Statistical Analysis Plan

A Phase 1, Single Ascending Dose, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Xisomab 3G3 in Healthy Adult Subjects

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Compound Name: xisomab 3G3

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from this study. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within protocol, after the unblinding, or locking of the database will be documented in the clinical study report (CSR). The section referred to as Table Shells within this SAP describes the traceability of the tables, figures, and listings (TFLs) back to the data. Note that the header for this page will be the one used for the main body of the CSR.

Any additional exploratory analyses not addressed within this statistical analysis plan (SAP) and/or driven by the data, or requested by the Aronora Inc., will be considered out of scope and must be described in the CSR.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

The primary objective of the study is to assess the safety and tolerability of single intravenous (IV) doses of xisomab 3G3 when administered to healthy adult subjects.

The secondary objectives of the study are as follows:

- To assess the pharmacokinetics (PK) of single IV doses of xisomab 3G3 when administered to healthy adult subjects.

- To assess the pharmacodynamics (PD) of single IV doses of xisomab 3G3 when administered to healthy adult subjects. The activated partial thromboplastin time (aPTT) will be used as a surrogate PD marker.

2.2 Endpoints

The primary endpoints of the study will be the number and severity of treatment-emergent adverse events (TEAEs) following single doses of xisomab 3G3 and placebo. Other safety endpoints include clinical laboratories, vital signs, electrocardiograms, physical examinations, and immunogenicity.

- The following PK parameters of free xisomab 3G3 in plasma following single IV dose, will be calculated, as appropriate: AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, T½, MRT, CL, and Vss.

- aPTT values will be listed with descriptive statistics and presented graphically.

3. STUDY DESIGN

This is a randomized, double-blind, placebo-controlled, SAD study conducted at one study center in the US.

Four (4) cohorts of either 6 subjects (Cohort 1 [4 active and 2 placebo]) or 5 subjects (Cohorts 2, 3, and 4 [4 active and 1 placebo]) are planned for evaluation. In each cohort, subjects will be randomized to receive a single IV infusion of xisomab 3G3 or placebo. In each cohort, at least 30% of the subjects were to be of a race/ethnicity minority group. An attempt will be made to include at least 2 females per cohort. Subjects will participate in only one cohort.

Two (2) sentinel subjects will be dosed (one placebo, one active) in Cohort 1 and data will be collected through Day 8. The next subject in the cohort will be dosed after evaluation of the sentinel subjects' Day 8 safety data. Each subject following these sentinel subjects will be dosed with an interval of 24-hours between subjects. Subjects in Cohorts 2, 3, and 4 will be dosed at an interval of 24 hours between subjects.

Screening of subjects will occur within 28 days prior to dosing.

Subjects will receive a single IV infusion dose of the assigned formulation (xisomab 3G3 or placebo) on the morning of Day 1.

Subjects will be housed on Day -1, at the time indicated by the Clinical Research Unit (CRU), until after the 24-hour blood draw and/or study procedures. Subjects will only be discharged if the prothrombin time (PT)/international normalized ratio (INR) values are ≤ 3.5 and judged not clinically significant by the PI or designee. Subjects will need to return to the CRU at least 2 days after discharge to confirm the PT/INR values.

Blood samples will also be collected for the PK (free xisomab 3G3) and PD (aPTT) assessments of xisomab 3G3 at scheduled time points for at least 672 hours postdose. The planned time points are at predose, and at 0.083, 0.25, 0.5, 1, 3, 8, 24, 72, 120, 168, 216, 336, 504, and 672 hours after xisomab 3G3 start of infusion. Following the 672-hour time point, sample collection for PK and PD assessments will continue every 7 days (±2 days) until aPTT values return within ±10% of the baseline value or the normal range.

Safety and tolerability will be monitored throughout the study by repeated clinical and laboratory evaluations.

Subjects for whom aPTT value reaches ± 10% of the baseline value or within the normal range by Day 29 will return to the CRU for the follow-up visit on Day 36 to perform scheduled follow-up procedures and to determine if any adverse event has occurred since the last study visit.

Subjects for whom aPTT did not reach ±10% of the baseline value or within the normal range on Day 29, will return every 7 days (±2 days) until aPTT reaches ±10% of the baseline value or within the normal range and for the follow-up visit.

Subjects who terminate the study early will be asked to continue aPTT monitoring until it reaches ±10% of the baseline value or within the normal range. They will return to the CRU approximately 7 days (±2 days) after aPTT reaches ± 10% of the baseline value or within normal range for the follow up (FU) visit to perform scheduled follow-up procedures and to determine if any AE has occurred since the last study visit. They will also be asked to return on Days 15 and 29 to collect the anti-drug antibody (ADA) samples.

ADA sample collection will be performed on Days 15 and 29 for all subjects. If aPTT values remain elevated past Day 29, an additional ADA sample collection will occur at the follow-up visit.

Dose escalation to the next dose level (i.e., next cohort) will not take place until the safety review committee (SRC) has determined that adequate safety and tolerability of xisomab 3G3 from the current and previous cohorts has been demonstrated to permit proceeding to the next cohort.

The total planned duration of subject participation is up to 63 days from screening to follow-up, if aPTT value returns within ± 10% of the baseline value or the normal range by Day 29. This participation could be prolonged if aPTT values did not reach ± 10% of the baseline value or within the normal range by Day 29.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety Population

The safety population will include all subjects who received at least one dose of study drug (active or placebo).

Pharmacokinetic Population

The PK population will include data from all subjects who received at least one dose of active study drug and completed at least one PK blood draw resulting in at least one quantifiable plasma concentration. Samples from all subjects will be assayed even if the subjects do not complete the study. All subjects who comply sufficiently with the protocol and display an evaluable PK profile (e.g., exposure to treatment, availability of measurements and absence of major protocol violations) will be included in the PK parameter summary and statistical analyses.

Pharmacodynamic Population

The PD population will include all subjects who received the study drug (active or placebo) and have at least one predose and one postdose quantifiable PD biomarker value. All subjects who comply sufficiently with the protocol and display an evaluable PD profile will be used for summary statistics.

4.2 Preliminary Data and Interim Analysis

Please note that Celerion Data Management and Biometrics has not participated in providing any of these following outputs. At this point Celerion has not been contracted to complete any interim safety, PK, and PD analyses, if required to do so an additional interim analysis plan would be required.

Safety:

All available blinded safety data will be reviewed by the SRC prior to dose escalation.

The protocol states that at the Sponsor's request unblinded safety tables, figures, and data listings may be presented to the sponsor's medical expert and head of regulatory for the purposes of planning the next initial Phase 2 studies prior to database lock.

PK:

The protocol states that preliminary PK analysis may be performed to evaluate the sampling time points as the study progresses and to guide the dose escalation decision.

PD:

The protocol states that preliminary PD analysis may be performed to evaluate the sampling time points as the study progresses and to guide the dose escalation decision.

5. TREATMENT DESCRIPTIONS

Planned doses for each cohort of the study are as follows:

Cohort 1: 4 subjects, 0.1 mg/kg xisomab 3G3, and 2 subjects, matching placebo

Cohort 2 4 subjects, 0.5 mg/kg xisomab 3G3, and 1 subject, matching placebo

Cohort 3: 4 subjects, 2 mg/kg xisomab 3G3, and 1 subject, matching placebo

Cohort 4: 4 subjects, 5 mg/kg xisomab 3G3, and 1 subject, matching placebo

The subject weight recorded at check-in will be used to calculate the study drug dose.

Treatments will be described as follows:

Cohort	Treatment	Short Description (used in text)	Long Description (used in Tables Figures and Listings)
Cohorts 1-4	Treatment P	Pooled Placebo	Single IV Infusion of Placebo (Pooled)
Cohort 1	Treatment A	0.1 mg/kg xisomab 3G3	Single IV Infusion of 0.1 mg/kg xisomab 3G3
Cohort 2	Treatment B	0.5 mg/kg xisomab 3G3	Single IV Infusion of 0.5 mg/kg xisomab 3G3
Cohort 3	Treatment C	2 mg/kg xisomab 3G3	Single IV Infusion of 2 mg/kg xisomab 3G3
Cohort 4	Treatment D	5 mg/kg xisomab 3G3	Single IV Infusion of 5 mg/kg xisomab 3G3

Additional subjects (N = 5 subjects per cohort; 4 active and 1 placebo) may be enrolled if it is deemed appropriate by the SRC to repeat a dose level or to study an interim dose level (lower than those planned) in a new cohort of subjects. If cohorts are reassigned to different dose levels, treatment descriptions will be updated in the TFLs and CSR accordingly.

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

For all subjects, blood samples for the determination of xisomab 3G3 will be collected at predose, and at 0.083, 0.25, 0.5, 1, 3, 8, 24, 72, 120, 168, 216, 336, 504, and 672 hours after xisomab 3G3 start of infusion. Following the 672-hour time point, sample collection for PK assessment will continue every 7 days (± 2 days) until aPTT values return within ± 10% of the baseline value or the normal range.

All concentration data will be included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). However, if there are any significant deviations from nominal sample times, some concentration data may be excluded from mean concentration-time plots and/or additional concentration-time plots of the mean data may be provided. All deviations and excluded data will be provided and discussed in the CSR.

6.2 Bioanalytical Method

Plasma concentrations of xisomab 3G3 will be determined using enzyme-linked immunosorbent assay (ELISA) validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Celerion, Lincoln, Nebraska. The analytical range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for xisomab 3G3 is expected to be 50 – 5000 ng/mL.

6.3 Investigational Product and PK Analyte Information

6.3.1 Xisomab 3G3

Xisomab 3G3 is a novel, injectable, therapeutic monoclonal antibody (IgG4, S241P hinge-modified) that prevents activation of the contact (intrinsic) pathway of coagulation and is intended to address the problem of dose limiting bleeding side effects of current antithrombotic agents. Xisomab 3G3 was developed by Aronora, Inc. and is intended for IV administration. The proposed indication for xisomab 3G3 is as a therapeutic treatment of venous thromboembolism. The goal of xisomab 3G3 treatment is to achieve safe anticoagulation for several days with a single dose.

Xisomab 3G3 is provided as sterile powder for injection via the IV route, upon reconstitution.

6.4 Pharmacokinetic Concentrations

Plasma concentrations of xisomab 3G3 as determined at the collection times and per the bioanalytical method described in Section 6.1 and Section 6.2, respectively, will be used for the calculation of the plasma xisomab 3G3 PK parameters.

6.5 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation

6.5.1 Plasma Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated from the plasma xisomab 3G3 concentration-time data using Phoenix® WinNonlin® Version 6.3 or higher. Actual sample times will be used in the calculations of the PK parameters. The calculation of the actual time for xisomab 3G3 will be in respect to the start of infusion time of xisomab 3G3 on Day 1. All PK parameters included in the protocol are listed in Table 6.1 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Pharmacokinetic Parameters to be Calculated

Parameter	Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC_{0-t}	AUC0-t	Area under the concentration-time curve from time 0 to the time of the last measurable non-zero concentration	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC_{0-inf}	AUC0-inf	Area under the concentration-time curve from time 0 extrapolated to infinity	AUC0-inf = AUC0-t + (Clast/kel) where Clast is the last observed/measured concentration
$AUC_{\%extrap}$	AUC%extrap	Percent of AUC0-inf extrapolated	AUC%extrap = (1 - AUC0-t/AUC0-inf)*100
$AUMC_{0-inf}$*	AUMC0-inf	Area under the moment curve from time 0 extrapolated to infinity	AUMC0-inf = AUMC0-t + [(tlast x Clast)/ Kel]+ [Clast/$(Kel)^2$]
C_{max}	Cmax	The maximum observed concentration	Taken directly from bioanalytical data
T_{max}	Tmax	The time to reach Cmax. If the maximum value occurs at more than one time point, Tmax is defined as the first time point with this value	Taken from clinical database as the difference in the start time of the infusion and the time of the blood draw which is associated with the Cmax.
K_{el}	Kel	Apparent first-order terminal elimination rate constant calculated from a semi-log plot of the plasma concentration versus time curve	The parameter will be calculated by linear least-squares regression analysis using the maximum number of points in the terminal log-linear phase (e.g., three or more non-zero plasma concentrations).

Parameter	Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
$T_{1/2}$	T1/2	Apparent first-order terminal elimination half-life	Calculated as: 0.693/ Kel
CL	CL	The apparent total plasma clearance after IV administration	Calculated as: Dose/(AUC0-inf)
MRT *	MRT	Mean residence time of unchanged drug in the systemic circulation when the drug concentrations are extrapolated to infinity	Calculated as: (AUMC0-inf/AUC0-inf) – (TI/2) Where TI is the duration of infusion
V_{ss}	Vss	Total apparent volume of distribution following single IV dose administration	Calculated as: MRT x CL

* AUMC0-inf and MRT values will be used for Vss calculation but will not be listed in the PK tables.
* Note for the programmer: Parameters which are calculated for use in the calculation of a separate parameter but that are not summarized in the PK tables (i.e., AUMC0-inf and MRT) will be included in the study data tabulation model (SDTM) PP(Pharmacokinetic Parameters) domain, but not included in the analysis data model (ADaM) ADPP (Pharmacokinetic Parameters Analysis) domain.

PK parameters will not be calculated for subjects with less than 3 consecutive postdose time points with quantifiable concentrations. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only and excluded from the statistical analysis.

For the calculation of the PK parameters, plasma concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration will be set to 0 and plasma concentrations BLQ after the first quantifiable concentration will be treated as missing.

The Kel will be determined using linear regressions composed of least 3 data points. The Kel will not be assigned if 1) the terminal elimination phase is not apparent, 2) if Tmax is one of the 3 last data points, or 3) if the R^2 value is less than 0.8. In cases where the Kel interval is not assigned, the values of AUC0-inf, AUC%extrap, AUMC0-inf, T1/2, CL, MRT, and Vss are considered not calculable and will not be reported. Wherever the resulting T1/2 is more than half as long as the sampling interval, the Kel values and associated parameters (AUC0-inf, AUC%extrap, AUMC0-inf, T1/2, CL, MRT, and Vss) may not be presented as judged appropriate and in accordance with Celerion SOPs.

6.6 Data Summarization and Presentation

All plasma xisomab 3G3 PK concentrations and/or PK parameters descriptive statistics will be generated using SAS® version 9.3 or higher. A concentration table will be presented for pooled placebo samples without descriptive statistics.

The plasma concentrations of xisomab 3G3 will be listed and summarized by treatment and time points for all subjects in the PK Population. Plasma concentrations of xisomab 3G3 will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum will be calculated for all nominal concentration time points. Excluded subjects will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the concentration listings and footnoted accordingly.

Mean and individual concentration-time profiles will be presented on linear and semi-log scales. Linear mean plots will be presented with and without SD.

Plasma xisomab 3G3 PK parameters will be listed and summarized by treatment for all subjects in the PK Population. Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of T1/2 and Tmax, which will be presented with 2 decimal places. Summary statistics (n, Mean, SD, CV%, SEM, minimum, median, maximum, geometric mean [Geom Mean] and geometric CV% [Geom CV%]) will be calculated for plasma xisomab 3G3 PK parameters. Excluded subjects will be listed in the PK parameter tables, but will be excluded from the summary statistics and noted as such in the tables.

The level of precision for each concentration and PK parameter statistic will be presented as follows:

- minimum/maximum: in same precision as in the bioanalytical data for concentrations and same precision for PK parameters presentation
- Mean/median/Geom Mean: in one more level of precision than minimum/maximum
- SD/SEM: in one more level of precision than Mean/median/Geom Mean
- n will be presented as an integer
- CV% and Geom CV% will be presented to the nearest tenth

7. PHARMACODYNAMIC ANALYSIS

7.1 Measurement and Collection Schedule

For all subjects, blood samples for the assessment of aPTT will be collected at predose, and at 0.083, 0.25, 0.5, 1, 3, 8, 24, 72, 120, 168, 216, 336, 504, and 672 hours after xisomab 3G3 start of infusion. Following the 672-hour time point, sample collection for PD assessment will continue every 7 days (± 2 days) until aPTT values return within ± 10% of the baseline value or the normal range.

7.2 Biomarker Method

aPTT will be determined using a light scattering method. This method is a Food and Drug Administration (FDA) approved kit for diagnostic testing and has been validated with respect to accuracy and precision at Celerion, Tempe, Arizona in accordance with the College of American Pathologists (CAP) and the Clinical Laboratory Improvement Amendments (CLIA) requirements for coagulation testing. The reference range for aPTT coagulation time is 23 – 32 seconds.

7.3 Activated Partial Thromboplastin Time

Inhibition of the blood coagulation contact pathway by xisomab 3G3 or its murine precursor, xisomab 14E11, is anticoagulant, as demonstrated by both in vitro and in vivo activated partial thromboplastin time (aPTT) prolongation.

7.4 Activated Partial Thromboplastin Time Values

aPTT values as determined at the collection times and per the biomarker method described in Section 7.1 and Section 7.2, respectively, will be used for the calculation of change from baseline.

7.5 Data Summarization and Presentation

aPTT values will be extracted from the clinical laboratory database and descriptive statistics will be generated using SAS® version 9.3 or higher. A table will be presented for the aPTT change from baseline with descriptive statistics. Change from baseline will be calculated by subtracting the predose aPTT value from the postdose aPTT value at each time point. The mean change from baseline will be calculated using the individual change from baseline values. If change from baseline results in a negative value, this value will be set to '0' for the calculation of the summary statistics.

aPTT values will be listed and summarized by treatment and time points for all subjects in the PD Population. aPTT values will be presented with the same level of precision as received from the clinical laboratory database. Summary statistics, including n, Mean, SD, CV%, SEM, minimum, median, and maximum will be

calculated for all nominal values time points. Excluded subjects will be included in the aPPT values tables, but will be excluded from the summary statistics and noted as such in the tables.

Mean and individual aPTT values-time and change from baseline-time profiles will be presented on linear scale. Linear mean plots will be presented with and without SD.

The level of precision for the aPPT values summary statistic will be presented as follows:

- minimum/maximum: in same precision as in the clinical laboratory database
- Mean/median: in one more level of precision than minimum/maximum
- SD/SEM: in one more level of precision than Mean/median
- n will be presented as an integer
- CV% will be presented to the nearest tenth

8. SAFETY

No inferential statistics will be performed on safety data.

All case report form (CRF) data will be listed by subject and chronologically by assessment time points. This will include rechecks, unscheduled assessments, and early termination.

Applicable continuous variables will be summarized using n, arithmetic mean, SD, minimum, median, and maximum. Data from subjects who received the placebo treatment will be pooled across cohorts.

The level of precision will be presented as follows: minimum/maximum in the same precision as in the database, mean/median in one more precision level than minimum/maximum, SD in one more precision level than mean/median, and n will be presented as an integer.

Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

8.1 Subject Discontinuation

Subjects will be summarized by number of subjects dosed, completed, and discontinued the study with discontinuation reasons by treatment (pooled placebo and xisomab 3G3 dose levels), pooled active, and overall. Any screen failure data will be listed.

8.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index) by treatment (pooled placebo and xisomab 3G3 dose levels), pooled active, and overall. Age will be derived from date of birth to date of first dosing and reported as an integer. Any screen failure data will be listed.

Frequency counts will be provided for categorical variables (race, ethnicity, and sex) by treatment (pooled placebo and xisomab 3G3 dose levels) and overall.

8.3 Adverse Events and Injection Site Reaction

All adverse events (AEs) occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 20.0.

All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, treatment, severity, relationship to study drug, and action; however, only treatment-emergent AEs (TEAEs) will be summarized.

A TEAE is defined as an AE that is starting or worsening at the start time of study drug administration or after. Each TEAE will be attributed to a treatment based on the onset date and time of the AE.

If an AE increases in severity, that AE will be given a resolution date and time and a new record will be initiated with the new severity. If the severity of an AE remains the same or decreases, the AE will be kept open through to resolution.

If the onset time of an AE is missing and the onset date is the same as the treatment dosing date or after the treatment dosing date, then the AE will be considered treatment emergent. If the onset date of an AE is missing, then the AE will be considered treatment emergent.

TEAEs will be tabulated by System Organ Class (SOC) and Preferred Term. Summary tables will include number of subjects reporting the AE and as percent of number of subjects dosed by treatment (pool placebo and xisomab 3G3 dose levels) and pooled active (xisomab 3G3 doses pooled). The number of AEs will be tabulated in a similar manner. Tables which tabulate the number of TEAEs by severity and relationship to study treatment will also be included.

Injection site reaction will be assessed and any abnormal finding will be reported as an adverse event.

Serious adverse events (SAEs), if present, will also be listed. Applicable narratives will be included in the CSR.

8.4 Clinical Laboratory Tests (Coagulation, Serum Chemistry, Hematology, Urinalysis)

Clinical laboratory tests for serum chemistry, hematology, and urinalysis will be performed at Screen, Check-in (Day -1), Hour 8 postdose on Day 1, Day 2, Day 8, Day 29, and Follow-up (Day 36) or prior to early termination. Bleeding time, which is contained in the hematology panel was performed at Check-in (Day -1), Predose, Hour 1 postdose on Day 1, and Day 2. Clinical laboratory tests for coagulation will be performed at Screen, Check-in (Day -1), and Follow-up (Day 36) or prior to early termination, with additional assessments at Hour 1 postdose on Day 1, Day 2, Day 4, Day 8, and Day 29 for PT and INR.

Out-of-normal range flags will be recorded as follows: high (H) and low (L) for numerical results and did-not-match (*) for categorical results. If a value fails the reference range, it will automatically be compared to a computer clinically significant (CS) range. If the value falls within the computer CS range, it will be noted as “N” for not clinically significant. If the value fails (i.e., fall outside of the CS range) the computer CS range, it will be flagged with a “Y” which prompts the PI to determine how the out-of-range value should be followed using 4 Investigator flags: "N", not clinically significant, "R", requesting a recheck, "^", checking at the next scheduled visit, or "Y", clinically significant. To distinguish the PI flag from the computer CS range flags, the PI flags of “N” and “Y” will be presented as “-“ and “+”, respectively, in the data listing. Additionally, a derived flag based on a search of the PI comments for a comment of “CS” or “Clinically Significant” will be used. The derived flag will be populated with “+” if the positive clinically significant determination is found in the comments for cases when the PI flag is populated with a “^” or a “R”.

Out-of-range values and corresponding recheck results will be listed. Results that are indicated as CS by the PI (either in the PI flag or in PI comments) will be listed in a table.

Bleeding time will be listed with the hematology results and will be included in the hematology out-of-range table but will be summarized with the coagulation results.

All coagulation results for PD endpoint aPTT will be listed with the clinical laboratory results and included in the out-of-range table, but for the time points outlined in Section 7.1 summaries will not be included in the clinical laboratory summary tables.

For all numeric laboratory values, descriptive statistics will be presented for each laboratory test by assessment time point and treatment (pooled placebo and xisomab 3G3 dose levels). Change from baseline will be summarized in a similar manner. Baseline is defined as the result closest and prior to dose which may include unscheduled or recheck results. This will typically be the result collected on Day -1.

Postdose unscheduled events or rechecks will not be included in summaries. Similarly early termination results will not be included in summaries.

For each laboratory test, a shift table will be developed to compare the frequency of the results at baseline (above normal, normal, or below normal) with the respective postdose results. For urinalysis tests, the categories are normal and outside normal.

8.5 Vital Signs

Vital signs (heart rate, blood pressure, respiration rate, and temperature) will be performed at Screen, predose, Hour .25 postdose on Day 1, as well as Day 8, Day 29, and Follow-up (Day 36) or prior to early termination.

Descriptive statistics will be presented for each vital sign measurement by assessment time point and treatment (pooled placebo and xisomab 3G3 dose levels). Change from baseline will be summarized in a similar manner. Baseline is defined as the result closest and prior to dose which may include unscheduled or recheck results. This will typically be the result collected predose on Day 1. Postdose unscheduled events or rechecks will not be included in summaries. Similarly early termination results will not be included in summaries.

8.6 Electrocardiogram

Single 12-Lead Electrocardiograms will be performed at Screen, predose, Hour .25 postdose on Day 1, as well as Day 8, Day 29, and Follow-up (Day 36) or prior to early termination. ECG parameters include heart rate, PR, QRS, QT, QTcF (QT corrected for heart rate using Fridericia's correction), and overall interpretation.

Descriptive statistics will be presented for each ECG parameter by assessment time point and treatment (pooled placebo and xisomab 3G3 dose levels). Change from baseline will be summarized in a similar manner. Baseline is defined as the result closest and prior to dose which may include unscheduled or recheck results. This will typically be the result collected predose on Day 1. Postdose unscheduled events or rechecks will not be included in summaries. Similarly early termination results will not be included in summaries.

8.7 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary Version 01MAR2017 and listed.

8.8 Physical Examination

Full physical examinations will be performed at Screen and Check-in (Day -1), and abbreviated physical examinations will be performed at Hour 1 postdose on Day 1, Day 2, Day 29, and Follow-up (Day 36) or prior to early termination. Symptom-

driven physical examinations may be performed at other times, at the PI's or designee's discretion. All data found in the CRF will be listed. Any changes in physical examinations will be captured and summarized with the adverse events and described in the text of the report.

8.9 Medical History

All medical and surgical history will be will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 20.0 and listed.

8.10 Immunogenicity

Blood samples will be collected from each subject for ADA detection at predose, Day 15, Day 29, and at the Follow-up visit only in the event that the Follow-up visit occurs after Day 36. Immunogenicity testing will be done at Celerion, Lincoln, Nebraska.

A qualitative screening assay will be performed on all samples and results reported as positive or negative for ADA detection. If the screening assay is positive, a qualitative confirmatory assay will be performed on the sample to confirm that the antibodies are specific to xisomab 3G3, with results reported as positive or negative. Confirmed positive samples for ADA will be reassayed, at a series of 2-fold dilutions prior to analysis. The greatest dilution that results in a mean response greater than the assay cut point will be reported as the titer for that sample.

On the other hand, if the screening result is negative, confirmatory and titer assays will not be performed. In the case where the confirmatory result is negative, but the screening result was positive, the titer assay will not be performed.

Results from the qualitative screening and confirmatory ADA detections will be listed as positive or negative. For samples with a positive confirmatory assay, a titer value will be presented with the same level of precision as received from the bioanalytical laboratory.

Frequency counts of positive and negative ADA detection will be presented by collection time, assay type (screening or confirmatory) and treatment (pooled placebo and xisomab 3G3 dose levels).

9. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

Per the protocol, immunogenicity data will be summarized descriptively. ADA detection is categorical data and thus descriptive summaries cannot be calculated. Frequency counts of positive and negative ADA detection will be presented instead.

10. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Note that all PK, PD, and Safety summary tables and figures will be generated using SAS® Version 9.3 or higher.

10.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the CSR. Tables and figures will be numbered appropriately during compilation of the CSR.

Section 10:

Table 10-1 Disposition Summary

Section 11:

Table 11-1 Demographic Summary

Table 11-2 Summary of Plasma Xisomab 3G3 Pharmacokinetics Following a Single IV Infusion of 0.1, 0.5, 2, and 5 mg/kg Xisomab 3G3

Figure 11-1 Arithmetic Mean Plasma Xisomab 3G3 Concentration -Time Profiles Following a Single IV Infusion of 0.1, 0.5, 2, and 5 mg/kg Xisomab 3G3 (Linear Scale)

Figure 11-2 Arithmetic Mean aPPT Values Versus Time Following a Single IV Infusion of 0.1, 0.5, 2, and 5 mg/kg Xisomab 3G3 and Pooled Placebo (Linear Scale)

Figure 11-3 Arithmetic Mean aPPT Change From Baseline Versus Time Following a Single IV Infusion of 0.1, 0.5, 2, and 5 mg/kg Xisomab 3G3 and Pooled Placebo (Linear Scale)

Section 12:

Table 12-1 Adverse Event Frequency by Treatment - Number of Subjects Reporting the Event (% of Subjects Dosed)

10.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report. Table and figure titles may be renumbered as appropriate during the compilation of the report.

14.1 Demographic Data Summary Tables

Table 14.1.1 Summary of Disposition (Safety Population)

Table 14.1.2 Demographic Summary (Safety Population)

14.2 Pharmacokinetic and Pharmacodynamic Data Summary Tables and Figures

14.2.1 Plasma Pharmacokinetic Xisomab 3G3 Tables

Table 14.2.1.1 Plasma Xisomab 3G3 Concentrations (ng/mL) Following a Single IV Infusion of 0.1 mg/kg Xisomab 3G3 (Treatment A) (Pharmacokinetic Population)

Table 14.2.1.2 Plasma Xisomab 3G3 Concentrations (ng/mL) Following a Single IV Infusion of 0.5 mg/kg Xisomab 3G3 (Treatment B) (Pharmacokinetic Population)

Table 14.2.1.3 Plasma Xisomab 3G3 Concentrations (ng/mL) Following a Single IV Infusion of 2 mg/kg Xisomab 3G3 (Treatment C) (Pharmacokinetic Population)

Table 14.2.1.4 Plasma Xisomab 3G3 Concentrations (ng/mL) Following a Single IV Infusion of 5 mg/kg Xisomab 3G3 (Treatment D) (Pharmacokinetic Population)

Table 14.2.1.5 Plasma Xisomab 3G3 Concentrations (ng/mL) Following a Single IV Infusion of Placebo (Pooled) (Treatment P)

Table 14.2.1.6 Plasma Xisomab 3G3 Pharmacokinetic Parameters Following a Single IV Infusion of 0.1 mg/kg Xisomab 3G3 (Treatment A) (Pharmacokinetic Population)

Table 14.2.1.7 Plasma Xisomab 3G3 Pharmacokinetic Parameters Following a Single IV Infusion of 0.5 mg/kg Xisomab 3G3 (Treatment B) (Pharmacokinetic Population)

Table 14.2.1.8 Plasma Xisomab 3G3 Pharmacokinetic Parameters Following a Single IV Infusion of 2 mg/kg Xisomab 3G3 (Treatment C) (Pharmacokinetic Population)

Table 14.2.1.9 Plasma Xisomab 3G3 Pharmacokinetic Parameters Following a Single IV Infusion of 5 mg/kg Xisomab 3G3 (Treatment D) (Pharmacokinetic Population)

Table 14.2.1.10 Intervals (Hours) Used for Determination of Plasma Xisomab 3G3 Kel Values (Pharmacokinetic Population)

14.2.2 Plasma Pharmacokinetic Xisomab 3G3 Figures

Figure 14.2.2.1 Mean (SD) Plasma Xisomab 3G3 Concentration Versus Time Profiles Following a Single IV Infusion of 0.1, 0.5, 2, and 5

Table 14.3.5.7 Clinical Laboratory Summary – Urinalysis (Safety Population)

Table 14.3.5.8 Clinical Laboratory Change From Baseline – Urinalysis (Safety Population)

Table 14.3.5.9 Clinical Laboratory Shift From Baseline – Urinalysis (Safety Population)

Table 14.3.5.10 Clinical Laboratory Summary – Coagulation & Bleeding Time (Safety Population)

Table 14.3.5.11 Clinical Laboratory Change From Baseline – Coagulation & Bleeding Time (Safety Population)

Table 14.3.5.12 Clinical Laboratory Shift From Baseline – Coagulation & Bleeding Time (Safety Population)

Table 14.3.5.13 Vital Sign Summary (Safety Population)

Table 14.3.5.14 Vital Sign Change From Baseline (Safety Population)

Table 14.3.5.15 12-Lead Electrocardiogram Summary (Safety Population)

Table 14.3.5.16 12-Lead Electrocardiogram Change From Baseline (Safety Population)

Table 14.3.5.17 ADA Detection Summary by Collection Time and Treatment (Safety Population)

10.3 Section 16 Data Listings

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in any database transfer.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the TFLs for the CSR. The following is a list of appendix numbers and titles that will be included as data listings:

16.1 Study Information

Appendix 16.1.9 Statistical Methods

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

16.2 Subject Data Listings

16.2.1 Subject Discontinuation

Appendix 16.2.1 Subject Disposition (Safety Population)

16.2.2 Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3 Subjects Excluded from Pharmacokinetic/Pharmacodynamic Analysis

Appendix 16.2.3.1 Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3.2 Subjects Excluded from Pharmacodynamic Analysis

Note: Appendices 16.2.2, 16.2.3.1, and 16.2.3.2 are generated in MS Word for inclusion in the study report.

16.2.4 Demographic Data

Appendix 16.2.4.1 Demographics (Safety Population)
Appendix 16.2.4.2 Physical Examination (Safety Population)
Appendix 16.2.4.3 Medical History (Safety Population)
Appendix 16.2.4.4 Substance Use (Safety Population)

16.2.5 Compliance and/or Drug Concentration Data

Appendix 16.2.5.1.1 Inclusion Criteria
Appendix 16.2.5.1.2 Exclusion Criteria
Appendix 16.2.5.2 Subject Eligibility (Safety Population)
Appendix 16.2.5.3 Check-in Criteria and Return Responses (Safety Population)
Appendix 16.2.5.4.1 Test Compound Description (Safety Population)
Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)
Appendix 16.2.5.5 Blood Draw Times (Safety Population)
Appendix 16.2.5.6 Meal Times (Safety Population)
Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

16.2.6 Individual Pharmacokinetic/Pharmacodynamic Response Data

Appendix 16.2.6.1 Individual Plasma Xisomab 3G3 Concentrations Versus Time Profiles Following a Single IV Infusion of <X> mg/kg Xisomab 3G3 (Linear and Semi-Log Scale) for <Subject #>

Appendix 16.2.6.2 Individual aPTT Values (sec) Following a Single IV Infusion of <X> mg/kg Xisomab 3G3 <or Placebo>

Appendix 16.2.6.3 Individual aPTT Values Versus Time Profiles Following a Single IV Infusion of <X> mg/kg Xisomab 3G3 <or Placebo> (Linear) for <Subject #>

Appendix 16.2.6.4 Individual Change from Baseline aPTT Values (sec) Following a Single IV Infusion of <X> mg/kg Xisomab 3G3 <or Placebo>

Appendix 16.2.6.5 Individual Change From Baseline aPTT Values Versus Time Profiles Following a Single IV Infusion of <X> mg/kg Xisomab 3G3 <or Placebo> (Linear) for <Subject #>

16.2.7 Adverse Events Listings

Appendix 16.2.7.1.1 Adverse Events (I of II) (Safety Population)

Appendix 16.2.7.1.2 Adverse Events (II of II) (Safety Population)

Appendix 16.2.7.2 Adverse Event Non-Drug Therapy (Safety Population)

Appendix 16.2.7.3 Adverse Event Preferred Term Classification (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Appendix 16.2.8.1.2 Clinical Laboratory Report - Hematology (Safety Population)

Appendix 16.2.8.1.3 Clinical Laboratory Report - Urinalysis (Safety Population)

Appendix 16.2.8.1.4 Clinical Laboratory Report - Coagulation (Safety Population)

Appendix 16.2.8.1.5 Clinical Laboratory Report - Urine Drug Screening (Safety Population)

Appendix 16.2.8.1.6 Clinical Laboratory Report - Comments (Safety Population)

Appendix 16.2.8.2 Vital Signs (Safety Population)

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Appendix 16.2.8.4 Immunogenicity Response Results (Safety Population)

11. TABLE AND FIGURE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included in the final report. Unless otherwise noted, all tables will be presented in Times New Roman font size 8. These tables will be generated off of the Celerion ADaM Version 2.1 data structure.

11.1 In-text Summary Tables Shells

In-text Table 10-1 will be in the following format:

Table 10-1 Disposition Summary

	Treatment						
Disposition	**A**	**B**	**C**	**D**	**Pooled Placebo**	**Pooled Active**	**Overall**
Dosed	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)
Completed	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Discontinued Early	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
<Reason>	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
Source: Table 14.1.1
Program: /CAXXXXX/sas_prg/stsas/intext/t_disp.sas 08OCT2015 16:36

In-text Table 11-1 will be in the following format:

Table 11-1 Demographic Summary

		Treatment						
Trait	**Category/Statistics**	**A**	**B**	**C**	**D**	**Pooled Placebo**	**Pooled Active**	**Overall**
Sex	Male	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Female	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
Race	Asian	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Black or African American	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	White	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
Ethnicity	Not Hispanic or Latino	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Hispanic or Latino	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
Age (yrs)	n	X	X	X	X	X	X	X
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX	XX	XX
Weight (kg)	n	X	X	X	X	X	X	X
	Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	SD	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX
	Minimum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Maximum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Height (cm)	n	X	X	X	X	X	X	X
	Mean	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XXX	XXX	XXX	XXX	XXX	XXX	XXX
	Median	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
	Maximum	XXX	XXX	XXX	XXX	XXX	XXX	XXX
BMI (kg/m²)	n	X	X	X	X	X	X	X
	Mean	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX
	SD	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
	Minimum	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX
	Maximum	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX

Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
BMI = Body mass index
Age is calculated at the time of dosing and reported as an integer.
Source: Table 14.1.2
Program: /CAXXXXX/sas_prg/stsas/intext/t_dem.sas 08OCT2015 16:36

In-text Table 11-2 will be in the following format:

Table 11-2: Summary of Plasma Xisomab 3G3 Pharmacokinetics Following a Single IV Infusion of 0.1, 0.5, 2, and 5 mg/kg Xisomab 3G3

Pharmacokinetic Parameters	Single IV Infusion of 0.1 mg/kg xisomab 3G3	Single IV Infusion of 0.5 mg/kg xisomab 3G3
Param1 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param2 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param3 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param4 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3 Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3 Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3 Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3 AUCs and Cmax values are presented as geometric mean and geometric CV%. Tmax values are presented as median (min, max). Other parameters are presented as arithmetic mean (± SD). Source: Tables 14.2.1.6 through 14.2.1.9		

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order and with following units: AUC0-t <ng*hr/mL>, AUC0-inf <ng*hr/mL>, AUC%extrap <%>, Cmax <ng/mL>, Tmax <hr>, Kel <1/hr>, T1/2 <hr>, CL <L/hr>, Vss <L>
- n will be presented as an integer (with no decimal);
- Summary statistics will be presented with same precision as defined in post-text shells
- Internal template ITPar1

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell: addition of a third and fourth column for Treatment C and D, respectively

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

In-text Table 12-1 will be in the following format:

Table 12-1 Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed)

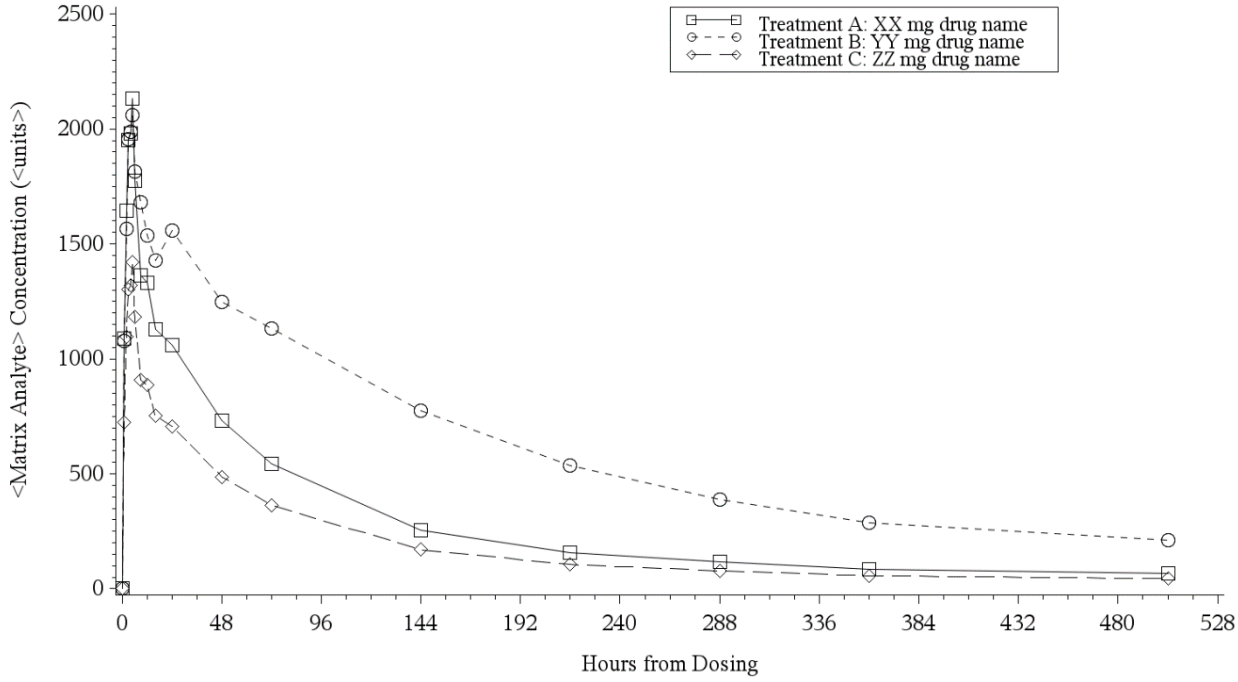
	Treatment					
TE Adverse Events*	**A**	**B**	**C**	**D**	**Pooled Placebo**	**Pooled Active**
Number of Subjects Dosed	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)
Number of Subjects With TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects Without TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
General disorders and administration site conditions	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Vessel puncture site pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Vessel puncture site reaction	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
*Adverse events are classified according to MedDRA® Version 20.0
TE = Treatment-emergent
Although a subject may have had 2 or more clinical adverse experiences, the subject is counted only once within a category. The same subject may appear in different categories.
Source: Table 14.3.1.1
Program: /CAXXXXX/sas_prg/stsas/intext/t_ae.sas 08OCT2015 16:36

11.2 Figures Shells

In-text Figures 11-1 through 11-3, post-text Figures 14.2.2.1 through 14.2.2.3, post-text Figures 14.2.4.1 through 14.2.4.4, and Individual Listings in 16.2.6.3 and 16.2.6.5 will be in the following format:

Figure 11-1 Arithmetic Mean Plasma Xisomab 3G3 Concentration-Time Profiles Following a Single IV Infusion of 0.1, 0.5, 2, and 5 mg/kg Xisomab 3G3 (Linear Scale)



Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYY HH:MM

Notes for Generating the Actual Mean Figure:

- Figures 11-1, 14.2.2.1 through 14.2.2.3
  - y-axis: Plasma Xisomab 3G3 Concentration (ng/mL)
  - X-axis: Hours From Start of Infusion
- Figures 11-2, 14.2.4.1 through 14.2.4.2, 16.2.6.3
  - y-axis: Arithmetic Mean aPTT (sec)
  - X-axis: Hours From Start of Infusion
- Figures 11-3, 14.2.4.3 through 14.2.4.4, 16.2.6.5
  - y-axis: aPTT Mean Change from Baseline (sec)
  - X-axis: Hours From Start of Infusion
- Source tables
  - Figure 11-1: 14.2.1.1 through 14.2.1.4
  - Figure 11-2: 14.2.3.1
  - Figure 11-3: 14.2.3.1

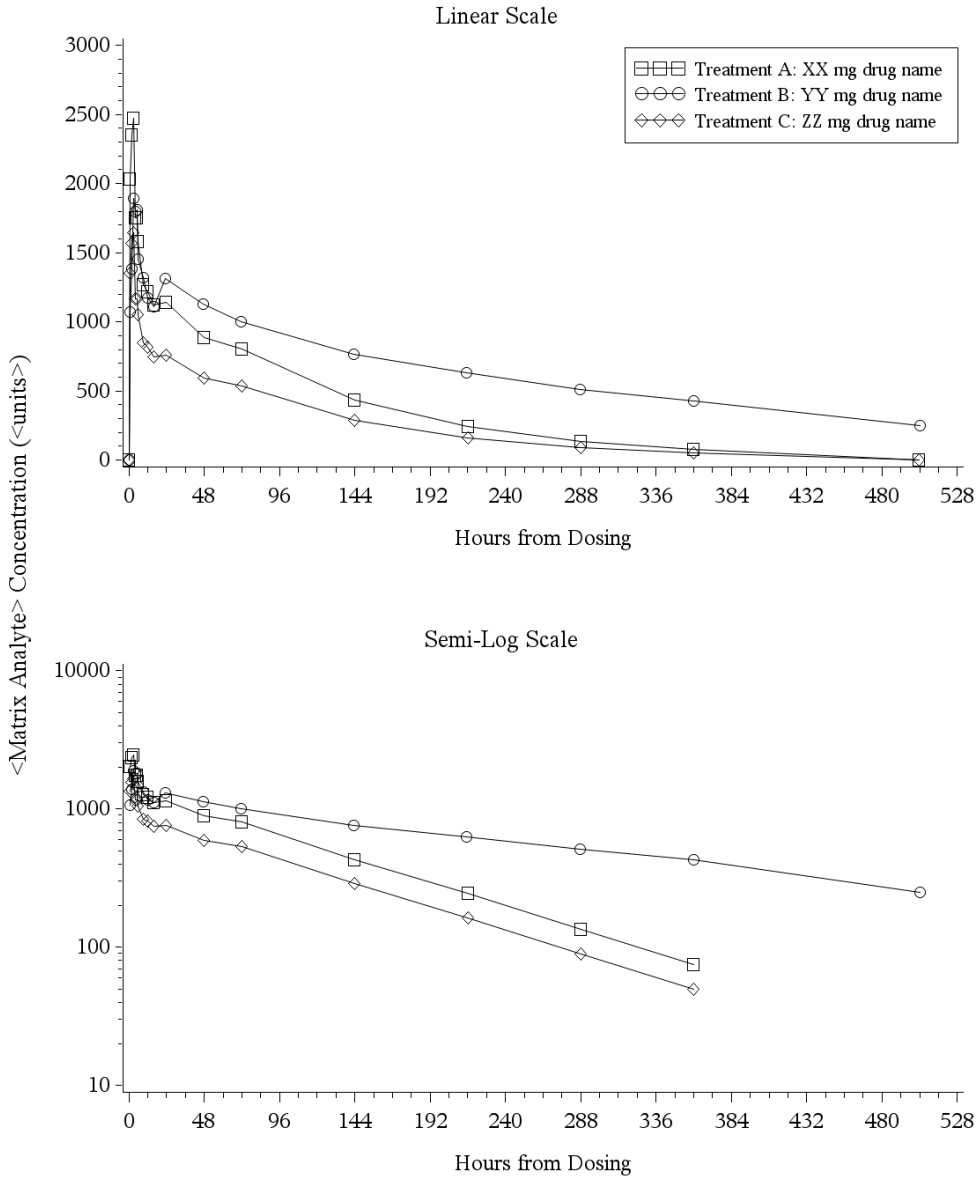
Figure Legend:

Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
Treatment P: Single IV Infusion of Placebo (Pooled)

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Figures in Appendix 16.2.6.1 will be in the following format:

Appendix 16.2.6.1 Individual Plasma Xisomab 3G3 Concentrations Versus Time Profiles Following a Single IV Infusion of 0.1, 0.5, 2, and 5 mg/kg Xisomab 3G3 (Linear and Semi-Log Scale) for Subject X



Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYY HH:MM

Notes for Generating the Actual Individual Figure:

- Appendix 16.2.6.1
  - y-axis: Plasma Xisomab 3G3 Concentration (ng/mL)
  - X-axis: Hours From Start of Infusion

Figure Legend:

Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
Treatment P: Single IV Infusion of Placebo (Pooled)

Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYYY HH:MM

11.3 Section 14 Summary Tables Shells

Part 1 of X

Table 14.1.1 Summary of Disposition (Safety Population)

	Treatment						
Disposition	A	B	C	D	Pooled Placebo	Pooled Active	Overall
Dosed	XX	XX	XX	XX	XX	XX	XX
Completed	XX	XX	XX	XX	XX	XX	XX
Discontinued Early	X	X	X	X	X	X	X
<Reason>	X	X	X	X	X	X	X

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /AAXXXXX/ECR/sas_prg/stsas/tab prog_name.sas DDMMMYYYY HH:MM

Table 14.1.2 Demographic Summary (Safety Population)

		Treatment						
Trait		A	B	C	D	Pooled Placebo	Pooled Active	Overall
Sex	Male	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Female	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
Race	American Indian	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Asian	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Black	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
Ethnicity	Hispanic or Latino	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Not Hispanic or Latino	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
Age* (yrs)	n	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX
Weight (kg)	n	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX

Programmer Note: Add Height (cm) and Body Mass Index (kg/m2) to the following page

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
*Age is calculated at the time of dosing and reported as an

integer. Program:

/AAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Tables 14.2.1.1 through 14.2.1.5 and Appendix 16.2.6.2 and 16.2.6.4 will be in the following format:

Table 14.2.1.1 Plasma Xisomab 3G3 Concentrations (ng/mL) Following a Single IV Infusion of 0.1 mg/kg Xisomab 3G3 (Treatment A)
(Pharmacokinetic Population)

Subject	Sample Times (hr)								
Number	Predose	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
n	XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX	XX	XX	XX	XX	XX	XX	XX	XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum	XX	XX	XX	XX	XX	XX	XX	XX	XX

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 50 ng/mL are treated as 0 before the first quantifiable concentration and as missing elsewhere.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

- Please use CPConc1 template
- Per study design needs, the following changes are made to this table relative to Celerion standard: columns <Treatment Sequence> and <Study Period> will be removed.
- Concentrations will be presented to the same precision as in the bio data.
- aPTT values will be presented to the same precision as in the clinical laboratory data.
- Summary statistics presentation with respect to the precision of the bio data or clinical laboratory data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal
- PK and PD Time points are: predose and 0.083, 0.25, 0.5, 1, 3, 8, 24, 72, 120, 168, 216, 336, 504, and 672 hours postdose (additional time points might be added depending on the conduct of the study)

Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables-sig.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_conc.sas DDMMMYYYY HH:MM

Tables 14.2.1.6 through 14.2.1.9 will be in the following format:

Table 14.2.1.6 Plasma Xisomab 3G3 Pharmacokinetic Parameters Following a Single IV Infusion of 0.1 mg/kg Xisomab 3G3 (Treatment A) (Pharmacokinetic Population)

	Parameters					
Subject Number	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n	XX	XX	XX	XX	XX	XX
Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median	XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum	XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

. = Value missing or not reportable.

Notes for Generating the Actual Table:

- Please use CPPar1 template
- Per study design needs, the following changes are made to this table relative to Celerion standard: columns <Treatment Sequence> and <Study Period> will be removed.
- PK Parameters will be presented in the following order and with following units: AUC0-t <ng*hr/mL>, AUC0-inf <ng*hr/mL>, AUC%extrap <%>, Cmax <ng/mL>, Tmax <hr>, Kel <1/hr>, T1/2 <hr>, CL <L/hr>, Vss <L>
- n will be presented as an integer (with no decimal);
- Exposure parameters (i.e. AUCs, Cmax, Vss, CL) will be presented with, at maximum, the precision of the bio data, and, at minimum, 3 significant figures (to be determined by the PKist once bio data are received).
    - Summary statistics will be presented with respect to the precision of the bio data: Mean, Median, and Geom Mean = +1; SD and SEM = +2, Min and Max = +0.
- Time parameters (i.e. Tmax, T1/2) will be presented with 2 decimals.
    - Summary statistics will be presented with respect to the number of decimals: Mean, Median, and Geom Mean = +1; SD and SEM = +2, Min and Max = +0.
- Values for rate constants (i.e. Kel) will be presented with 3 significant figures.
    - Summary statistics for Kel will be presented as: Mean, Median, and Geom Mean = +1; SD and SEM = +2, Min and Max = +0.
- CV% and Geom CV% for all parameters will be presented with 1 decimal

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Table 14.2.1.10 will be in the following format:

Table 14.2.1.10 Intervals (Hours) Used for Determination of Plasma Xisomab 3G3 Kel Values (Pharmacokinetic Population)

Subject Number	Treatment Sequence	<Treatment A> Interval	R2	n	<Treatment B> Interval	R2	n
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X

Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
R2 = Coefficient of determination
n = Number of points used in Kel calculation
. = Kel value not reportable.

Notes for Generating the Actual Table:

- Please use CPKel1 template
- Per study design, the "Treatment Sequence" column will be replaced with 'Treatment' and the data will be presented vertically instead of horizontally.
- Interval start and stop times will be presented to 1 decimal or 3 significant figures minimum
- R2 will be presented to 3 decimals
- n will be presented as an integer

Program: /CAXXXXX/sas_prg/pksas/kel-tables-xover.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_kel.sas DDMMMYYYY HH:MM

Table 14.2.3.1 will be presented in the following format:

Table 14.2.3.1 Mean aPTT Values (sec) and Mean Change from Baseline aPTT Values (sec) Following a Single IV Infusion of 0.1, 0.5, 2.0, and 5 mg/kg Xisomab 3G3 and Placebo (Pharmacodynamic Population)

				Mean aPTT Values				Mean Change From Day 1 Predose			
Measurement	Day	Hour	Statistic	P	A	B	C	P	A	B	C
aPTT Values (sec)	1	0	N	X.XX	X.XX	X.XX	X.XX				
			Mean	X.XX	X.XX	X.XX	X.XX				
			SD	X.XX	X.XX	X.XX	X.XX				
			Median	X.XX	X.XX	X.XX	X.XX				
			Minimum	X.XX	X.XX	X.XX	X.XX				
			Maximum	X.XX	X.XX	X.XX	X.XX				
	1	0.083	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	1	0.25	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	1	0.5	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Notes for Generating the Actual Table:

- Per study design, an additional column for treatment D will be added
- aPTT values will be presented with the same level of precision as received from the clinical laboratory database

- Summary statistics presentation with respect to the precision of the clinical laboratory data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal
- PD Time points are: predose and 0.083, 0.25, 0.5, 1, 3, 8, 24, 72, 120, 168, 216, 336, 504, and 672 hours postdose (additional time points might be added depending on the conduct of the study)

Add the following to the footnote:

Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
Treatment P: Single IV Infusion of Placebo (Pooled)

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

	Treatment					
Adverse Event*	A	B	C	D	Pooled Placebo	Pooled Active
- Number of Subjects Dosed	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Number of Subjects With TEAEs	X (X%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects Without TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nervous system disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Headache NOS	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Reproductive system and breast disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vaginal discharge	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Respiratory, thoracic and mediastinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Epistaxis	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Skin and subcutaneous tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Sweating increased	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
*Adverse events are classified according to MedDRA Version 20.0. TEAEs = Treatment-emergent adverse

events Program: /AAXXXXX/ECR/sas_prg/stsas/tab progrname.sas

DDMMMYYYY HH:MM

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

	Treatment					
Adverse Event*	A	B	C	D	Pooled Placebo	Pooled Active
- Number of TEAEs	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nervous system disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Headache NOS	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Reproductive system and breast disorder	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vaginal discharge	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Respiratory, thoracic and mediastinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Epistaxis	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Skin and subcutaneous tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Sweating increased	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
*Adverse events are classified according to MedDRA Version 20.0. TEAEs = Treatment-emergent adverse

events Program: /AAXXXXX/ECR/sas_prg/stsas/tab programname.sas

DDMMMYYYY HH:MM

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Drug - Number of Adverse Events (Safety Population)

		Number of Subjects	Number	Severity/Intensity				Relationship to Study Drug				
Adverse Event*	Treat-ment	With TEAEs	of TEAEs	Mild (Grd 1)	Moderate (Grd 2)	Severe (Grd 3)	PLT^ (Grd 4)	Unrelated	Unlikely	Possibly	Probably	Likely
Abdominal pain	A	X	X	X	X	X	X	X	X	X	X	X
Constipation	C	X	X	X	X	X	X	X	X	X	X	X
Dry throat	B	X	X	X	X	X	X	X	X	X	X	X
Dysmenorrhoea	B	X	X	X	X	X	X	X	X	X	X	X
Dyspepsia	D	X	X	X	X	X	X	X	X	X	X	X
Headache	A	X	X	X	X	X	X	X	X	X	X	X
	B	X	X	X	X	X	X	X	X	X	X	X
	Pooled Active	X	X	X	X	X	X	X	X	X	X	X
Myalgia	P	X	X	X	X	X	X	X	X	X	X	X
Nasal congestion	B	X	X	X	X	X	X	X	X	X	X	X
Skin laceration	B	X	X	X	X	X	X	X	X	X	X	X
Treatment A		X	X	X	X	X	X	X	X	X	X	X
Treatment B		X	X	X	X	X	X	X	X	X	X	X
Treatment C		X	X	X	X	X	X	X	X	X	X	X
Treatment D		X	X	X	X	X	X	X	X	X	X	X
Pooled Placebo		X	X	X	X	X	X	X	X	X	X	X
Pooled Active		X	X	X	X	X	X	X	X	X	X	X

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
*Adverse events are classified according to MedDRA Version 20.0. TEAEs = Treatment-emergent adverse events
^PLT = Potentially Life-threatening; Grd = Grade

Program: /AAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Will match 16.2.7

Or contain statement as follows:

"There were no serious adverse events recorded during the study."

Program: /AAXXXXX/ECR/sas_prg/stsas/programname.sas DDMMMYYYY HH:MM

Tables 14.3.4.1 to 14.3.4.4 will have the following format:

Table 14.3.4.1 Out-of-Range Values and Recheck Results - Serum Chemistry (Safety Population)

Cohort	Subject Number	Age#/ Sex	Study Period	Treat-ment	Day	Hour	Date	Time	Parameter1 <Range> (Unit)	Parameter2 <Range> (Unit)	Parameter3 <Range> (Unit)	Parameter4 <Range> (Unit)	Parameter5 <Range> (Unit)
X	X	XX/X	Screen				DDMMMYYYY	HH:MM:SS	XX HN				XX HN
			1	X	-X	-XX.XX	DDMMMYYYY	HH:MM:SS	XX LY^	XX LN		XX LYR+	

Programmer notes: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Programmer notes: Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.6 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional CS flag for PI flag (+) based on positive comments (i.e. CS/Clinically Significant). Present this derived 4th column in all tables, and list only subjects/tests which are PI-determined clinically significant lab values in Table 14.3.4.5.

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
#Age is calculated from the date of first dosing. F = Female, M = Male
H = Above reference range, L = Below reference range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.4.5 Clinically Significant Values and Corresponding Results (Safety Population)

Cohort	Subject Number	Age#/ Sex	Study Period	Treatment	Day	Hour	Date	Time	Department	Test	Result		Reference Range	Unit
X	X	XX/X	1	X	-X	-XX.XX	DDMONYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX		XX – XX	mg/dL
					X	XX.XX	DDMONYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HYR+	XX – XX	mg/dL
					X	XX.XX	DDMONYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HYR+	XX – XX	mg/dL

Programmer notes: All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table.

If no event meets this criteria then include a statement as follows:
"There were no clinical laboratory results documented as clinically significant by the PI."

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
#Age is calculated from the date of first dosing. F = Female, M = Male
H = Above reference range, L = Below reference range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Tables 14.3.5.4 (hematology), 14.3.5.7 (urinalysis), and 14.3.5.10 (coagulation & bleeding time) will resemble 14.3.5.1.

Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

				Treatment				
Laboratory Test (units)	Reference Range	Time Point	Statistic	A	**B**	C	D	Pooled Placebo
Testname (unit)	< - >#	Screen	n	X	X	X	X	X
			Mean	X.X*	X.X	X.X	X.X	X.X
			SD	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	XX	XX	XX	XX	XX
			Median	X.X	X.X	X.X	X.X	X.X
			Maximum	XX	XX	XX	XX	XX
		Baseline	n	X	X	X	X	X
			Mean	XX.XX	XX.XX	XX.XX*	XX.XX	XX.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	XX.X	XX.X	XX.X	XX.X	XX.X
			Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
			Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Programmer note: Time points are Screen, Baseline, Day 1 Hour 8, Day 2, Day 8, Day 29, and Follow-up. Coagulation time points are Screen, Baseline, Day 1 Hour 1, Day 2, Day 4, Day 8, Day 29, and Follow-up. aPTT samples for PD time points are not presented here. Bleeding time is presented with coagulation with time points Check-in, Baseline, Day 1 Hour 1, and Day 2.

Programmer note: Treatment means at specific time points will be flagged (with a *) if they are above or below the reference range. This only applies to the clinical laboratory treatment results (i.e., not the change from baseline or any other endpoints).

Programmer note: The following footnote only presented on Coagulation summary tables
Summaries for aPTT associated with PD time points can be found in Table 14.X.X.X.

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Baseline is the last predose measurement.
= Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
*Outside reference range

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Tables 14.3.5.5 (hematology), 14.3.5.8 (urinalysis), and 14.3.5.11 (coagulation & bleeding time) will resemble 14.3.5.2.

Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

			Treatment				
Laboratory Test (units)	Time Point	Statistic	A	**B**	C	D	Pooled Placebo
Testname (unit)	Day 1 Hour 8	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Day 2	n	X	X	X	X	X
		Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Programmer note: Time points are Day 1 Hour 8, Day 2, Day 8, Day 29, and Follow-up. Coagulation time points are Day 1 Hour 1, Day 2, Day 4, Day 8, Day 29, and Follow-up. aPTT samples for PD time points are not presented here. Bleeding time is presented with coagulation with time points Day 1 Hour 1 and Day 2.
Programmer note: The following footnote only presented on Coagulation summary tables
Change from baseline summaries for aPTT associated with PD time points can be found Table 14.X.X.X.

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Baseline is the last predose measurement.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Tables 14.3.5.6 (hematology), 14.3.5.9 (urinalysis), and 14.3.5.12 (coagulation & bleeding time) will resemble 14.3.5.3

Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

			Baseline L			Baseline N			Baseline H		
			Postdose			Postdose			Postdose		
Laboratory Test (units)	Treatment	Time Point	L	N	H	L	N	H	L	N	H
Testname (unit)	X	Day 1 Hour 8	X	XX	X	X	XX	X	X	XX	X
		Day 2	X	XX	X	X	XX	X	X	XX	X
		Day 8	X	XX	X	X	XX	X	X	XX	X
		Day 29	X	XX	X	X	XX	X	X	XX	X
		Follow-up	X	XX	X	X	XX	X	X	XX	X
Testname (unit)	X	Day 1 Hour 8	X	XX	X	X	XX	X	X	XX	X
		Day 2	X	XX	X	X	XX	X	X	XX	X
		Day 8	X	XX	X	X	XX	X	X	XX	X
		Day 29	X	XX	X	X	XX	X	X	XX	X
		Follow-up	X	XX	X	X	XX	X	X	XX	X

Programmer note: Time points are Day 1 Hour 8, Day 2, Day 8, Day 29, and Follow-up. Coagulation time points are Day 1 Hour 1, Day 2, Day 4, Day 8, Day 29, and Follow-up. aPTT samples for PD time points are not presented here. Bleeding time is presented with coagulation with time points Day 1 Hour 1 and Day 2.
Programmer note: For urinalysis, the following footnote is used since the categories of N and O will be used instead of L, N, and H
Note: N = Within reference range, O = Outside reference range

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
N = Within reference range, L = Below reference range, H = Above reference range
Baseline is the last predose measurement.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programame.sas DDMMMYYYY HH:MM

Change From Baseline Table 14.3.5.14 will resemble 14.3.5.13

Table 14.3.5.13 Vital Sign Summary (Safety Population)

			Treatment				
Vital Sign (units)	Time Point	Statistic	A	B	C	D	Pooled Placebo
Testname (unit)	Screen	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Baseline	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Day 1 Hour 0.25	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX

Programmer note: Time points are Screen, Baseline, Day 1 Hour 0.25, Day 8, Day 29, and Follow-up.

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Baseline is the last predose measurement.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Change From Baseline Table 14.3.5.16 will resemble 14.3.5.15

Table 14.3.5.15 12-Lead Electrocardiogram Summary (Safety Population)

			Treatment				
Measurement (units)	Time Point	Statistic	A	B	C	D	Pooled Placebo
Testname (unit)	Screen	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Baseline	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Day 1 Hour 0.25	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX

Programmer note: Time points are Screen, Baseline, Day 1 Hour 0.25, Day 8, Day 29, and Follow-up.

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Baseline is the last predose measurement.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.5.17 ADA Detection Summary by Collection Time and Treatment (Safety Population)

			Treatment				
Time Point	Assay Type	Result	A	B	C	D	Pooled Placebo
Predose	Screening	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
	Confirmatory	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
Day 15	Screening	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
	Confirmatory	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
Day 29	Screening	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
	Confirmatory	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
Follow-up	Screening	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
	Confirmatory	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
Overall*	Screening	Negative	X	X	X	X	X
		Positive	X	X	X	X	X
	Confirmatory	Negative	X	X	X	X	X
		Positive	X	X	X	X	X

Note: Follow-up ADA detection sample only collected if Follow-up visit occurred after Day 36.
*For overall counts, if the response of a subject is positive at least once, the subject will be counted as positive; otherwise, the subject will be considered negative.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

12. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final report. These listings will be generated off of the Celerion SDTM Version 3.2 data structure. All listings will be presented in Courier New size font 9. Subject listings will be provided in subject order within cohort order.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Sex	Age Category	Reference Range	Unit
Serum Chemistry	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
Hematology	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units
	Test name	XXX	XX – XX	XX – XX	units

<Similar for all remaining laboratory groups and test names, note that age category will only be presented when different normal ranges exist>

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_lno.sas 27NOV2015 18:34

Appendix 16.2.1 Subject Disposition (Safety Population)

Cohort	Subject Number	Treatment	Study Period	Date	Completed Study?	Primary Discontinuation Reason
X	1	X	Post	DDMONYYYY	YES	
	2	X	Post	DDMONYYYY	YES	
	3	X	Post	DDMONYYYY	NO	Adverse Event

Programmer Note: Add any potential screen failure subjects to the end of this listing

Note: Treatment A: Single IV Infusion of 0.1 mg/kg xisomab 3G3
Treatment B: Single IV Infusion of 0.5 mg/kg xisomab 3G3
Treatment C: Single IV Infusion of 2 mg/kg xisomab 3G3
Treatment D: Single IV Infusion of 5 mg/kg xisomab 3G3
Treatment P: Single IV Infusion of Placebo

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_dis.sas 27NOV2015 18:35

Appendix 16.2.4.1 Demographics (Safety Population)

Cohort	Subject Number	Date Of Birth	Age* (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m²)	Informed Consent Date
X	1	DDMONYYYY	47	Male	< >	Not Hispanic or Latino	XXX	XX.X	XX.XX	DDMONYYYY
	2	<similar to above.								

Programmer Note: Add any potential screen failure subjects to the end of this listing

Note: *Age is calculated at the time of dosing and reported as an integer.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_dem.sas 27NOV2015 18:35

Appendix 16.2.4.2 Physical Examination (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Question	Result Description or Comment
X	1	Screen				DDMONYYYY	Was PE performed? (Yes/No)	YES
		1	X	-1	-19.25	DDMONYYYY	Was PE performed? (Yes/No)	NO
				1	1.25	DDMONYYYY	Was PE performed? (Yes/No)	NO
	2	Screen				DDMONYYYY	Was PE performed? (Yes/No)	YES
		1	X	-1	-19.25	DDMONYYYY	Was PE performed? (Yes/No)	NO
				1	1.25	DDMONYYYY	Was PE performed? (Yes/No)	NO

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_phy_best_practice.sas 27NOV2015 18:35

Appendix 16.2.4.3 Medical History (Safety Population)

Cohort	Subject Number	Any History?	System Reviewed	System Organ Class/ Preferred Term*	Category	Date Start	Date End	Ongoing?	Condition or Event
X	1	No							
	2	Yes	XXXXXXXXXXXXX	XXXXXXXXX/XXXXXXXX	Medical	YYYY		YES	< >

<Note date can be YYYY, MONYYYY, or DDMONYYYY based on individual subject data.>

Note: *Medical history events are classified according to MedDRA Version 20.0.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_mh.sas 27NOV2015 18:35

Appendix 16.2.4.4 Substance Use (Safety Population)

Cohort	Subject Number	Study Period	Substance	Description of Use	Start Date	End Date
X	1	Screen	Tobacco Use	NON-SMOKER	03DEC1967	06OCT2016
				0-4 CIGARETTES WEEK	06OCT2016	
	2	Screen	Tobacco Use	NON-SMOKER	DDMONYYYY	

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_su.sas 27NOV2015 18:35

Appendix 16.2.5.1.1 Inclusion Criteria

1. Healthy adult male and/ or female (non-childbearing potential only), 18 to 48 years of age, inclusive, at screening.
2. < >
3. < >
4. < >

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_inc.sas 27NOV2015 18:35

Appendix 16.2.5.1.2 Exclusion Criteria

1. Subject is mentally or legally incapacitated or has significant emotional problems at the time of the screening visit or expected during the conduct of the study.
2. < >
3. < >
4. < >
5. < >

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_exc.sas 27NOV2015 18:35

Appendix 16.2.5.2 Subject Eligibility (Safety Population)

Cohort	Subject Number	Study Period	Did subject meet all eligibility criteria?	Specify
X	1	Screen	YES	
	2	Screen	NO	<This column prints only if data are present.>

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ie.sas 27NOV2015 18:35

Appendix 16.2.5.3 Check-in Criteria and Return Responses (Safety Population)

Cohort	Subject Number	Study Period	Day	Hour	Date	Time	Check-in Criteria 1	Check-in Criteria 2	Specify
X	1	1	-1	-22.50	DDMONYYYY	MM:HH	NO	NA	
			4	71.50	DDMONYYYY	MM:HH	YES	YES	<This column prints only
			6	119.50	DDMONYYYY	MM:HH	NO	NA	if data are present>
			8	167.50	DDMONYYYY	MM:HH	NO	NA	

Note: Check-in Criteria 1 = Did the Subject report any study restriction violations since the last study visit?
2 = IF YES TO ANY QUESTION, WAS SUBJECT APPROVED FOR STUDY?
NA = Not Applicable

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_chk1.sas 27NOV2015 18:35

Appendix 16.2.5.4.1 Test Compound Description (Safety Population)

Compound	Interval	Form	Route
< >	XX.XX TO XX.XX	SOLUTION	INJECTION IV BOLUS/PUSH

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_med.sas 27NOV2015 18:35

Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Interval	Date	Time		Compound	Dosage	Comments
							Start	Stop			
X	1	1	X	1	XX.XX TO XX.XX	DDMONYYYY	HH:MM:SS	HH:MM:SS	XXXXXXX	< >	<This column prints only if data are present.>

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_med2.sas 27NOV2015 18:35

Appendix 16.2.5.5 Blood Draw Times (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Actual Time	Vacutainer ID	Bioassay	Comments
X	1	1	X	1	-0.50	DDMONYYYY	HH:MM:SS	XXXXXXXXXXX	XXXXXXX	<This column prints only
					0.08	DDMONYYYY	HH:MM:SS	XXXXXXXXXXX	XXXXXXX	if data are present.>
				<similar for all other time points and subjects>						

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_bld.sas 27NOV2015 18:35

Appendix 16.2.5.6 Meal Times (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Event	Start Date	Start Time	Stop Time	Comments
X	1	1	X	-1	-19.50	LUNCH	DDMONYYYY	HH:MM:SS	HH:MM:SS	
					-15.00	DINNER	DDMONYYYY	HH:MM:SS	HH:MM:SS	
					-11.00	SNACK	DDMONYYYY	HH:MM:SS	HH:MM:SS	
				1	1.50	BREAKFAST	DDMONYYYY	HH:MM:SS	HH:MM:SS	DID NOT CONSUME 10% OF MEAL

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_mel.sas 27NOV2015 18:35

Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

Cohort	Subject Number	Any Medications?	Treatment	Medication (WHO DD*)	Dosage	Route	Start Date	Start Time	Stop Date	Stop Time	Frequency	Indication	Continuing?	Prior to Study?
X	1	NO		None										
	2	NO		None										
	3	YES		CETIRIZINE (CETIRIZINE)	X MG	XXXXXXXXX	DDMONYYYY	UNK	DDMONYYYY	HH:MM	XXXXXXX	XXXXXXX	NO	Yes
			X	PARACETAMOL (PARACETAMOL)	X MG	XXXXXXXXX	DDMONYYYY	HH:MM	DDMONYYYY	HH:MM	XXXXXXXX	XXXXXXXX	XX	

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
*Concomitant medications are coded with WHO Dictionary Version 01MAR217.
UNK = Unknown, WHO DD = World Health Organization Drug

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_con.sas 27NOV2015 18:35

Appendix 16.2.7.1.1 Adverse Events (I of II) (Safety Population)

Cohort	Subject Number	Treatment	TE?	Adverse Event	Preferred Term*	Time From (DD:HH:MM)	Date	Time	Date	Time	Time From (DD:HH:MM)
X	1			None							
	2			None							
	3		No	XXXXXXXXXXXXX XXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXX XXXXXXXXXXX	XX:XX:XX	DDMONYYYY	HH:MM	DDMONYYYY	HH:MM	DD:HH:MM
		X	Yes	XXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	<similar to above>					

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
*Adverse events are classified according to MedDRA Version 20.0.
TE = Treatment-emergent

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ae.sas 27NOV2015 18:35

Appendix 16.2.7.1.2 Adverse Events (II of II) (Safety Population)

Cohort	Subject Number	Treatment	Adverse Event	Date	Time	Frequency	Severity/ Intensity	Serious	Outcome	Relationship to Study Drug	Action
X	1		None								
	2		None								
	3		XXXXXXXXXXXXXXXXXXXX	DDMONYYYY	XX:XX	Cont.	Mild	NS	Resolved	Unrelated	None
		X	XXXXXXXXXXXXXXXXXXXX	DDMONYYYY	XX:XX	<similar to above>					

Programmer Note: Shorten Frequency and Serious headers to Freq^ and Ser*, respectively and add 'Freq^ represents Frequency:' and 'Ser* represents Serious:' before their respective decodes in the footnotes as necessary.

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
NS = Not Serious
SE = Single Episode, Inter. = Intermittent, Cont. = Continuous

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ae2.sas 27NOV2015 18:35

Appendix 16.2.7.2 Adverse Event – Non Drug Therapy (Safety Population)

Cohort	Subject Number	Treatment	Adverse Event	Onset Date	Onset Time	Therapy Date	Therapy Time	Therapy Description
X	6	X	< >	DDMONYYYY	HH:MM	DDMONYYYY	HH:MM	TRENDELENBURG POSITION

Programmer Note: If there are no non drug therapies the listing will contain the statement "There were no non drug therapies administered during the study."

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >

Program: /CAXXXXX/sas_prg/stsas/lis_dev/cdash_lis_ae3.sas 02DEC2015 9:51

Appendix 16.2.7.3 Adverse Event Preferred Term Classification (Safety Population)

Cohort	Subject Number	Treatment	Adverse Event	Preferred Term*	System Organ Class	Onset Date	Onset Time
X	1		None				
	2		None				
	3		XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	DDMONYYYY	HH:MM
		X	XXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXX	DDMONYYYY	HH:MM

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
*Adverse events are classified according to MedDRA Version 20.0.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ae4.sas 27NOV2015 18:35

Appendices 16.2.8.1.1 to 16.2.8.1.5 will have the following format:

Page 1 of X

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Cohort	Subject Number	Age#/ Sex	Study Period	Treat-ment	Day	Hour	Date	Time	Parameter1 <Range> (Unit)	Parameter2 <Range> (Unit)	Parameter3 <Range> (Unit)	Parameter4 <Range> (Unit)
X	1	XX/M	Screen				DDMONYYYY	HH:MM:SS	XXX	X.X	X.X	XXX HN
			1	X	-1	-22.50	DDMONYYYY	HH:MM:SS	XXX HYR	X.X	X.X	XXX HYR+
			Recheck				DDMONYYYY	HH:MM:SS	XXX	X.X	X.X	XXX

<similar to above for all subjects/time points>

Programmer Notes: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Programmer Notes: Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.1.6 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional flag for PI flag (+) based on positive CS/Clinically Significant comments. Present this derived 4th column in all tables, and list only PI-determined out-of-range clinically significant lab values in Table 14.3.4.5.

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
#Age is calculated from the date of first dosing. F = Female, M = Male
H = Above reference range, L = Below reference range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_lab.sas 27NOV2015 18:44

Appendix 16.2.8.1.6 Clinical Laboratory Report – Comments (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Department	Test	Result	Unit	Comment
X	2	1	X	X	X.XX	DDMONYYYY	Serum Chemistry	Chloride	XXX	mg/dL	NOT SIGNIFICANT IN CONTEXT OF STUDY
	3	Screen				DDMONYYYY	Serum Chemistry	Direct Bilirubin	X.X	mg/dL	LESS THAN 0.1 MG/DL

Programmer Note: Footnote NCS = Not clinically significant, CS = Clinically significant, WNL = Within normal limits, etc. as needed

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_lco.sas 27NOV2015 18:35

Appendix 16.2.8.2 Vital Signs (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Test	Blood Pressure (mmHg) Systolic/Diastolic	Pulse (bpm)	Respiration (rpm)	Temperature (°C)	Weight (kg)	Comment
X	1	Screen				DDMONYYYY	HH:MM:SS						XX.X	<This
								column SIT1		XXX/	XX	XX	XX	XX.X
										prints only				
						R	HH:MM:SS	SIT1	XXX/ XX	XX	XX	XX.X		if data are
						R	HH:MM:SS	SIT1	XXX/ XX	XX	XX	XX.X		present.>
	1		X	-1	-21.00	DDMONYYYY	HH:MM:SS	SIT1	XXX/ XX	XX	XX	XX.X		

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
SIT1 = 1-minute sitting, R = Recheck value

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_vit.sas 27NOV2015 18:35

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Result	Heart Rate (bpm)	PR (msec)	QRS (msec)	QT (msec)	QTcF* (msec)	Comments
X	1	Screen				DDMONYYYY	HH:MM:SS	ANCS	XX	XXX	XX	XXX	XXX	EARLY REPOLARIZATION; LEFT AXIS DEVIATION
		1	X	-1	-18.50	DDMONYYYY	HH:MM:SS	ANCS	XX	XXX	XX	XXX	XXX	LEFT AXIS DEVIATION
				1	0.17	DDMONYYYY	HH:MM:SS	< >	XX	XXX	XX	XXX	XXX	SINUS BRADYCARDIA
				8	167.75	DDMONYYYY	HH:MM:SS	< >	XX	XXX	XX	XXX	XXX	

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
ANCS = Abnormal, not clinically significant
QTcF* = QT corrected for heart rate using Fridericia's correction.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ecg.sas 27NOV2015 18:35

Appendix 16.2.8.4 Immunogenicity Response Results (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Screening Result	Confirmatory Result	Titer Value*	Comments
X	1	1	X	1	-0.50	DDMONYYYY	HH:MM:SS	Negative			<This column prints only if data are present.>
				15	336.00	DDMONYYYY	HH:MM:SS	Negative			
				29	672.00	DDMONYYYY	HH:MM:SS	Positive	Positive	XX	

Note: Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment P: < >
*If the screening result is negative, confirmatory and titer assays will not be performed. If confirmatory result is negative, but the screening was positive, the titer assay will not be performed.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ada.sas 27NOV2015 18:35