Statistical Analysis Plan

A Phase 1, Single Ascending Dose, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Pharmacodynamics of E-WE Thrombin as an Intravenous Bolus in Healthy Adult Subjects

Protocol No: CA19169
Sponsor Project No.: EWE-17-01
US PIND No.: PTS #PS003017; CRMTS #10353; IND No. 018154
Final Protocol Date: 19 February 2018
Amendment 1 Date: 27 March 2018
Amendment 2 Date: 14 May2018
Compound Name: E-WE thrombin

Celerion Project CA19169
Final Version 1.0
Date: 25 July 2018

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Statistical Analysis Plan Signature Page

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Issue Date: 25 July 2018

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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 SAP and/or driven by the data, or requested by 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) bolus doses of E-WE thrombin when administered to healthy adult subjects.

The **secondary objective** is to assess the pharmacodynamics (PD) of single IV bolus doses of E-WE thrombin when administered to healthy adult subjects. The activated protein C/protein C inhibitor complex (APC-PCI) will be used as a surrogate biomarker for drug exposure.

2.2 Endpoints

The **primary endpoints** of the study will be the number and severity of treatment-emergent adverse events (TEAEs) following single IV bolus doses of E-WE thrombin and placebo. In addition, physical examinations, vital signs, electrocardiograms (ECGs), clinical laboratory tests (including coagulation), thrombin time, immunogenicity, and injection site reaction will be assessed throughout the study.

The **secondary endpoints** are the PD (i.e., APC-PCI) of E-WE thrombin following single IV bolus doses. PD will act as a surrogate for pharmacokinetics (PK) of E-WE thrombin.

3. STUDY DESIGN

This is a randomized, double-blind, placebo-controlled, single ascending dose (SAD) study conducted at one study center in the United States (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 receive a single IV bolus of E-WE thrombin or placebo. Subjects will participate in only 1 cohort.

Cohort 1 will contain a sentinel group of 2 subjects (1 placebo and 1 active) who will be dosed at least 28 days before the remaining group of subjects. The remaining subjects in Cohort 1, and subjects in each of Cohorts 2, 3, and 4 will be dosed in 2 groups separated by at least 14 days (2 subjects in each group [Cohort 1] or 2 subjects in the first group and 3 subjects in the second group [Cohorts 2-4]). The placebo will be randomized to one of the groups.

Dose escalation to the next dose level (i.e., next cohort) will not take place until after the Principal Investigator (PI) has reviewed the safety data. If any findings in the safety data are of concern, then the Safety Review Committee (SRC) comprised of but not limited to, the Sponsor, medical monitor, and the PI will convene to determine if adequate safety and tolerability from the previous cohort has been demonstrated to permit proceeding to the next cohort. Data from all subjects in the cohort will be used and reviewed for a dose escalation decision and a minimum of 4 subjects must complete the study (up to Day 14) before proceeding to the next higher dosing cohort.

Subjects will participate in only one cohort. An attempt will be made to have at least 30% of the total subjects of a race/ethnicity minority group. An attempt will be made to include at least 2 females per cohort.

Safety (i.e., physical examinations, vital signs, ECGs, clinical laboratory tests [including coagulation], thrombin time, immunogenicity, injection site reaction, and AEs) will be assessed throughout the study.

Blood samples will be collected for PD assessment (i.e., APC-PCI) of E-WE thrombin.

Blood samples will be also collected for the ADA evaluation.

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. At all times, a subject may be required to remain at the CRU for longer at the discretion of the PI or designee.

Subjects (including those who terminate early) will return on Days 14 and 28 for follow-up (FU) procedures (coagulation sample collection, thrombin time measurement, and immunogenicity sample collection) and to determine if any AE has occurred since the last study visit). Subjects who terminate the study early will be asked to continue aPTT and thrombin time monitoring as scheduled until Day 28.

Any subjects for whom aPTT and/or thrombin time did not reach ± 10% of the baseline value or within the normal range by Day 14, will return every 7 days (±2 days) until aPTT and thrombin time reach ±10% of the baseline value or within

the normal range and for a FU visit (i.e., FU procedures and AE evaluation listed on Day 28 will be repeated) 7 days (± 2 days) after it was reached.

The total planned duration of subject participation is approximately 56 days from screening to last FU.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety population: All subjects who received the study drug (active or placebo) will be included in the safety summary.

PD population: All subjects receiving the study drug (active or placebo) and having any measurable PD data will be included in the PD data set. The Sponsor will assess the real time aPTT on-site. The protein C samples will be processed by Celerion associates and then shipped to Aronora for later analysis.

4.2 Preliminary Data and Interim Analysis

If there are safety concerns, all available blinded safety/tolerability data (i.e., physical examinations, ECGs, vital signs, clinical laboratory tests [including coagulation], thrombin time, injection site reaction, and AEs available for all subjects who have completed up to Day 14 procedures) will be reviewed by the SRC prior to dose escalation.

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. These interim analyses will be performed on data that will be edit-checked and monitored.

A safety programmer and a biostatistician at Celerion who are not involved with the present study will be unblinded to prepare the required unblinded safety tables, figures, and data listings. All the personnel related to the present study will remain blinded.

5. TREATMENT DESCRIPTIONS

E-WE thrombin will be supplied as sterile, non-pyrogenic, preservative-free liquid for IV administration. E-WE thrombin will be supplied as 0.1 mg/mL for IV use and given as a single IV bolus, according to the planned dose (mcg/kg) for each cohort, as noted Table 5.1. Matching placebo will be supplied as sterile formulation buffer for injection via IV route.

Table 5.1 Dosing Duration

Dose Level	Manual Push Time
Cohort 1: 0.5 mcg/kg	~ 15 seconds
Cohort 2: 1.0 mcg/kg	~ 15 seconds
Cohort 3: 2.0 mcg/kg	~ 30 seconds
Cohort 4: 4.0 mcg/kg	~ 1 minute

Dose levels will be used in the presentation of tables, figures, and listings. Dose levels will be described as proposed in Table 5.2 below:

Table 5.2 Description of Dose Levels

Dose Level	Abbreviated Description
0.5 mcg/kg	0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg	1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg	2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg	4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo	Placebo Solution (IV bolus)

Note: The planned dose levels described above may be revised up or down or a dose level may be repeated based upon data from a previous dose level, however, doses will not exceed 4.0 mcg/kg without a protocol amendment.

6. PHARMACODYNAMIC ANALYSIS

There will be 5 dose levels consisting of 4 active drug and 1 pooled placebo. The placebo subjects from all dose levels will be pooled into a single placebo group for all summaries and presentations.

Individual, mean, and median data will be presented graphically for all dose levels as well as pooled placebo group.

Additional analyses may be performed as deemed necessary upon review of the data.

6.1 APC-PCI

APC-PCI values will be listed and presented graphically.

Plasma for APC-PCI will be collected at predose, 0.083, 0.25, 0.5, 1, 2, 4, and 24 hours postdose. The sample times and Hour 0 are in relation to start of IV bolus.

Sample analysis for APC-PCI will be performed by Celerion (Lincoln, NE).

6.2 Real-Time aPTT

Blood samples for real-time aPTT will be analyzed by Aronora on site. Samples will be collected in blood collection tubes containing 3.2% sodium citrate by a Celerion employee and transferred directly to an Aronora employee for sample processing as per their internal procedures.

At the end of the study, platelet poor plasma samples obtained by centrifugation of citrated blood will be shipped to the Sponsor for their internal analyses.

Blood samples for the assessment of real-time aPTT will be collected at predose, 0.083, 0.25, 0.5, 1, 2, 4, and 24 hours postdose.

Data for real-time aPTT will not be analyzed by Celerion.

6.3 Protein C

Blood sample for the assessment of protein C will be collected at the following timepoints: predose, 1, 2, and 24 postdose. The protein C samples will be processed by Celerion associates and then shipped to Aronora for their internal analyses.

Data for protein C will not be analyzed by Celerion.

6.4 Data Summarization and Presentation

All PD markers will be tabulated by dose level and a pooled placebo group. Summary statistics, including the number of observations (n), arithmetic mean (mean), standard deviation (SD), coefficient of variation (%CV), minimum, median, and maximum will be computed.

The level of precision will be presented as follows: n will be presented without decimal, mean, SD, minimum, median, and maximum will be presented to 1 decimal place. All percentages will be presented to 1 decimal place.

7. IMMUNOGENICITY

Plasma and serum samples for immunogenicity testing will be collected on Days -1, 14, and 28. If ADA are detected on Days 14 and 28, the check-in sample on Day -1 will be also evaluated. ADA detection will be reported and summarized.

Assessment of ADA will be performed by Haemtech Biopharma Services, Inc.

For samples with a positive confirmatory assay, titers of ADA will be presented with the same level of precision as received from the bioanalytical laboratory. A table will be provided for ADA positive duration for each dose level, where duration is defined

as the time interval between the first postdose and last postdose occurrence of positive ADA.

8. SAFETY

No inferential statistics will be performed on the safety endpoints.

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 results.

Applicable continuous variables will be summarized using the number of observations (n), mean, SD, minimum, median, and maximum. Frequency counts will be reported for categorical data, when appropriate. The placebo subjects from all cohorts will be pooled into a single group for summarization.

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.

For laboratory, ECGs, and vital signs, 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

Subject disposition will be listed and summarized by number of subjects dosed, completed, and discontinued the study with discontinuation reasons by dose level, pooled placebo, and for overall the study.

8.2 Demographics

Demographic data will be listed and summarized. Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index [BMI]) by dose level, pooled placebo, and for overall the study. Frequency counts will be provided for categorical variables (race, ethnicity, and sex) by dose level, pooled placebo, and for overall the study. Age will be derived from date of birth to date of first dosing.

8.3 Adverse Events

All AEs occurring during this clinical trial will be coded using the MedDRA®, Version 21.0 or a later version if available. All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, dose level, placebo, severity, relationship to study drug, and action; however, only treatment-

emergent AEs (TEAEs) will be summarized. Any non-drug procedure performed due to an AE will be listed by subject.

A TEAE is defined as an AE that is starting or worsening at the time of or after the study drug dose administration. 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 and the maximum severity will be recorded. If the onset time of an AE is missing and the onset date is the same as the treatment dosing date or does not fall on a dosing date, 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 TEAE and corresponding percentage by dose level, pooled placebo, and overall the study. The number of TEAEs will be summarized in a similar way. Percentages will be based on the total number of subjects dosed or total number of TEAEs, respectively, for each dose level, pooled placebo, or overall the study, as appropriate. In addition, the number of TEAEs will be summarized by severity and relationship to study drug.

If present, serious adverse events (SAEs) will be listed, displayed in a table, and a narrative included in the study CSR.

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

Clinical laboratory reference ranges will be listed by laboratory group, test, sex, and age category, where appropriate.

Serum chemistry, hematology, coagulation, and urinalysis will be performed at the following time points:

Table 8.1 Laboratory Data Time Points

Test	Period	Day	Hour
Serum Chemistry/ Hematology/ Urinalysis	Screen		
	1	-1	Check-in
		2*	24
Coagulation	Screen		
		1	Predose, 0.083, 0.25, 0.5, 1, 2, 4
		2*	24
		14	FU
		28	FU
*Prior to discharge from CRU or at early termination from the study. FU = Follow-up			

Out-of-normal range flags (1st flag) will be recorded as follows:

- for numerical results: high (H) and low (L);
- for categorical results: did-not-match (*).

If a value fails the reference range, it will automatically be compared to a computer clinically significant (CS) range (2nd flag).

- If the value falls within the computer CS range, it will be noted as “N” for not clinical significant.
- If the value fails the 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 PI flags (3rd flag):
  - "N", not clinically significant,
  - "R", requesting a recheck,
  - "^", checking at the next scheduled visit,
  - "Y", clinically significant.

To distinguish the PI flags from the computer CS range flags, the PI flags “N” and “Y” will be presented as “-“ and “+” in the data listing, respectively.

In addition, a derived flag (a 4th 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. Out-of-range values are considered to be values that are out-of- normal range as defined by the clinical laboratory. Results that are indicated as CS by the PI (either in the PI flag or in PI comments) will be also listed in a separate table.

For all safety values that are numeric, descriptive statistics will be presented for each laboratory test by dose level, pooled placebo, and time point. Change from baseline will be summarized in a similar way. In addition, for the activated partial thromboplastin time (aPTT) (coagulation test), the fold change from baseline will be calculated and summarized in a similar way. The following formula will be used for the calculation: postdose/baseline. Baseline is defined as the result closest and prior to the dose on Day 1 (i.e., Day 1 for Coagulation and Day -1 for the rest of tests) which may include unscheduled or recheck results, whichever is later. 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

Single measurements of systolic and diastolic blood pressure, heart rate, body temperature, and respiratory rate will be obtained in supine position at the following time points:

Table 8.2 Vital Signs Data Time Points

Measurement	Period	Day	Hour
Blood Pressure / Heart Rate/ Respiratory Rate / Body Temperature	Screen		
	1	1	Predose, 0.25, 0.5, 1, 2, 4
		2*	24
*Prior to discharge from CRU or at early termination from the study.			

Vital signs tests will be summarized by dose level, pooled placebo, and time point. Change from baseline will be summarized in a similar way. Baseline is defined as the result closest and prior to the dose on Day 1, which may include unscheduled or recheck results, whichever is later. 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 ECGs (i.e., HR, PR, QRS, QT, and QTcF [i.e., QT corrected for heart rate using Fridericia's correction]) will be measured at the following time points:

Table 8.3 12-Lead Electrocardiogram Data Time Points

Parameter	Period	Day	Hour
HR, PR, QRS, QT, QTcF	Screen		
	1	1	Predose
		2*	24
*Prior to discharge from CRU or at early termination from the study.			

ECGs will be summarized by dose level, pooled placebo, and time point. Change from baseline will be summarized in a similar way. Baseline is defined as the result closest and prior to the dose on Day 1, which may include unscheduled or recheck results, whichever is later. Postdose unscheduled events or rechecks will not be included in summaries. Similarly early termination results will not be included in summaries.

The QTcF values that are > 450 ms and increase from baseline > 30 ms, will be flagged in the data listings.

8.7 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary Version 01-Mar-2018 or a later version if available and listed.

8.8 Physical Examination

Full physical examination will be performed at screening. A symptom-driven physical examination will be performed at check-in and FU or may be performed at other scheduled times, at the PI's or designee's discretion. Abnormal findings will be reported as medical history or adverse events. All data found in the CRF will be listed.

8.9 Injection Site

Injection and needle puncture site reactions for drug administration will be evaluated at the following time points:

Table 8.4 Injection Site Reaction

Parameter	Period	Day	Hour
Site Reaction	Screen		
	1	1	Predose, 1
		2*	24
*Prior to discharge from CRU or at early termination from the study.			

Abnormal findings will be reported as adverse events.

9. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

The analyses described in this SAP are aligned with those analyses described in the protocol.

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 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 Subject Disposition Summary (Safety Population)

Section 11:

Table 11-1 Demographic Summary (Safety Population)

Pharmacodynamics

Table 11-2 Summary of APC-PCI Pharmacodynamics Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, and 4.0 mcg/kg E-WE Thrombin

Figure 11-1 Mean Plots of APC-PCI Pharmacodynamics Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, and 4.0 mcg/kg E-WE Thrombin

Immunogenicity

Table 11-3 Summary of Anti- E-WE Thrombin Plasma ADA Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, and 4.0 mcg/kg E-WE Thrombin

Table 11-4 Summary of Anti-WT Thrombin Serum ADA Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, and 4.0 mcg/kg E-WE Thrombin

Section 12:

Table 12-1 Adverse Event Frequency by Dose Level - Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

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 CSR. Table and figure titles may be renumbered as appropriate during the compilation of the CSR.

14.1 Demographic Data Summary Tables

Table 14.1.1 Subject Disposition Summary (Safety Population)
Table 14.1.2 Demographic Summary (Safety Population)

14.2 Pharmacodynamic/Immunogenicity Data Summary Tables and Figures

Pharmacodynamic Tables

14.2.1 Plasma APC-PCI Tables

Table 14.2.1.1 Plasma APC-PCI Levels (<units>) Following a Single IV Dose of 0.5 mcg/kg E-WE Thrombin (Pharmacodynamic Population)

Immunogenicity Tables

14.2.2 Anti-E-WE and Anti-WT Thrombin Antibody

Pharmacodynamic Figures

14.2.3 Plasma APC-PCI Figures

14.3.4 Abnormal Laboratory Value Listing (each patient)

Table 14.3.4.1 Out-of-Range Values and Recheck Results – Serum Chemistry (Safety Population)
Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology (Safety Population)
Table 14.3.4.3 Out-of-Range Values and Recheck Results – Coagulation (Safety Population)
Table 14.3.4.4 Out-of-Range Values and Recheck Results – Urinalysis (Safety Population)
Table 14.3.4.5 Clinically Significant Laboratory and Corresponding Results (Safety Population)

14.3.5 Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data

Table 14.3.5.1 Clinical Laboratory Summary – Serum Chemistry (Safety Population)
Table 14.3.5.2 Clinical Laboratory Change from Baseline – Serum Chemistry (Safety Population)
Table 14.3.5.3 Clinical Laboratory Shift from Baseline – Serum Chemistry (Safety Population)
Table 14.3.5.4 Clinical Laboratory Summary – Hematology (Safety Population)
Table 14.3.5.5 Clinical Laboratory Change from Baseline – Hematology (Safety Population)
Table 14.3.5.6 Clinical Laboratory Shift from Baseline – Hematology (Safety Population)
Table 14.3.5.7 Clinical Laboratory Summary – Coagulation (Safety Population)
Table 14.3.5.8 Clinical Laboratory Change from Baseline – Coagulation (Safety Population)
Table 14.3.5.9 Clinical Laboratory Fold Change from Baseline – Activated Partial Thromboplastin Time (Safety Population)
Table 14.3.5.10 Clinical Laboratory Shift from Baseline – Coagulation (Safety Population)
Table 14.3.5.11 Clinical Laboratory Summary - Urinalysis (Safety Population)
Table 14.3.5.12 Clinical Laboratory Change from Baseline – Urinalysis (Safety Population)
Table 14.3.5.13 Clinical Laboratory Shift from Baseline – Urinalysis (Safety Population)

Table 14.3.5.14 Vital Sign Summary (Safety Population)

Table 14.3.5.15 Vital Sign Change from Baseline (Safety Population)

Table 14.3.5.16 12-Lead Electrocardiogram Summary (Safety Population)

Table 14.3.5.17 12-Lead Electrocardiogram Change from Baseline (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 Discontinuation (Safety Population)

16.2.2 Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3 Subjects Excluded from Pharmacodynamic Analysis

Appendix 16.2.3 Subjects Excluded from Pharmacodynamic/Immunogenicity Analysis

Note: Appendices 16.2.2 and 16.2.3 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 and Surgical 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 16.2.5.3.1 Check-in and Return Criteria
Appendix 16.2.5.3.2 Check-in Criteria and Responses (Safety Population)
Appendix 16.2.5.4.1 Test Compound Description
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 Efficacy/Pharmacokinetic/Pharmacodynamic Response Data

Appendix 16.2.6.1 Individual Plasma APC-PCI Levels Versus Time Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, 4.0 mcg/kg, or Placebo (Linear Scale) for <Subject #>
Appendix 16.2.6.2 Plasma Anti-E-WE Thrombin Antibodies

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 Related Procedure (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 - Coagulation (Safety Population)
Appendix 16.2.8.1.4 Clinical Laboratory Report - Urinalysis (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 CSR. 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.

11.1 In-text Summary Tables Shells

Table 10-1 Subject Disposition Summary (Safety Population)

	Dose Level				Pooled	
Disposition	**0.5 mcg/kg**	**1.0 mcg/kg**	**2.0 mcg/kg**	**4.0 mcg/kg**	**Placebo**	**Overall**
Dosed	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Completed	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Discontinued	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
<Reason1>	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
<Reason2>	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
<AE = Adverse event>

Source: Table 14.1.1
Program: /CAXXXXX/sas_prg/stsas/intext/t_disp.sas DDMMMYYYY HH:MM

Table 11-1 Demographic Summary (Safety Population)

Trait	Category/ Statistics	Dose Level				Pooled Placebo	Overall
		0.5 mcg/kg	1.0 mcg/kg	2.0 mcg/kg	4.0 mcg/kg		
Sex	Female	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Race	Asian	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Black or African American	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	White	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Ethnicity	Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Not Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Age* (yrs)	n	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX	XX
Weight (kg)	n	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX	XX

0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
*Age is calculated at the time of first dosing.
BMI = Body mass index

Source: Table 14.1.2
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_dem.sas DDMMMYYYY HH:MM

Programmer Notes:

- This is just a mock table shell. Please use the race categories listed in the CRF.
- Height (cm) and BMI (kg/m^2) will be also summarized in this table.

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

Table 11-2 Summary of APC-PCI Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, and 4.0 mcg/kg E-WE Thrombin

Hour	0.5 mcg/kg (N=X)	1.0 mcg/kg (N=X)	2.0 mcg/kg (N=X)	4.0 mcg/kg (N=X)	Placebo (N=X)
XX	X ± X	X ± X	X ± X	X ± X	X ± X
XX	X ± X	X ± X	X ± X	X ± X	X ± X
XX	X ± X	X ± X	X ± X	X ± X	X ± X
XX	X ± X	X ± X	X ± X	X ± X	X ± X

N is the total number of subjects dosed at each dose level.
Source: Table XXX

Treatments:

- 0.5 mcg/kg E-WE thrombin (IV bolus)
- 1.0 mcg/kg E-WE thrombin (IV bolus)
- 2.0 mcg/kg E-WE thrombin (IV bolus)
- 4.0 mcg/kg E-WE thrombin (IV bolus)
- Pooled Placebo (IV bolus)

Programmer's note:

- Arithmetic mean ± SD will be presented.
- Table 11-2 the source table will be 14.2.1.1 through 14.2.1.5.

In-text Tables 11-3 and 11-4 will be in the following format.

Table 11-3 Summary of Anti- E-WE Thrombin Plasma ADA Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, and 4.0 mcg/kg E-WE Thrombin

	0.5 mcg/kg (n=x)	**1.0 mcg/kg (n=x)**	**2.0 mcg/kg (n=x)**	**4.0 mcg/kg (n=x)**	**Placebo (n=x)**
Predose (Day -1)					
ADA Test Result Number Negative/Positive	X/X	X/X	X/X	X/X	X/X
Confirmatory E-WE Thrombin Positive	X	X	X	X	X
Neutralizing Positive	X	X	X	X	X
Day 14					
ADA Test Result Number Negative/Positive	X/X	X/X	X/X	X/X	X/X
Confirmatory E-WE Thrombin Positive	X	X	X	X	X
Neutralizing Positive	X	X	X	X	X
Day 28					
ADA Test Result Number Negative/Positive	X/X	X/X	X/X	X/X	X/X
Confirmatory E-WE Thrombin Positive	X	X	X	X	X
Neutralizing Positive	X	X	X	X	X

Presentation of Data:

- The following outcomes will be presented as number of subjects (% of the population): confirmatory positive will be a percentage of the total subject in the dose level
- Number of subjects will be presented as an integer (no decimals)
- 4 dose levels will be presented instead on the same table
- Internal Table template: Table ITPar1

Programmer's note:

- Table 11-3 the source table will be 14.2.2.1.
- Table 11-4 the source table will be 14.2.2.2.
- ADA collection times: Predose, Day 14 and Day 28 postdose.

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

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

	Dose Level				Pooled	
Adverse Event*	**0.5 mcg/kg**	**1.0 mcg/kg**	**2.0 mcg/kg**	**4.0 mcg/kg**	**Placebo**	**Overall**
Number of Subjects With TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Subjects Without TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
System Organ Class 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
System Organ Class 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
*Adverse events are classified according to MedDRA Version 21.0.
TEAEs = Treatment-emergent adverse events
If a subject has 2 or more clinical adverse events, 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 DDMMMYYYY HH:MM

11.2 Section 14 Summary Tables Shells

Table 14.1.1 Subject Disposition Summary (Safety Population)

	Dose Level					
Disposition	0.5 mcg/kg	1.0 mcg/kg	2.0 mcg/kg	4.0 mcg/kg	Pooled Placebo	Overall
Dosed	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Completed	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Discontinued	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
<Reason 1>	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
<Reason 2>	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)

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

Table 14.1.2 Demographic Summary (Safety Population)

Trait	Category/ Statistics	Dose Level 0.5 mcg/kg	1.0 mcg/kg	2.0 mcg/kg	4.0 mcg/kg	Pooled Placebo	Overall
Sex	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Race	Asian	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Ethnicity	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age* (yrs)	n	X	X	X	X	X	X
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX	XX
Weight (kg)	n	X	X	X	X	X	X
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX	XX

Programmer Note: This is just a mock table shell. Please use the race categories listed in the CRF. Please also include Height (cm) and BMI (kg/m2).

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
*Age is calculated at the time of first dosing.

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

Tables 14.2.1.1 through 14.2.1.5 will be in the following format:

Table 14.2.1.1 Plasma APC-PCI Levels (<units>) Following a Single IV Dose of 0.5 mcg/kg E-WE Thrombin (Pharmacodynamic Population)

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

. = Value missing or not reportable.

Programmer Notes:

- PD time points for the 3 PD markers are presented in Sections 6.1 through 6.3 of the SAP
- Verify Section 6.4 for presentation of descriptive statistics.

Program: /AAXXXXX/ECR/sas prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.2.2.1 and 14.2.2.2 will be in the following format.

Table 14.2.2.1 Plasma Anti-E-WE Thrombin Antibody Detection Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, or 4.0 mcg/kg E-WE Thrombin Summary by Collection Time and Treatment - Number of Subjects (% Total Subjects)

		0.5 mcg/kg				1.0 mcg/kg			
		Day X	Day X	Day X	Overall*	Day X	Day X	Day X	Overall*
Test	Result	N=X	N=X	N=X	N = X	N=X	N=X	N=X	N = X
Initial	Negative	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Positive	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Confirmatory	Negative	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Positive	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Neutralizing	Negative	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Positive	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

N is the total number of subjects dosed at each dose level.

Programmer Note:
- Immunogenicity sampling times: Day -1, Day 14, and Day 28
- Treatments:
  - 0.5 mcg/kg E-WE thrombin (IV bolus)
  - 1.0 mcg/kg E-WE thrombin (IV bolus)
  - 2.0 mcg/kg E-WE thrombin (IV bolus)
  - 4.0 mcg/kg E-WE thrombin (IV bolus)
  - Pooled Placebo: Placebo Solution (IV bolus)

Note: * if the response of a subject is positive at least once postdose, it will be counted as "positive"; otherwise will be considered as
"negative".
Only screening positives will be reassayed for confirmatory analysis.

Program: /AAXXXXX/ECR/sas_prg/pksas PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.2.2.3 through 14.2.2.4 will be in the following format:

Table 14.2.2.3 Summary of Titers for Plasma Anti-E-WE Thrombin Antibody

Subject	0.5 mcg/mL	1.0 mcg/mL
X	XX	XX
n	X	X
Mean	XX.X	XX.X
SD	X.XX	X.XX
Minimum	XX	XX
Median	XX.X	XX.X
Maximum	XX	XX

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)

Programmer note: 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.

Tables 14.2.2.5 and 14.2.2.6 will be in the following format.

Table 14.2.2.5 Anti-E-WE Thrombin Antibody +Duration by Dose Level Following Administration of a Single IV Dose of 0.5, 1.0, 2.0, or 4.0 mcg/kg E-WE Thrombin

E-WE Thrombin	Subject	Duration*
0.5 mcg/kg	X	X Days
	X	X Days
1.0 mcg/kg	X	X Days
	X	x Days

Programmer note:

- Treatments:
  - 0.5 mcg/kg E-WE thrombin (IV bolus)
  - 1.0 mcg/kg E-WE thrombin (IV bolus)
  - 2.0 mcg/kg E-WE thrombin (IV bolus)
  - 4.0 mcg/kg E-WE thrombin (IV bolus)
  - Pooled Placebo: Placebo Solution (IV bolus)

Note: * duration is defined as the time interval between the first postdose and last postdose occurrence of positive ADA. If positive ADA is only on Day 28 the duration will be N/A.

Note: Figures of 14.2.3 and In-text Figure 11-1 will be in the following format.

Figure 14.2.3.1

Mean <Matrix Analyte> Concentrations Versus Time
(Linear Scale)

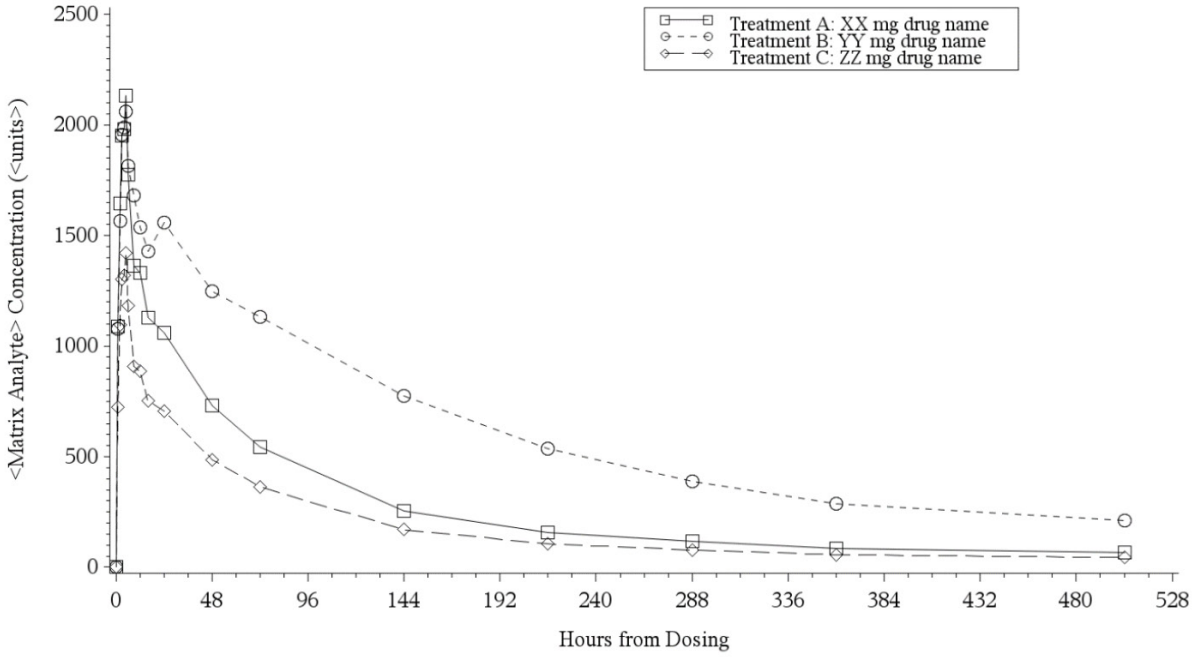
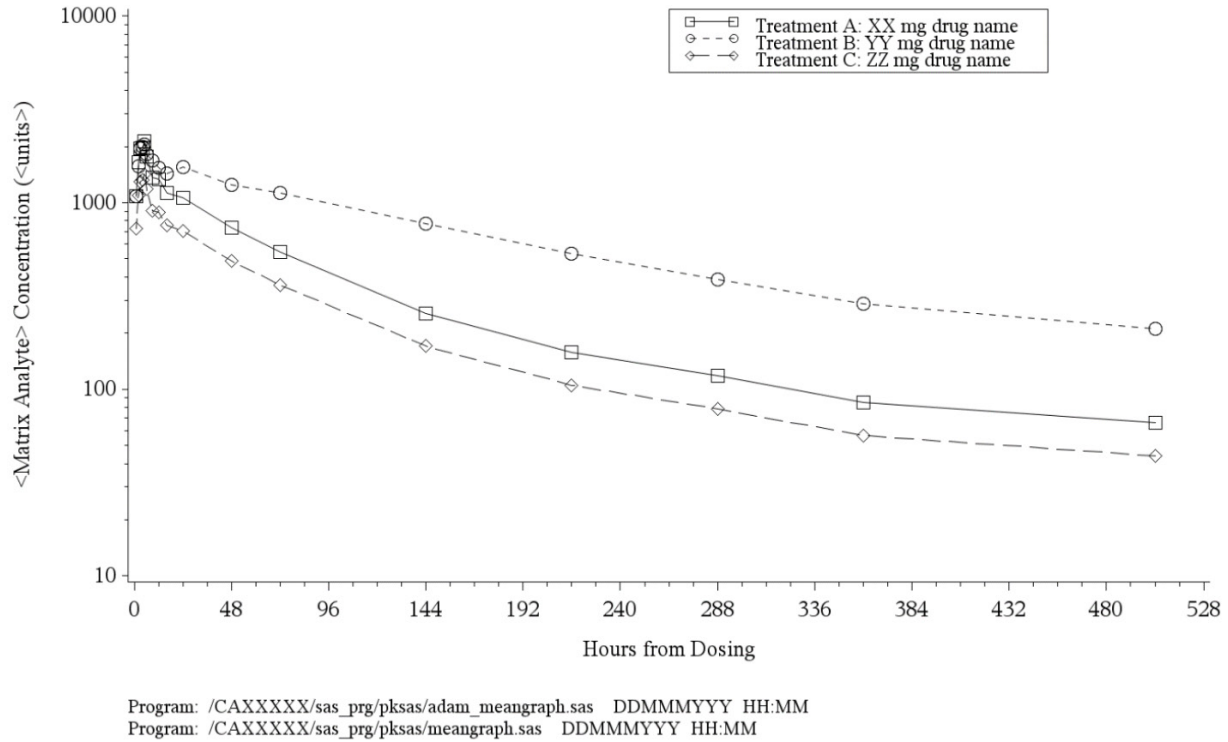


Figure 14.2.3.2

Median <Matrix Analyte> Concentrations Versus Time
(Linear Scale)

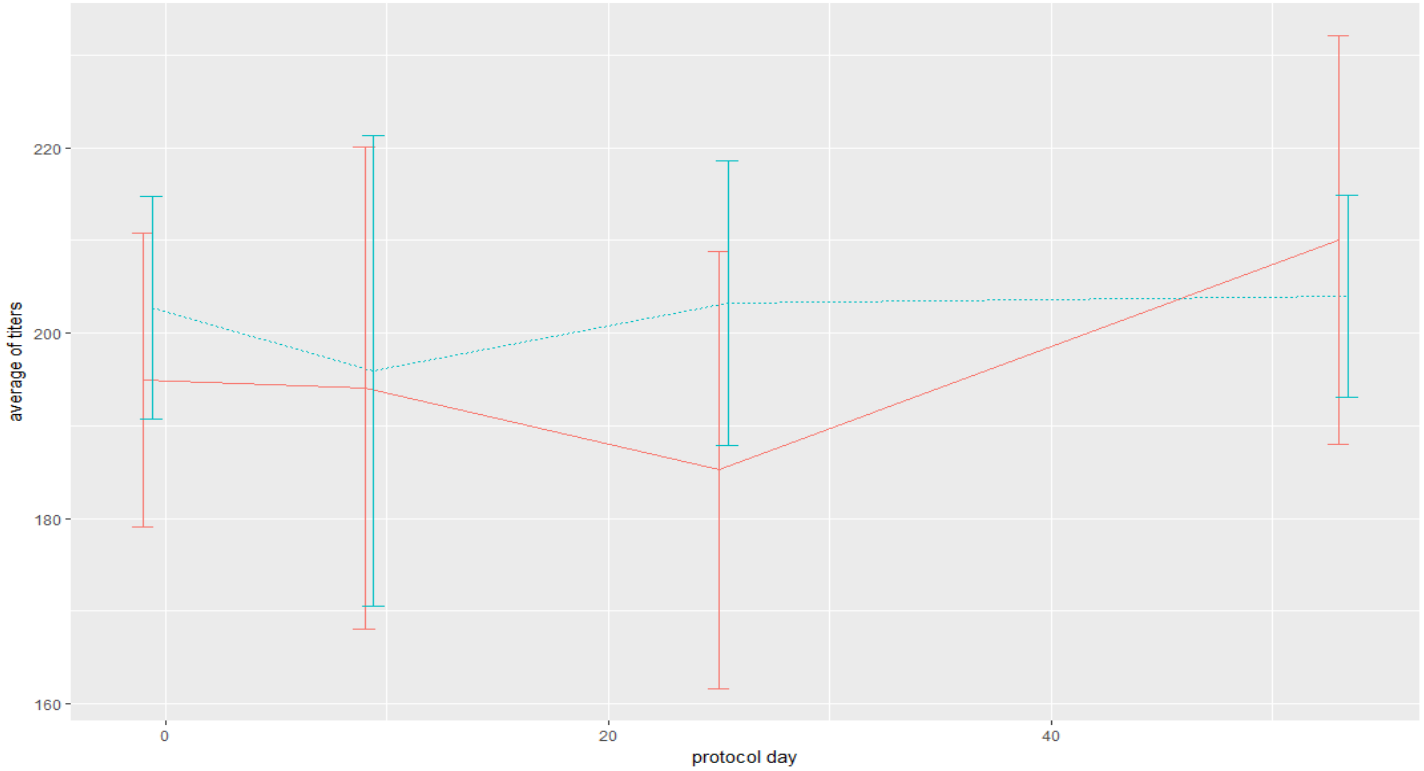


Notes for Generating the Actual Mean Figure:

- Legend will be <> and <>
- Y axis label will be <Matrix> <Analyte> Concentration (<unit>)
- X axis label will be "Hours From Dosing"
- Mean plots will have 4 dose levels and placebos overlayed.
- Please generate figures in color. Please use the same color and symbol for each treatment throughout.

Note: Figures of 14.2.4.1 and 14.2.4.3 will be in the following format.

Figure 14.2.4.1 Summary of Titers for Plasma Anti-E-WE Thrombin Antibody by Treatment – Line Plot (Mean ± SD) for Confirmatory Test Results

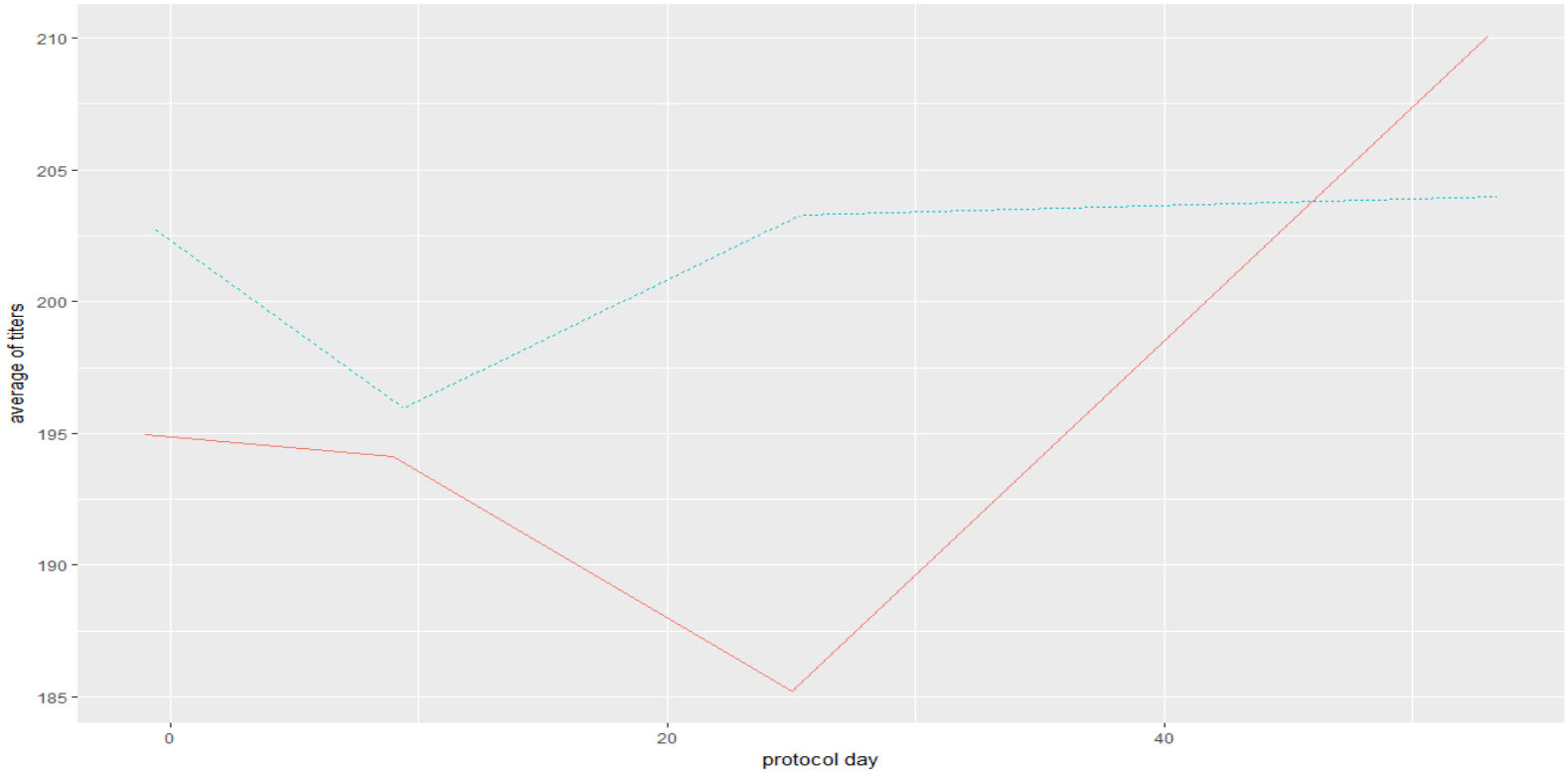


Programmer Note: If data for neutralizing test are available, please present similar figure. Plots to be generated in SAS.

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

Note: Figures of 14.2.4.2 and 14.2.4.4 will be in the following format.

Figure 14.2.4.2 Summary of Titers for Plasma Anti-E-WE Thrombin Antibody by Treatment – Line Plot (Mean) for Confirmatory Test Results



Programmer Note: If data for neutralizing test are available, please present similar figure. Plot to be generated in SAS.

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

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

	Dose Level					
Adverse Event*	0.5 mcg/kg	1.0 mcg/kg	2.0 mcg/kg	4.0 mcg/kg	Pooled Placebo	Overall
Number of Subjects Dosed	XX (XX%)	XX (XX%)	XX (XX%)	XX (XXX%)	XX (XX%)	XX (XXX%)
Number of Subjects With TEAEs^	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects Without TEAEs^	XX (XX%)	XX (XX%)	XX (XX%)	XX (XXX%)	XX (XX%)	XX (XXX%)
Nervous system disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dizziness	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Headache	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Presyncope	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Respiratory, thoracic and mediastinal disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dry throat	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Oropharyngeal pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sinus congestion	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sneezing	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%)
Fatigue	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Thirst	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
*Adverse events are classified according to MedDRA Version 21.0. ^ = Treatment-emergent adverse events
If a subject has 2 or more clinical adverse events, the subject is counted only once within a category. The same subject may appear in different categories.

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

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

	Dose Level					
Adverse Event*	0.5 mcg/kg	1.0 mcg/kg	2.0 mcg/kg	4.0 mcg/kg	Pooled Placebo	Overall
Number of TEAEs	X (100%)	X (100%)	X (100%)	X (100%)	X (XX%)	X (XX%)
Nervous system disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dizziness	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Headache	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Presyncope	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Respiratory, thoracic and mediastinal disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dry throat	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Oropharyngeal pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sinus congestion	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sneezing	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%)
Fatigue	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Thirst	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
*Adverse events are classified according to MedDRA Version 21.0. ^ = Treatment-emergent adverse events

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

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

Adverse Event*	Dose Level/ Pooled Placebo	Number of Subjects With TEAEs	Number of TEAEs	Severity/Intensity				Relationship to Study Drug				
				Grade 1	Grade 2	Grade 3	Grade 4	Unrelated	Unlikely	Possibly	Probably	Likely
Dizziness	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
Dry eye	X	X	X	X	X	X	X	X	X	X	X	X
Dry mouth	X	X	X	X	X	X	X	X	X	X	X	X
Dry throat	X	X	X	X	X	X	X	X	X	X	X	X
Ear pain	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
Fatigue	X	X	X	X	X	X	X	X	X	X	X	X
Headache	X	X	X	X	X	X	X	X	X	X	X	X
Dizziness	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
Hyperhidrosis	X	X	X	X	X	X	X	X	X	X	X	X
Laceration	X	X	X	X	X	X	X	X	X	X	X	X
Limb crushing injury	X	X	X	X	X	X	X	X	X	X	X	X
Muscle twitching	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X	X	X
Pooled Placebo		XX	XX	X	X	X	X	X	X	X	X	X
Overall		XX	XX	X	X	X	X	X	X	X	X	X

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
*Adverse events are classified according to MedDRA Version 21.0. ^ = Treatment-emergent adverse events
If a subject experience the same adverse event (AE) at more than one level of severity during a treatment, each AE is counted separately. If a subject experience the same AE at more than one level of drug relationship during a treatment, each AE is counted separately.
Severity/Intensity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially life-threatening

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

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Dose Level/ Placebo	Subject Number	Adverse Event	Onset Date	Onset Time	Frequency	Severity/ Intensity	Serious	Outcome	Relationship to Study Drug	Action
XXX <units>	X	XXXXXXXXXX	DDMMMYYYY	XX:XX	XXXXXXXXX	XXXX	XXXX	Resolved	XXXXXXXX	XXXXXXXXX

Programmer Note: If no SAE, then table will contain the statement: "There were no serious adverse events recorded during the study."

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)

Program: /AAXXXXX/sas_prg/stsas/tab_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)

Dose Level/ Placebo	Subject Number	Age#/ Sex	Study Period	Day	Hour	Date	Time	Parameter1 <Range> (Unit)	Parameter2 <Range> (Unit)	Parameter3 <Range> (Unit)	Parameter4 <Range> (Unit)	Parameter5 <Range> (Unit)
XXX <units>	X	XX/X	Screen	.	.	DDMMMYYYY	HH:MM:SS	XX HN				XX LN
			1	-X	-XX.XX	DDMMMYYYY	HH:MM:SS	XX LY-	XX IN	XX HN	XX LYR+	
			Recheck			DDMMMYYYY	HH:MM:SS				XX	

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.

Clinically significant lab values will be generally 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 flag for PI flag -/+ based on comments (i.e. NCS/CS). 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: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
#Age is calculated at the time 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 Laboratory and Corresponding Results (Safety Population)

Dose Level/ Placebo	Subject Number	Age#/ Sex	Study Period	Day	Hour	Date	Time	Department	Test	Result	Reference Range	Unit
XXX <units>	X	XX/X	X	X	-X.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	X - X	mg/dL
				X	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HYR+	X - X	mg/dL
				X	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HY-	X - X	mg/dL
				X	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HN	X - X	mg/dL

Programmer Note: 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 there were no CS values as deemed by PI (i.e., no "CS" or "Clinically Significant" in the PI comment field in the laboratory dataset), then this table will contain only the statement: "There were no laboratory values deemed clinically significant by the PI in the study."

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
#Age is calculated at the time of first dosing.
H = Above reference range
Computer: Y = Clinically significant
PI Interpretation: R = Recheck requested, + = Clinically significant

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

Tables 14.3.5.1, 14.3.5.4, 14.3.5.7, and 14.3.5.11 will be in the following format:

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

Laboratory Test (unit)	Reference Range	Time Point	Statistic	Dose Level <dose level 1>	<dose level 2>	<dose level 3>	<dose level 4>	Pooled Placebo
XXXXXXXXX (unit)	X.X-XX.X#	Screen	n	XX	XX	XX	XX	XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.X	X.X	X.X	X.X	X.X
			Maximum	XX.X	XX.X	XX.X	XX.X	XX.X
		Baseline*	n	XX	XX	XX	XX	XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.X	X.X	X.X	X.X	X.X
			Maximum	XX.X	XX.X	XX.X	XX.X	XX.X
		Day X, Hour X.XX	n	XX	XX	XX	XX	XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.X	X.X	X.X	X.X	X.X
			Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
= Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
* Baseline is defined as the result closest and prior to dose on Day 1.

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

Tables 14.3.5.2, 14.3.5.5, 14.3.5.8, 14.3.5.9 and 14.3.5.12 will be in the following format:

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

Laboratory Test (unit)	Reference Range	Time Point	Statistic	Dose Level <dose level 1>	<dose level 2>	<dose level 3>	<dose level 4>	Pooled Placebo
XXXXXXXXX (unit)	X.X-XX.X#	Day X, Hour X.XX	n	XX	XX	XX	XX	XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.X	X.X	X.X	X.X	X.X
			Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
= Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
Baseline is defined as the result closest and prior to dose on Day 1.

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

Tables 14.3.5.3, 14.3.5.6, 14.3.5.10, and 14.3.5.13 will be in the following format:

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

Laboratory Test (unit)	Reference Range	Dose Level/ Pooled Placebo	Time Point	Baseline* L			Baseline* N			Baseline* H		
				L	N	H	L	N	H	L	N	H
XXXXXXX (unit)	X.X-XX.X#	XXX <units>	Day X, Hour X.XX	X (X%)	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)

Programmer Note: For Urinalysis tests, the categories will be N = Normal and O = Outside Normal.

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
N = Within Normal Range, L = Below Normal Range, H = Above Normal Range
# = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
* Baseline is defined as the result closest and prior to dose on Day 1.

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

Table 14.3.5.14 Vital Sign Summary (Safety Population)

Vital Sign (unit)	Time Point	Statistic	Dose Level: <dose level 1>	<dose level 2>	<dose level 3>	<dose level 4>	Pooled Placebo
XXXXXXXXX (unit)	Screen	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X
	Baseline*	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X
	Day X, Hour X.XX	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
* Baseline is defined as the result closest and prior to the dose on Day 1.

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

Table 14.3.5.15 Vital Sign Change from Baseline (Safety Population)

Vital Sign (unit)	Time Point	Statistic	Dose Level: <dose level 1>	<dose level 2>	<dose level 3>	<dose level 4>	Pooled Placebo
XXXXXXXXX (unit)	Day X, Hour X.XX	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
Baseline is defined as the result closest and prior to the dose on Day 1.

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

Table 14.3.5.16 12-Lead Electrocardiogram Summary (Safety Population)

Measurement (unit)	Time Point	Statistic	Dose Level <dose level 1>	<dose level 2>	<dose level 3>	<dose level 4>	Pooled Placebo
XXXXXXXXX (unit)	Screen	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X
	Baseline*	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X
	Day X, Hour X.XX	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
* Baseline is defined as the result closest and prior to the dose on Day 1.

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

Table 14.3.5.17 12-Lead Electrocardiogram Change From Baseline (Safety Population)

			Dose Level				
Measurement (unit)	Time Point	Statistic	<dose level 1>	<dose level 2>	<dose level 3>	<dose level 4>	Pooled Placebo
XXXXXXXXX (unit)	Day X, Hour X.XX	n	XX	XX	XX	XX	XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Pooled Placebo: Placebo Solution (IV bolus)
Baseline is defined as the result closest and prior to the dose on Day 1.

Program: /AAXXXXX/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 CSR. These listings will be generated off of the Celerion SDTM Tabulation Model 1.4 mapped in accordance with SDTM Implementation Guide 3.2. All listings will be presented in Courier New size font 9.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

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

<similar for remaining Laboratory Groups and Test Names>

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

Appendix 16.2.1 Subject Discontinuation (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Date	Completed Study?	Reason for Discontinuation	Specify
XXX <units>	X	Post	DDMMMYYYY	Yes		
	X	Post	DDMMMYYYY	Yes		
	X	Post	DDMMMYYYY	Yes		
	X	Post	DDMMMYYYY	Yes		
	X	Post	DDMMMYYYY	No	Personal Reason	XXXXXXXX
	X	Post	DDMMMYYYY	Yes		

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.1 Demographics (Safety Population)

Dose Level/ Placebo	Subject Number	Date of Birth	Age* (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m^2)	Informed Consent Date
XXX <units>	X	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY
	X	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY
	X	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY
	X	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY
	X	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY
	X	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY
	X	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
*Age is calculated from the date of first dosing.

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2 Physical Examination (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Day	Hour	Date	Was PE Performed?	Comment
XXX <units>	X	Screen	.	.	DDMMMYYYY	XXX	
	X	X	-X	-XX.X	DDMMMYYYY	XXX	
			X	XX.X	DDMMMYYYY	XXX	

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
PE = Physical Examination

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3 Medical and Surgical History (Safety Population)

Dose Level/ Placebo	Subject Number	Any History?	Study Period	Body System	Category	Date Start	Date End	Condition or Event
XXX <units>	X	XXX	Screen	XXXXXX XXXXX XXXXXXX	Medical	DDMMMYYYY	Ongoing	XXXXXXX XXXXXX XXXXXXXX
				XXXXXXXXX	Surgical	DDMMMYYYY	DDMMMYYYY	
	X	XXX	Screen	XXXXXXXX XXXXX XXXXXX	Medical	DDMMMYYYY	DDMMMYYYY	

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.4 Substance Use (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Substance	Date		Description
				Start	End	
XXX <units>	X	Screen	XXXXXXXX XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXX XXXXXX XXXX

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.1 Inclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.2 Exclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.2 Subject Eligibility (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Date	Did subject meet all eligibility criteria?	Criterion Not Met*	Specify
XXX <units>	X	Screen	DDMMMYYYY	Yes		
	X	Screen	DDMMMYYYY	Yes		
	X	Screen	DDMMMYYYY	No	EXCLUSION X	XXXXXXXXXXXXXX XXXX

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
*Please refer to Appendices 16.2.5.1.1 and 16.2.5.1.2 for specific inclusion and exclusion criteria.

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3.1 Check-in and Return Criteria

X. Did the Subject report any study restriction violations since the last study visit?
X. IF YES TO ANY QUESTION, WAS SUBJECT APPROVED FOR STUDY?

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3.2 Check-in Criteria and Return Responses (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Day	Hour	Date	Time	Check-in Criteria 1	Check-in Criteria 2	Specify
XXX <units>	X	X	-X	-XX.X	DDMMMYYYY	HH:MM:SS	No	NA	Will only be present and populated if there is a comment present in the study database.
			X	XX.X	DDMMMYYYY	HH:MM:SS	No	NA	
			X	XX.X	DDMMMYYYY	HH:MM:SS	No	NA	
	X	X	-X	-XX.X	DDMMMYYYY	HH:MM:SS	No	NA	
			X	XX.X	DDMMMYYYY	HH:MM:SS	No	NA	
			X	XX.X	DDMMMYYYY	HH:MM:SS	No	NA	

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
Please refer to Appendix 16.2.5.3.1 for the Check-in criteria.
NA = Not applicable

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.1 Test Compound Description

Compound	Form	Route
XXXXXXXXXXXXX	< >	XXXX
XXXXXXXXXXXXX	< >	XXXX

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Day	Interval	Start Date	Start Time	End Time	Compound	Dosage	Comments
XXX <units>	X	X	X	X.XX - X.XX	DDMMMYYYY	X:XX:XX	X:XX:XX	XXXXXXXXX	< >	XXXXXXXXXXXXXXXXXX
			X	X.XX - X.XX	DDMMMYYYY	X:XX:XX	X:XX:XX	XXXXXXXXX	< >	
			X	X.XX - X.XX	DDMMMYYYY	X:XX:XX	X:XX:XX	XXXXXXXXX	< >	

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5 Blood Draw Times (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Day	Hour	Date	Actual Time	Vacutainer ID	Bioassay	Comment
XXX <units>	X	X	X	-X.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX
				XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXX
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXX
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	
			X	XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXXX	XXXXXXXXXXX	

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)

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

Appendix 16.2.5.6 Meal Times (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Day	Hour	Event	Actual Date	Start Time	Stop Time	Comments
XXX <units>	X	X	-X	-XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
			X	XX.XX	BREAKFAST	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

Dose Level/ Placebo	Subject Number	Any Med?	Medication (WHO* Term)	Dosage	Route	Start Date	Start Time	Stop Date	Stop Time	Frequency	Indication	Continuing?	Prior to Study?
XXX <units>	X	No	None										
	X	Yes	ACETAMINOPHEN (ACETAMINOPHEN)	620 mg	Oral	DDMMMYYYY	HH:MM:SS	DDMMMYYYY	HH:MM:SS	Once	Toothache	No	X

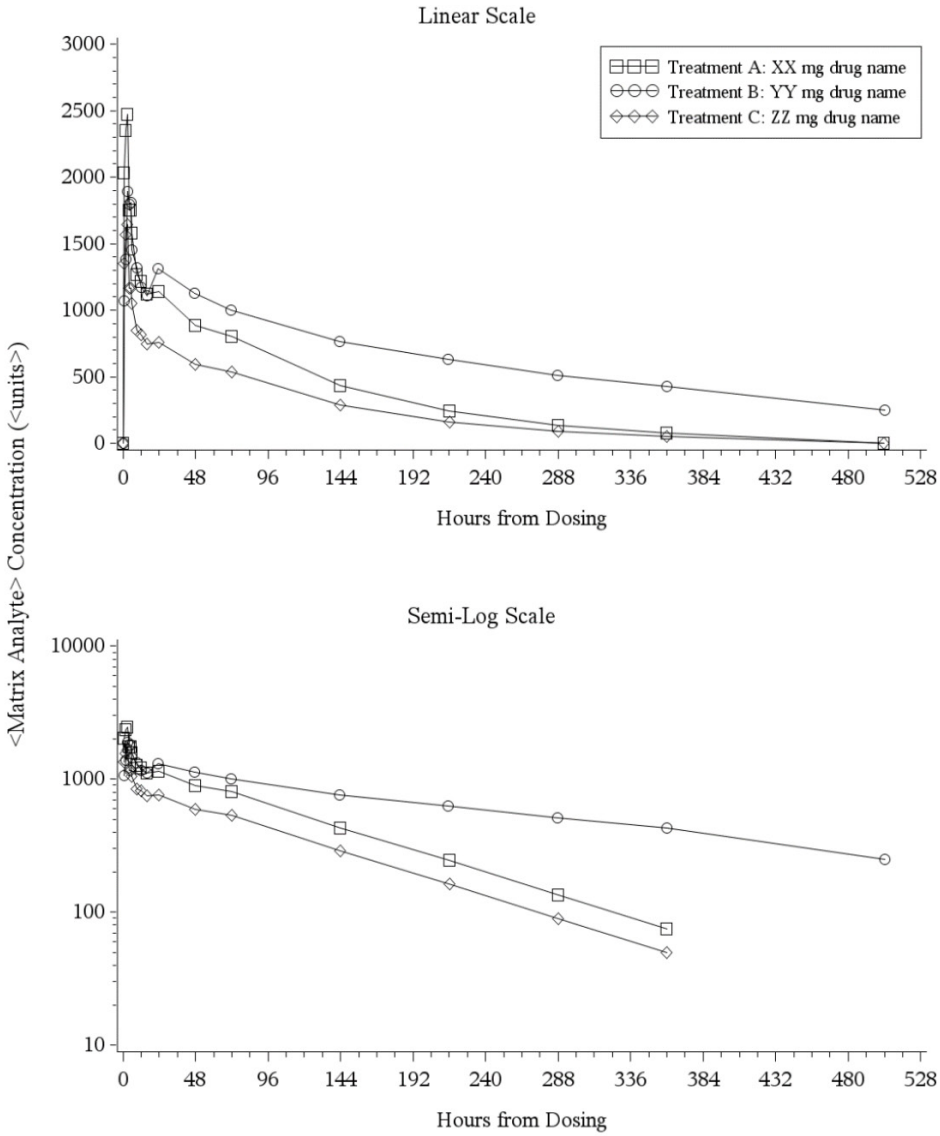
Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
*Concomitant medications are coded with World Health Organization (WHO) Drug Dictionary Version 01Mar2018.
Med = Medication

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Individual profiles in Appendix 16.2.6 will be in the following format.

Appendix 16.2.6.1

Individual <Matrix Analyte> Concentrations Versus Time 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:

- Legend will be <> and <>
- Y axis label will be <Matrix> <analyte> Concentration (unit)
- X axis label will be "Hours From Dosing"
- Please generate figures in color. Please use the same color and symbol for each treatment throughout.

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

Dose Level/ Placebo	Subject Number	TE?^	Adverse Event*	Preferred Term	Time From Last Dose (DD:HH:MM)	Onset Date	Onset Time	Resolved Date	Resolved Time	Duration (DD:HH:MM)
XXX <units>	X		None							
	X	Yes	XXXXXXXXXXXXX	XXXXXXXXXX XXXXXXX	XX:XX:XX	DDMMMYYYY	XX:XX	DDMMMYYYY	XX:XX	XX:XX:XX

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
*Adverse events are classified according to MedDRA Version 21.0.
^TE = Treatment-emergent

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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

Dose Level/ Placebo	Subject Number	TE?^	Adverse Event	Onset Date	Onset Time	Onset Freq*	Severity/ Intensity	Serious	Outcome	Relationship to Study Drug
XXX <units>	X		None							
	X	Yes	XXXXXXXXXXXXXXXXX	DDMMMYYYY	XX:XX	Inter.	Grade 1 Mild	Not serious	Resolved	XXXXXXXXXXXXXXX

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
^TE = Treatment-emergent
*Freq represents Frequency: SI = Single Episode, Inter. = Intermittent, Cont. = Continuous

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Event Related Procedure (Safety Population)

Dose Level/ Placebo	Subject Number	TE?^	Adverse Event	Onset Date	Onset Time	Procedure Date	Procedure Time	Procedure Description
XXX <units>	X	Yes	DRY LIPS	DDMMMYYYY	XX:XX	DDMMMYYYY	XX:XX	PETROLEUM JELLY

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
^TE = Treatment-emergent

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.3 Adverse Event Preferred Term Classification (Safety Population)

Dose Level/ Placebo	Subject Number	TE?^	Adverse Event*	Preferred Term	System Organ Class	Onset Date	Onset Time
XXX <units>	X	Yes	XXXXXXX XXXXX XXXX XXXXXX	XXXXXXXXXX XXXXXXX	XXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	XX:XX

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
*Adverse events are classified according to MedDRA Version 21.0.
^TE = Treatment-emergent

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendices 16.2.8.1.1 to 16.2.8.1.5 will have the following format.

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

Dose Level/ Placebo	Subject Number	Age#/ Sex	Study Period	Day	Hour	Date	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)	Parameter6 < Range> (Unit)
XXX <units>	X	XX/X	Screen	.	.	DDMMMYYYY	XX HN	XX	XX	XX	XX HN	XX
			X	-X	-XX.X	DDMMMYYYY	XX LYR+	XX LN	XX	XX LY-	XX	XX

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.
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 flag for PI flag (+) based on positive CS/Clinically Significant comments. Present this derived 4th column in all tables, and also list the PI-determined out-of-range clinically significant lab values in Table 14.3.4.5.

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
#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, + = Clinically Significant, R = To be rechecked
^ = Will be retested at a later event

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.1.5 Clinical Laboratory Report – Comments (Safety Population)

Dose Level/ Placebo	Subject Number	Age#/ Sex	Study Period	Day	Hour	Date	Department	Test	Result	Unit	Comment
XXX <units>	XX/X	X	X	-X	-XX.X	DDMMMYYYY	Other Tests	Fibrinogen	XXX	mg/dL	Not significant in the context of this study.

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
#Age is calculated from the date of first dosing. F = Female; M = Male

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.2 Vital Signs (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Day	Hour	Date	Time	Test	Blood Pressure (mmHg) Systolic/Diastolic	Pulse (bpm)	Respiration (rpm)	Temperature (°C)	Weight (kg)	Comment
XXX <units>		Screen	.	.	DDMMMYYYY	X:XX:XX	SUPX	XXX/ XX	XX	XX	XX	XX	XXXX
	X	X	-X	-XX.X	DDMMMYYYY	X:XX:XX	SUPX	XXX/ XX	XX	XX	XX	XX	XXXXXXXXX
			X	XX.X	DDMMMYYYY	X:XX:XX	SUPX	XXX/ XX	XX				

Programmer Note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
SUPX = X-minute supine; R = Recheck value

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Dose Level/ Placebo	Subject Number	Study Period	Day	Hour	Date	Time	Result	Heart Rate (bpm)	PR (ms)	QRS (ms)	QT (ms)	QTcF* (ms)	Comments
XXX <units>	X	Screen	.	.	DDMMMYYYY	X:XX:XX	Normal	XX	XXX	XX	XXX	XXX^#	
	X	X	X	XX.X	DDMMMYYYY	X:XX:XX	Normal	XX	XXX	XX	XXX	XXX	XXXXXXXXX
				XX.X	DDMMMYYYY	X:XX:XX	Normal	XX	XXX	XX	XXX	XXX	XXXXXXXXX

Programmer Note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled timepoint the recheck is for.

Note: 0.5 mcg/kg: 0.5 mcg/kg E-WE thrombin (IV bolus)
1.0 mcg/kg: 1.0 mcg/kg E-WE thrombin (IV bolus)
2.0 mcg/kg: 2.0 mcg/kg E-WE thrombin (IV bolus)
4.0 mcg/kg: 4.0 mcg/kg E-WE thrombin (IV bolus)
Placebo: Placebo Solution (IV bolus)
QTcF* = QT corrected for heart rate using Fridericia's correction.
Abnormal, NCS = Abnormal, Not clinically significant
^ = QTcF is > 450 ms
# = QTcF change from baseline is > 30 ms

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM