visit 2)	RAW						
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	RA	Screening (Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 (Visit 2)	RAW						
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
xxxxxxxx(xxx)	HC-1	Screening (Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 (Visit 2)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	Screening (Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 (Visit 2)	RAW						
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	RA	Screening (Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 (Visit 2)	RAW						
			CFB	xxx	xxx	xxx	xxx	xxx	xxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] 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 format repeats for Tables 26 and 27.

Page x of y

Table 28. Serum Chemistry Clinical Laboratory Parameters Shift Table by Arm
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Part 1 of 3: HC-1[a]

	Baseline Result/ Post-Injection Result								
Panel/Parameter (units)	Low/ Low	Low/ Normal	Low/ High	Normal/ Low	Normal/ Normal	Normal/ High	High/ Low	High/ Normal	High/ High
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format is repeated for Tables 29 (Hematology) and 30 (Urinalysis)

Page x of y

Table 28. Serum Chemistry Clinical Laboratory Parameters Shift Table by Arm
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Part 2 of 3: HC-2[a]

	Baseline Result/ Post-Injection Result								
Panel/Parameter (units)	Low/ Low	Low/ Normal	Low/ High	Normal/ Low	Normal/ Normal	Normal/ High	High/ Low	High/ Normal	High/ High
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format is repeated for Tables 29 (Hematology) and 30 (Urinalysis)

Page x of y

Table 28. Serum Chemistry Clinical Laboratory Parameters Shift Table by Arm
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Part 3 of 3: RA[a]

	Baseline Result/ Post-Injection Result								
Panel/Parameter (Units)	Low/ Low	Low/ Normal	Low/ High	Normal/ Low	Normal/ Normal	Normal/ High	High/ Low	High/ Normal	High/ High
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)
xxxxxxx/ xxxxxxxx(xxx)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)	xxx (xxx%)

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

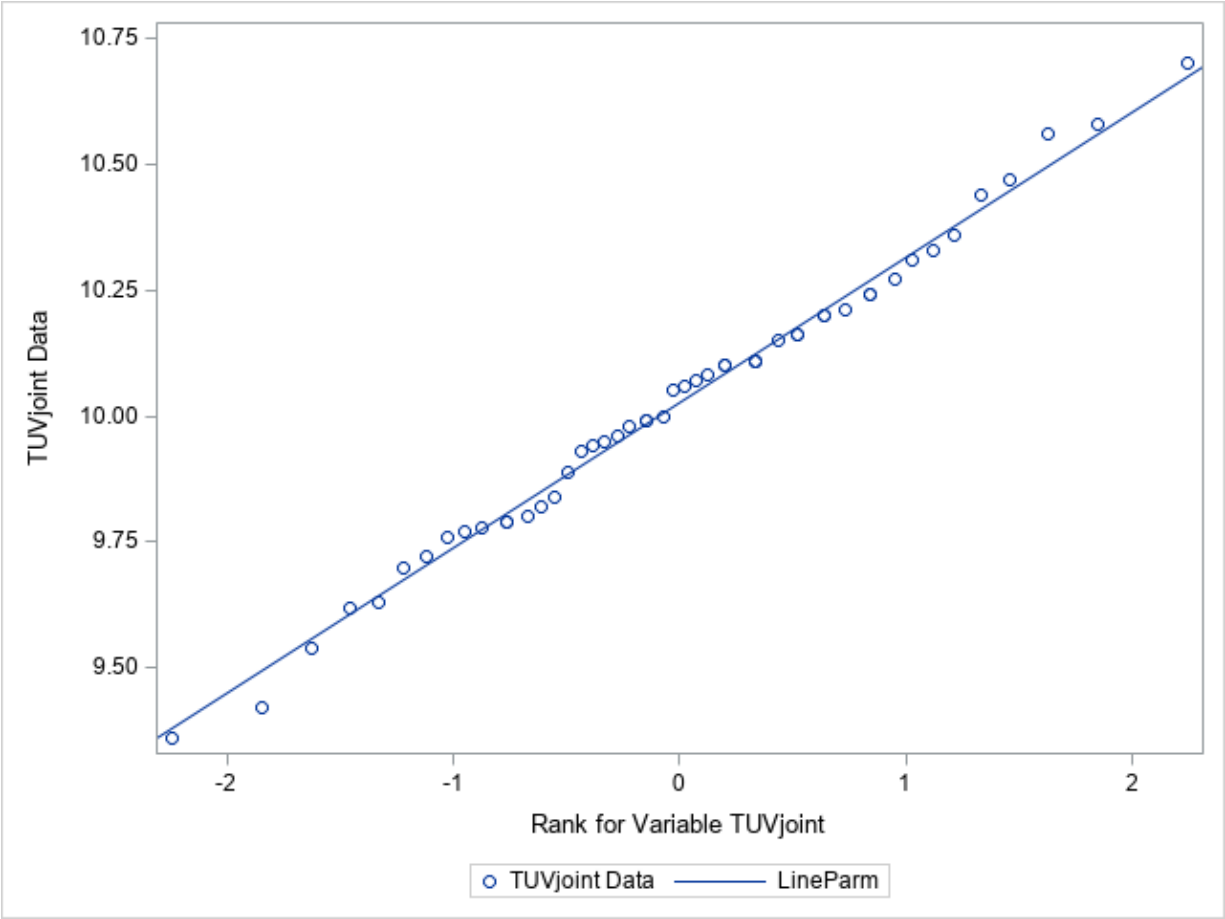
Table format is repeated for Tables 29 (Hematology) and 30 (Urinalysis)

Table 31. Vital Signs Summary Statistics by Arm
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Vital Sign Parameter (units)	Arm[a]	Visit	Data Type[b]	Mean	Std Dev	n	Min	Max	Median
xxxxxxxxx (xxx)	HC-1	Screening	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	Day 0 Pre-Injection(Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 Post-Injection	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	Screening	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	HC-2	Day 0 Pre-Injection(Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 Post-Injection	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	RA	Screening	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx
	RA	Day 0 Pre-Injection(Baseline)	RAW	xxx	xxx	xxx	xxx	xxx	xxx
		Day 0 Post-Injection	RAW	xxx	xxx	xxx	xxx	xxx	xxx
			CFB	xxx	xxx	xxx	xxx	xxx	xxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] 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

Figure 1. Normal QQ plot for TUV_{joint} Data - All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

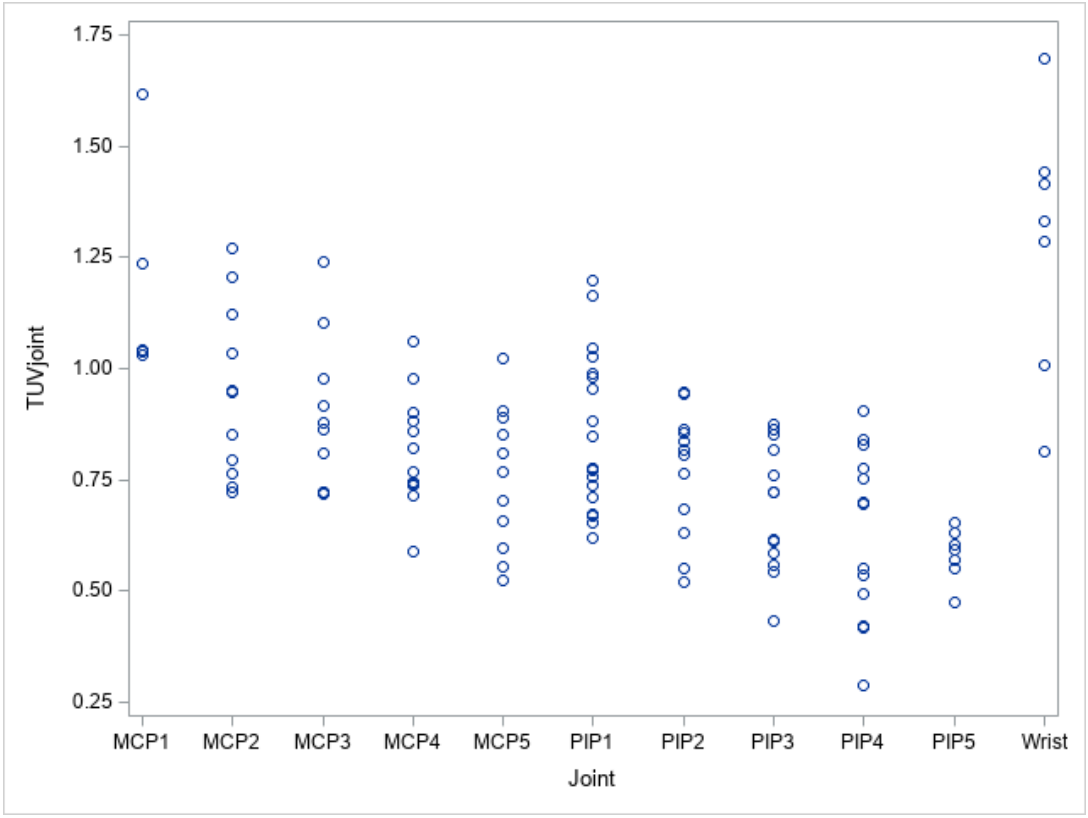


STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Figure format is repeated for the PP population.

Page x of y

Figure 3. Scatter Plot of TUV_{joint} Distribution of the Right Hand - All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

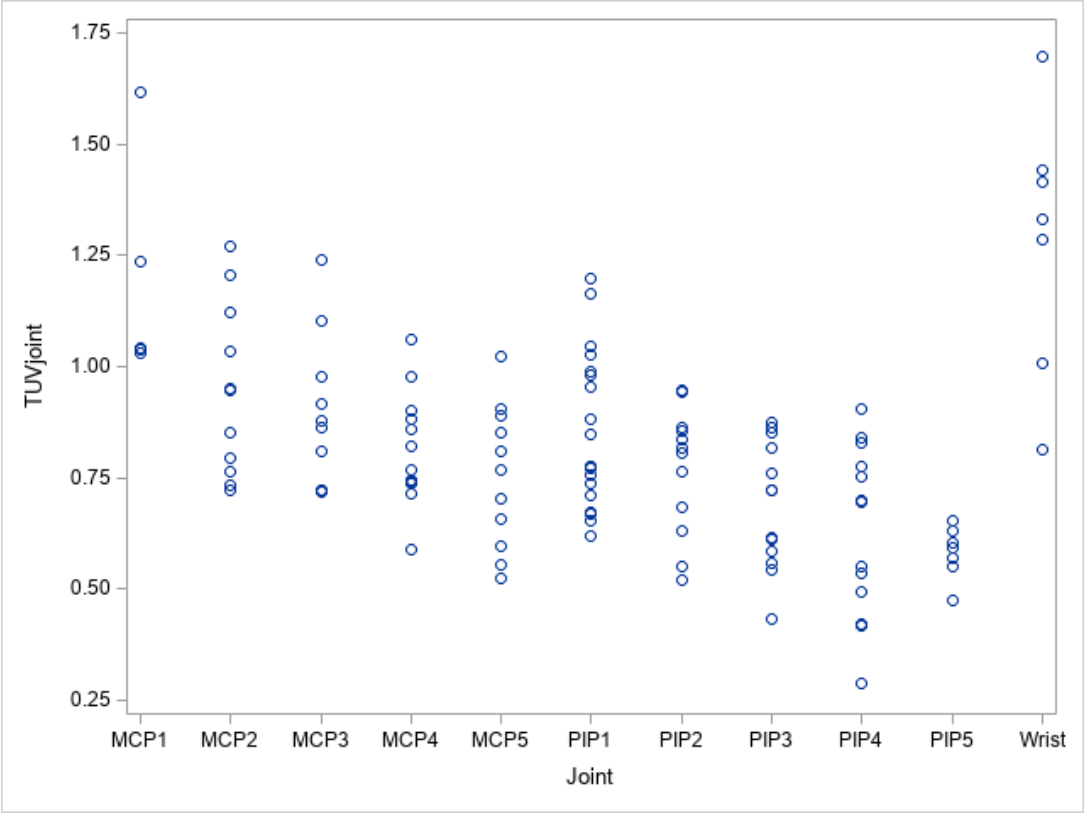


STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Figure format is repeated for the PP population.

Page x of y

Figure 5. Scatter Plot of TUVjoint Distribution of the Left Hand - All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)

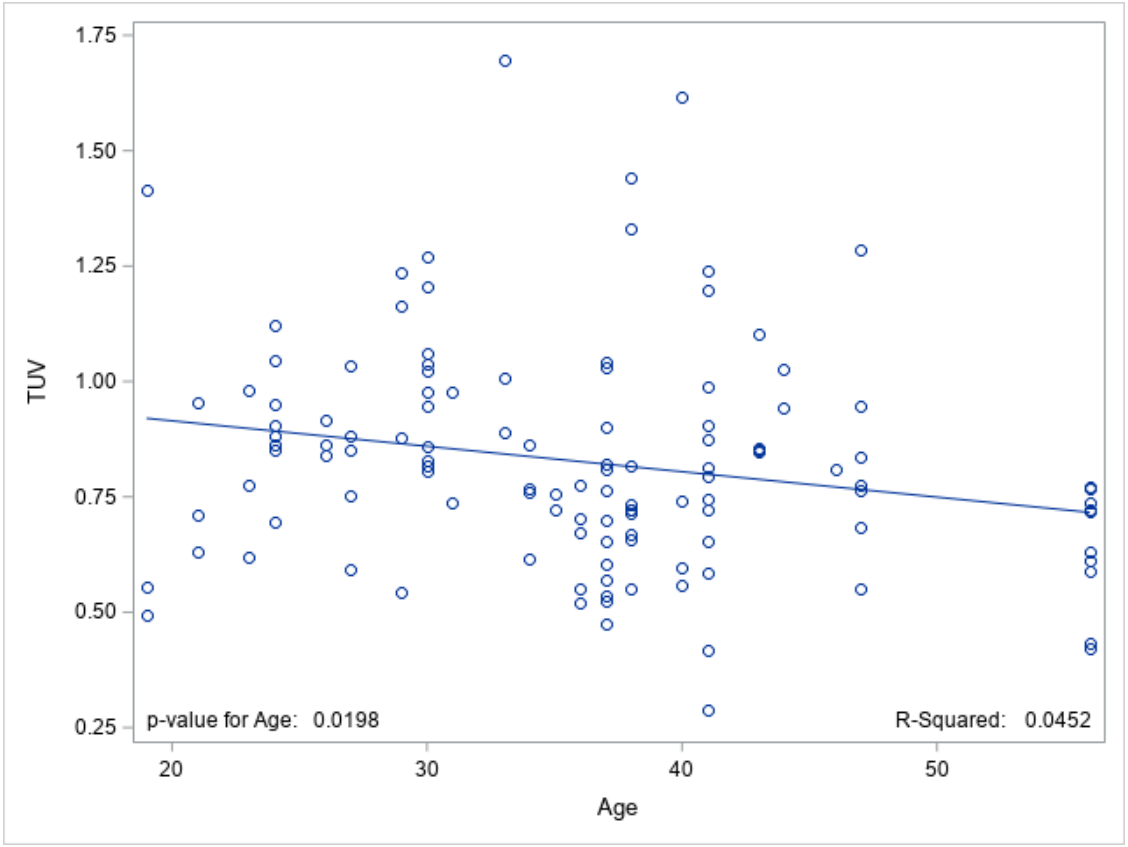


STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Figure format is repeated for the PP population.

Page x of y

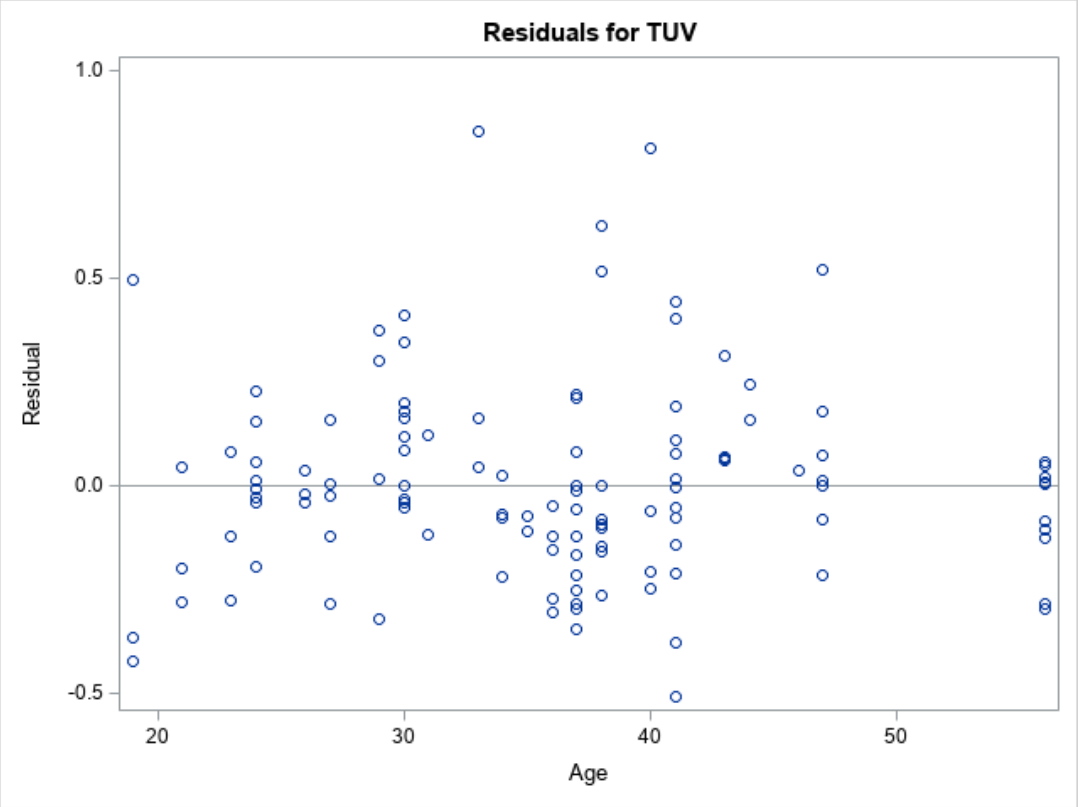
Figure 7. Scatter Plot of TUV_{joint} Distribution for MCP1 by Age – All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)



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

Figure format is repeated per joint and again for the PP population per joint. Repeat for Sex and BMI.

Figure 33. Scatter Plot of Residuals by Age – All Arm 1 and 2 Healthy Control Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
ITD Population (N=xxx)



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

Figure format is repeated the PP Population.

Data Listing 1. Subject Disposition Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35

Arm[a]	Subject No.	Disposition Status	Date of Completion or Withdrawal	Withdrawal Reason
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 2. Inclusion/Exclusion Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35

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

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 3. Protocol Deviations Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35

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

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Data Listing 4. Demographics Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=135)

Arm[a]	Subject No.	Informed Consent Date/Time	Date of Birth	Height (inches)	Weight (pounds)	Age (yrs)	Gender	Race	Ethnicity	Handedness	WOCBP?
xxxxxx	xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
xxxxxx	xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
xxxxxx	xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx
xxxxxx	xxxx	xxxxxx	xxxxxx	xxx	xxx	xxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 5. Subjects Excluded from ITD Population Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
All Enrolled Subjects (N=xxx)

Arm[a]	Subject No.	Reason for Exclusion
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 6. Subjects Excluded from PP Population Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
All Enrolled Subjects (N=xxx)

Arm[a]	Subject No.	Reason for Exclusion
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 7. Subjects Excluded from Safety Population Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
All Enrolled Subjects (N=xxx)

Arm[a]	Subject No.	Reason for Exclusion
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	xxxx	xxxxxxxxxxxxxxxxxxxxxxxx

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 8. Medical History Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

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

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] 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. NAV3-35
Safety Population (N=xxx)

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

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Medications coded with WHO Coding Dictionary xxxxxxxxx
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 10. Prior and Concomitant RA Medications Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

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

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Medications coded with WHO Coding Dictionary xxxxxxxxx
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Data Listing 11. Adverse Events Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

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

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Adverse events coded with MedDRA Coding Dictionary Version xxx
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Data Listing 12. Subject Laboratory Profiles - Hematology Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Arm[a]	Subject No.	Visit	Sample Date and Time	Lab Parameter (Units)	Result	Normal Range		Clin. Sig?
						Lab Low	Lab High	
xxxxxx	xxxx	xxxxxxxx	xxxxxxxx / xx:xx	xxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
				xxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
				xxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
				xxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
				xxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx
				xxxxxxxxxxxx (xxx)	xxx	xxx	xxx	xxx

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Table format is repeated for Serum Chemistry, Urinalysis, and Rheumatology Panel Listings (Listings 13, 14, 15).

Data Listing 16. Physical Exam Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

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

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 17. ACR/EULAR 2010 Classification Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

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

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 18. DAS-28 by Joint Data Listing – Arm 2 RA[a] Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
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

[a] RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 19. DAS-28 by Subject Data Listing – Arm 2 RA[a] Subjects
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

			DAS28				
Subject No.	Visit	Date	Tender Joint Count	Swollen Joint Count	Patient VAS Global (mm)	Erythrocyte Sedimentation Rate (ESR; mm/hr)	DAS28 Score
xxxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx	xxx	xxx
xxxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx	xxx	xxx

[a] RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Page x of y

Data Listing 20. Vital Signs Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

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

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 21. Study Drug Administration Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Arm[a]	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)	Source Recorded Administered Radioactivity (mCi)	Calculated Mass Dose (µg)	Volume Injected (mL)	Lot Number
xxxxxx	xxxx	xxxxxxxx/ xxxx	xxxxxxxx	xxx/ xxxx	xxx/ xxxx	xxx	xxx	xxx	xxx	xxx
xxxxxx	xxxx	xxxxxxxx/ xxxx	xxxxxxxx	xxx/ xxxx	xxx/ xxxx	xxx	xxx	xxx	xxx	xxx
		xxxxxxxx/ xxxx	xxxxxxxx	xxx/ xxxx	xxx/ xxxx	xxx	xxx	xxx	xxx	xxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 22. Post-Injection Imaging Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Arm[a,b]	Subject No.	Visit	Date of Imaging	Start Time of Planar Imaging	End Time of Planar Imaging	Start Time of SPECT/CT Imaging	End Time of SPECT/CT Imaging
xxxxxx	xxxx	xxxxxxxx	xxxxxx	xx:xx	xx:xx	xx:xx	xx:xx
xxxxxx	xxxx	xxxxxxxx	xxxxxx	xx:xx	xx:xx	xx:xx	xx:xx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] SPECT/CT imaging performed only in study Arm 2 - RA
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 23. SPECT/CT Reader Results Data Listing – Hands and Wrists
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Arm[a]	Subject No.	Post-Injection Imaging Time Point	Joint	SPECT/CT Localization?
xxxxxx	xxxx	xxxxxxx	xxxxxxxxxxx xxxxxxxxxxx	xxxx
xxxxxx	xxxx	xxxxxxx	xxxxxxxxxxx xxxxxxxxxxx	xxxx

[a] HC-1 = healthy control–Arm 1, HC-2 = healthy control–Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas

Data Listing 24. TUV Data Listing
Navidea Biopharmaceuticals - Study No. NAV3-35
Safety Population (N=xxx)

Arm[a]	Subject No.	Visit	Date/Time	Region of Interest[b]	TUV
xxxxxx	xxxx	xxxxxxx	xxxxxxxxxxxxx	xxxxxx	xxxxx
xxxxxx	xxxx	xxxxxxx	xxxxxxxxxxxxx	xxxxxx	xxxxx

[a] HC-1 = healthy control-Arm 1, HC-2 = healthy control-Arm 2, RA = rheumatoid arthritis (stable treatment regimen; Arm 2)
[b] Region of Interest is joint for all arms, and joint or Global for the Arm 2 - RA.
STATKING Clinical Services (DD-MMM-YYYY)
Source Program: xxxxxxx.sas