STATISTICAL ANALYSIS PLAN

A Phase 1, Partially-Blinded, Placebo-Controlled, Randomized, Multiple Ascending Dose Study to Include A Single Dose Food-Effect Study to Evaluate the Safety, Tolerability, and the Pharmacokinetic Profile of TBI-223 in Healthy Adult Subjects

Global Alliance for TB Drug Development

Protocol No: TBI-223-CL-002

TKL Study Number P1980121

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List of Abbreviations and Definitions of Terms

Abbreviation	Definition
ADaM	Analysis Data Model
AE	Adverse Event
AI	Accumulation Index
ANOVA	Analysis of Variance
AUC	Area under the plasma concentration versus time curve
AUC_{inf}	Area under the plasma concentration versus time curve from Time 0 to infinity (by extrapolation); also reported as $AUC_{(0\text{-}inf)}$
$AUC_{0\text{-}24}$	Area under the plasma concentration versus time curve from Time 0 to the end of the dosing period
BMI	Body Mass Index
BP	Blood Pressure
BPM	Beats Per Minute
C	Celsius (Centigrade)
CI	Confidence Interval
CL/F	Apparent Oral Clearance
C_{max}	Observed Maximum Plasma Concentration
C_{min}	Observed Minimum Plasma Concentration
CS	Clinically Significant
CRF	Case Report Form
CRO	Contract Research Organization
DBP	Diastolic Blood Pressure
DIC	Drug-in-Capsule
DMP	Data Management Plan
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
FDA	US Food and Drug Administration
GMR	Geometric Mean Ratio
IL-17	Interleukin-17
λ_z	Elimination Rate Constant
kg	Kilogram
mg	Milligram

Abbreviation	Definition
mL	Milliliter
msec	Millisecond
ODS	Output Delivery System
N/A	Not Applicable
NCS	Not Clinically Significant
PD	Pharmacodynamics
PK	Pharmacokinetics
PR	Duration between the beginning of the P wave and the beginning of the next QRS complex on the ECG
PT	Preferred Term
QRS	Duration between the start of the Q wave and the end of the S wave on the ECG. Also known as ventricular depolarization complex.
QT	Duration between the start of the Q wave and the end of the T wave on the ECG
QTc	QT interval corrected for heart rate
QTcB	Corrected QT interval using Bazett's Formula
QTcF	Corrected QT interval using Fridericia's Formula
RTF	Rich-Text Format
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SOP	Standard Operating Procedure
TEAE	Treatment-Emergent Adverse Event
$t_{½}$	Half-life
T_{max}	Time at which C_{max} occurs
T_{min}	Time at which C_{min} occurs
V_z/F	Apparent Volume of Distribution

1. INTRODUCTION

This Statistical Analysis Plan (SAP) is based on the study Protocol Version 1.0 dated 04 December 2020. This document specifies, prior to locking the database, a comprehensive description of the rationale, strategies, and statistical techniques that are planned to assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of multiple dose TBI-223 in normal healthy volunteers.

This document also provides additional details concerning the statistical analyses outlined in the protocol and reflects any changes to the protocol from any amendments. This plan will not repeat all the definitions given in the protocol but will provide further details of the summaries and analyses planned therein.

2. STUDY OBJECTIVES

The primary objective of the study is to evaluate the safety and tolerability of multiple doses of TBI-223 in healthy adult subjects.

The secondary objective of the study is:

• To determine the pharmacokinetics (PK) of TBI-223 and its metabolite, M2 after multiple ascending doses of TBI-223 in healthy adult subjects when administered after a high-calorie, high-fat meal

• For the TBI-223 sustained-release (SR1) formulation and for the combination of the SR and immediate-release (IR) formulations, to compare the PK profiles of a single dose when administered to healthy adult subjects in the fasting state versus after a high-calorie, high-fat meal

• To determine the pharmacokinetics (PK) of a single dose of the TBI-223 sustained-release (SR1) formulation in healthy adult subjects when administered fasted

3. STUDY DESIGN

This is a partially-blinded, placebo-controlled, randomized multiple ascending dose (MAD) study to be conducted at one study center.

Thirty-six (36) subjects will be enrolled in 3 cohorts with 12 subjects per cohort. Within each cohort, 9 subjects will be assigned to receive active treatment and 3 subjects will receive placebo. Each subject will participate in one dose level.

The first 2 cohorts (food-effect cohorts) will begin dosing of TBI-223 on Day 1 under fasted conditions, followed by a 3 day washout period and then by multiple doses of TBI-223

administered after a high-calorie, high-fat meal from Day 4 through Day 17 (total of 14 days). The third cohort (non-food-effect cohort) will begin dosing of TBI-223 on Day 1 and continue through Day 14, all doses administered after a high-calorie, high-fat meal.

Each subject will be administered TBI-223 tablets (SR1 or IR or a combination of both formulations) or placebo once daily for 14 days with corresponding pharmacokinetic measurements. After each dose cohort, the Sponsor and Investigator will review the pharmacokinetic and safety data before proceeding to the next dose level.

Dose escalation to the next cohort (i.e., dose level) or decisions regarding changed or additional cohorts will not take place until the Sponsor, in conjunction with the Principal Investigator and dose escalating committee, has determined that adequate safety, tolerability, and pharmacokinetics from the previous cohort(s) have been demonstrated to permit proceeding to the next cohort. The Institutional Review Board (IRB) should be immediately notified of the dose escalation or any revised approach for review and approval.

Safety will be assessed throughout the study for all subjects. Safety assessments will include physical and detailed neurological examinations, vital signs (blood pressure, pulse rate, respiration rate, temperature and pulse oximetry), electrocardiograms (ECGs), cardiac monitoring, adverse events (AEs), and clinical laboratory tests (including hematology, serology, serum chemistry, coagulation, and urinalysis).

Blood and urine will be collected for clinical laboratory evaluations.

The Principal Investigator, in conjunction with the Sponsor may collect additional blood if necessary, for repeat laboratory or safety evaluations including AE follow up.

Female subjects will have blood collected for serum pregnancy testing. Females claiming postmenopausal status will have blood collected to measure follicle stimulating hormone (FSH) levels.

During each cohort, blood samples (trough samples) will be obtained before each dose of study drug, and at the time points on the events schedule. Plasma pharmacokinetic samples will be analyzed for TBI-223 and M2 using validated analytical methods. Appropriate pharmacokinetic parameters will be calculated using non compartmental methods.

4. HARDWARE AND SOFTWARE

Statistical analysis will be performed following TKL standard operating procedures and on the TKL computer network. All statistical analyses will be performed using SAS Version 9.4 or higher with program code prepared specifically for the project by qualified TKL statisticians and SAS programmers.

The SAS programs will generate rich-text-formatted (RTF) output with the "RTF" extension using the SAS Output Delivery System (ODS). The summary tables and listings will be formatted using the Times New Roman font. The RTF output is included in report documents prepared with Microsoft Word and converted to PDF format without typographical change.

Study data tabulation model (SDTM) data sets and required analysis data model (ADaM) data sets will be created and taken as input to validated SAS programs to generate the report-ready tables, listings, and figures. Each output display will show the names of the data sets and SAS program used to produce it. Upon completion of the study report, the data sets will be provided to the sponsor as SAS XPT transport files with define.xml files including details of all derivations and imputations used.

5. STATISTICAL DATA REVIEW

Data verification activities to be performed prior to delivery of the SAS data sets to the project statistician are described in the approved Data Management Plan (DMP). After completion of the data verification activities, the SAS data sets will be reviewed by the project statistician along with documentation of any unresolved queries and data conventions applied that are not fully explained in the data or in the DMP. The project statistician will perform completeness and self-consistency checks of the study data. Questions will be issued to the Data Manager and resolved before closure of the database.

6. DATABASE CLOSURE

After completion of all data review procedures, validation of the project database, and approval of the data review document by the study sponsor, the clinical database will be closed, termed "Database Lock". Any change to the clinical database after this time will require written authorization, with explanation, by the Sponsor and the Biostatistician.

7. SAMPLE SIZE DETERMINATION

The sample size and the number of subjects for each cohort is expected to provide sufficient safety and tolerability data to evaluate whether escalation to the next dose level is warranted. This study has not been formally powered and the sample size was not based on statistical considerations.

8. HANDLING OF MISSING DATA

No imputation is planned for safety data unless otherwise specified below. All efforts will be made to ensure completeness for AE severity and AE drug-relationship data.

The handling of any missing drug concentration-time data to estimate PK parameters is described in the PK analysis section.

9. ANALYSIS POPULATIONS

Two populations will be defined for analysis detailed in this document: the Safety Population and the PK Population.

8.1 Safety Population

The Safety Population will include all randomized subjects who receive at least one dose of the study drugs (TBI-223 or placebo). Subjects will be analyzed according to the treatment subjects actually received regardless of the treatment to which they were randomized. Subjects who receive placebo will be pooled across dosing panels to form a single placebo group.

8.2 Pharmacokinetic (PK) Population

All subjects who receive TBI-223 and who have plasma concentration data available will be included in the PK population. This population will be used for the presentation of plasma concentration results as well as PK analysis. However, only subjects with profiles adequate to determine PK parameters will be included in PK analyses, which will be decided by a PK scientist upon review of all concentration profiles.

10. DATA CONVENTIONS FOR ANALYSIS

9.1 General Statistical Principles

All statistical processing will be performed using the SAS system (Version 9.4 or higher). The focus of the statistical analysis will be to assess the safety, tolerability, and PK of TBI-223 in normal healthy volunteers.

Descriptive statistics will be used to provide an overview of the safety and PK results. For categorical parameters, the number and percentage of subjects in each category will be presented. The denominator for percentage will be based on the number of subjects appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will include n (number of subjects), mean, standard deviation (SD), median, and range. In addition, coefficient of variation (%CV) and geometric mean will also be reported for appropriate PK parameters.

9.2 Study Day

Day 1 is defined as the date of first study drug administration. The day before Day 1 is Day -1; there is no Day 0. Study day is calculated relative to the date of Day 1.

Baseline is defined as the last available measurement prior to the first dose of the study drug on Day 1.

11. STATISTICAL EVALUATION

10.1 Subject Disposition

A subject disposition table will present the number of subjects screened, randomized, completed, and discontinued, along with the primary reason for discontinuation, as well as the number of subjects within each population. The summary will be presented for each TBI-223 dose, an "Any TBI-223" group including subjects receiving any TBI-223, and a pooled placebo group.

A listing of the subjects who are enrolled, randomized, and who complete or discontinue the study, along with the reason for and day of discontinuation, will be provided. Screen failures and protocol deviations will be presented in by-subject listings.

10.2 Demographic and Other Baseline Characteristics

The following demographic and baseline variables will be listed and summarized by treatment(TBI-223 by dose, any TBI-223, and pooled placebo) and overall:

- Age (years)
- Sex
- Race (American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Multiple)
- Ethnicity origin (Hispanic or Latino, Not Hispanic or Latino)
- Weight (kg)
- Height (cm)
- BMI (kg/m^2)

For continuous variables, descriptive statistics (mean, standard deviation, median, minimum, and maximum) will be provided. For categorical variables, the number and frequency of subjects in each category (sex, ethnicity, race) will be provided.

10.3 Study Drug Administration

A summary table for drug exposure will be provided by treatment (TBI-223 by dose, any TBI-223, and pooled placebo), and will include the number and percentage of subjects who receive at least one dose, at least one dose under fed conditions, all intended (i.e., 14 or 15) doses, as well as each single-dose treatment on each day. In addition, descriptive statistics (mean, standard deviation, median, minimum, and maximum) will be provided for the total number of doses for each dose group. A by-treatment, by-subject listing will be provided for date and time of each dose of study drug.

10.4 Prior and Concomitant Medications

Records of prior (with stop dates prior to Day 1) and concomitant medications (with stop dates on or after Day 1) will be provided in a by-treatment, by-subject listing.

10.5 Medical History

Current conditions and past medical conditions will be provided in a by-treatment, by-subject listing.

10.6 Efficacy Analysis

No efficacy analysis or hypothesis testing will be performed.

10.7 Safety Analysis

All safety analyses are based on the Safety Population according to the actual study drug and dose received. Detailed analyses will be described in sections below.

The following safety endpoints will be summarized:

- Adverse Events;
- Clinical safety laboratory testing;
- Standard 12-lead ECG data;
- Physical examinations;
- Vital signs

Interim analyses of safety results from each panel before dose escalation will be reviewed by the Investigator and Medical Monitor, but will not be analyzed statistically.

10.7.1 Adverse and Serious Adverse Events

AE terms will be coded using the MedDRA version 23.1 (2020) dictionary. A treatment-emergent AE (TEAE) is defined as an AE with a start date and time coinciding with or after the first dose of study drug received.

All AEs will be presented in a by-treatment, by-subject, detailing the verbatim term given by the investigator, the preferred term (PT), system organ class (SOC), onset date and time, end date and time, severity, outcome, relationship to study drug, action taken with study drug, other action taken, seriousness and criteria for seriousness. Serious AEs and AEs leading to study discontinuation will also be presented in a separate listing.

An overall summary of TEAEs will be presented by treatment (TBI-223 by dose, any TBI-223, and pooled placebo). The summary will include the total number of events, frequency counts and percentages with:

- Any TEAE
- Any serious TEAE
- Any treatment-related TEAE (that is, TEAEs that are probably and possibly related)
- Any treatment-related serious TEAE
- Any TEAE resulting in withdrawal from the study
- Any deaths

Summaries of the incidence of the following TEAEs will be displayed by treatment (TBI-223 by dose, any TBI-223, and pooled placebo):

- All TEAEs by PT in descending order of frequency of any TBI-223
- All treatment-related TEAEs by PT in descending order of frequency of any TBI-223
- All TEAEs by SOC, PT, and maximum severity (mild, moderate, or severe)
- All treatment-related TEAEs by SOC, PT, and maximum severity
- All TEAEs by SOC, PT, and maximum causality (not related, possible, probably) to the study drug

For purpose of the summary of the incidence, each subject will contribute only once (i.e., the first occurrence, the occurrence with the maximum severity or causality) within an SOC and a PT, regardless of the number of occurrences (events) the subjects experiences.

10.7.2 Clinical Laboratory Tests

Data listings by-treatment and by-subject will be provided for all laboratory parameters. Absolute values and changes from baseline will also be summarized for hematology and clinical chemistry parameters using descriptive statistics by treatment at the following time points: Baseline, Days 3, 5, 9, 10, 11 and follow-up visit).

Normal ranges and values outside the normal ranges will be identified by the central laboratory. A separate listing of out of normal range laboratory results will be provided. Shift tables will be provided for the number of subjects with clinical laboratory values below, within, or above normal ranges at each post-baseline visit relative to baseline, for each test.

Serum pregnancy, drug, alcohol, and cotinine screening results will be presented in a by-treatment, by-visit, by-subject listing.

10.7.3 Electrocardiogram

Tabulation of standard 12-lead ECG numeric results (ventricular rate, PR, QRS, QT, QTcF intervals) will be presented using descriptive statistics by treatment (TBI-223 by dose, any TBI-223, and pooled-placebo) for absolute values and changes from baseline for the following time points: Baseline, Day 1 post-dose, Day 4 post-dose, Day 14 or 17 pre-dose and post dose, and final assessment.

The number and percentage of subjects with post-baseline values of >450, >480, and >500 msec, as well as subjects with change from baseline of >30 (including subjects with >60 msec changes) and >60 msec at any post-baseline time point will be summarized for QTcF intervals.

Any clinically significant ECG results were to be captured as AEs by the PI. A by-treatment and by-subject listing of standard ECG results (numeric results and verbatim findings) will also be presented.

10.7.4 Vital Signs

Vital signs data will be presented in a by-treatment and by-subject listing for the following tests:

- Blood pressure (mmHg) – both systolic and diastolic
- Pulse rate (beats per min)
- Respiration rate (breaths per min)
- Body temperature (°C)
- Pulse Oximetry

Absolute values and changes from baseline (i.e., the last available measurement prior to Day 1 dosing) will be summarized using descriptive statistics by treatment for the following time points:

- Baseline
- Day 1 6 hours post-dose
- Days 4 – 17 or 2 to 14 pre-dose
- Day 17 or 14 pre-dose
- Day 17 or 14 6 hours post-dose, change from Day 4 or Day 2 pre-dose value will also be summarized
- Follow-up visits

10.7.5 Physical Examination

Physical examination results will be presented in a by-subject listing. Clinically significant physical examination results will be reported as AEs by the PI.

10.8 Pharmacokinetic Analysis

All analyses of pharmacokinetics (PK) will be based on the PK population. Plasma concentrations of TBI-223 and M2 will be listed and summarized by cohort for each nominal time point, giving number of subjects, mean, standard deviation, median, minimum, maximum, and coefficient of variation [CV]). Mean and individual concentrations (TBI-223 and M2) will be plotted versus time for each cohort, for the following time periods:

- 0 to 24 h post-dose, Cohorts 1 and 2, Days 1, 4, and 17, linear and semi-log scales
- 0 to 24 h post-dose, Cohort 3, Days 1 and 14, linear and semi-log scales
- 0 to 72 h post-dose, Cohorts 1 and 2, Days 1 and 17, linear and semi-log scales
- 0 to 72 h post-dose, Cohort 3, Day 14, linear and semi-log scales
- Trough (Pre-dose and 24 h) Concentrations (Approach to Steady State), Cohorts 1 and 2, Days 4 to 17
- Trough (Pre-dose and 24 h) Concentrations (Approach to Steady State), Cohort 3, Days 1 to 14

Pharmacokinetic parameters for TBI-223 and M2 will be calculated as defined in Table 1 below. Only subjects with measured concentrations adequate to determine PK parameters will be included in the PK analyses.

Table 1: Pharmacokinetic Parameters

PK parameter	Definition	Scope
C_{max}	Maximum plasma concentration	[a]
AUC_{0-24}	Area under the concentration curve from 0 to 24 h post-dose, calculated by trapezoidal integration	[a]
AUC_{inf}	Area under the concentration curve extrapolated to complete elimination, calculated as $AUC_{inf} = AUC_{last} + \frac{C_{last}}{\lambda_z}$ where C_{last} is the last measured post-dose concentration.	[b]
T_{max}	Time of the maximum plasma concentration, given as the nominal time point	[a]
C_{min}	Minimum concentration during dosing period at steady state	[d]
T_{min}	Time of minimum concentration during dosing period at steady state	[d]
C_{trough}	Trough concentrations (pre-dose or 24-hour)	[c]
λ_z	Elimination rate constant, calculated as the slope of log-transformed concentration vs time during the elimination phase.	[a]
$t_{½}$	Elimination half-life, calculated as $\frac{\ln 2}{\lambda_z}$	[a]
CL/F	Apparent plasma drug clearance, calculated as $\frac{Dose}{AUC_{0-inf}}$	[b]
CL_{ss}/F	Apparent plasma drug clearance at expected steady state, calculated as $\frac{Dose}{AUC_{0-24}}$	[d]
V_Z/F	Apparent volume of distribution, calculated as $\frac{CL/F}{\lambda_z}$	[b]
V_{zss}/F	Apparent volume of distribution at expected steady state, calculated as $\frac{CL_{ss}/F}{\lambda_z}$	[d]
R_{AUC}, R_{Cmax}	Accumulation ratio for AUC_{0-24} (C_{max}) calculated as the ratio of the value at steady state to the value during the first dosing period.	--

[a] Days 1, 4, and 17 (Cohorts 1 and 2); Days 1 and 14 (Cohort 3)
[b] Days 1 and 4 (Cohorts 1 and 2); Day 1 (Cohort 3)
[c] All dosing days
[d] Day 17 (Cohorts 1 and 2); Day 14 (Cohort 3)

Actual sample collection times will be used for the purpose of calculating PK parameters. Concentration data below the limit of quantitation (BLQ) will be marked as such in the data listings; they will be imputed as 0 for the calculations of descriptive statistics and for calculation of $AUC_{0\text{-}24}$. Parameters will be presented in by-subject listings and summarized by dose group using mean, standard deviation, median, minimum, and maximum, as well as coefficient of variation and geometric mean for appropriate parameters.

The elimination rate constant will be estimated by linear regression using no fewer than 3 sampling points during the elimination phase. The first sampling time to be included in the calculation will be determined by visual inspection of the by-subject plots.

The food effect will be estimated for $AUC_{0\text{-}24}$, AUC_{inf}, and C_{max} in Cohorts 1 and 2 by the ratio of geometric means of Day 4 (fed) to Day 1 (fasted) values. These will be presented along with the 90% 2-sided confidence intervals. These estimates will be calculated for each dose level using analysis of variance of the log-transformed values including the effects of subject and day. The differences of the least-squares means and confidence limits will then be back-transformed to provide the ratios of geometric means and their confidence limits. The food effect on T_{max} will be compared using the Wilcoxon Signed Rank test.

The achievement of steady state will be confirmed through analysis of trough (pre-dose / 24-hour concentrations) from Days 7 through 14 (Cohort 3) or Days 10 through 17 (Cohorts 1 and 2). (The 24-hour concentration for Day 17 may be used as a trough concentration at the end of the last dosing period.) These values will be analyzed in each cohort using analysis of variance with effects of subject and day (taking day as a 1-degree-of-freedom regressor effect, ie, not in the CLASS statement). If the effects of day and subject-day interaction are not found to be significant at the 5% level, then steady state will have been achieved. (Note that failure to reject the null hypothesis of the 5% 2-sided test of the effect of day in the proposed regression model is equivalent to a finding that the 95% 2-sided confidence limit on the slope includes the value 0.)

In a supplemental exploratory analysis, the values of $AUC_{0\text{-}24}$ and C_{max} will be analyzed for differences between males and females. This analysis will be performed separately for each cohort and study day (8 separate analyses for each parameter) using by-gender summary statistics and 2-sample *t* tests.

12. CHANGES FROM THE PROTOCOL AND PLANNED ANALYSES

There are no major changes to the planned analyses as stated in the protocol. Any minor changes were for the purpose of streamlining the analysis.

13. HEADINGS

Each page of the analysis will show the sponsor's name, the investigational product, and the protocol number. Report tables will be embedded in the MS Word report document from SAS program output without change. The footer of each table will show the name of the SAS program

module which generated it, the names of all data sets providing input data in the program and the date and time the table was generated.

14. ARCHIVING AND RETENTION OF DOCUMENTS

After finalization of the analysis, the following will be archived at TKL Research, Inc. and/or with the study sponsor:

- SAP and any amendments
- DMP and Database Specification
- All SAS code used in the project for statistical analysis, report tables generation, and analysis data set creation
- Tables, listings and figures as included in the clinical study report
- SAS study data tabulation model (SDTM) and analysis dataset model (ADaM) datasets
- Relevant correspondence
- Any other pertinent study document (i.e. study protocol, investigator's brochure, correspondence, study report(s), etc.).

15. REFERENCES

No references are included.

16. OUTLINE OF PROPOSED TABLES, FIGURES AND LISTINGS

All the mock-up shells will be included in a separate document.

15. OUTLINE OF PROPOSED TABLES, FIGURES AND LISTINGS

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14.2.A.1.3.2	Mean TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (single dose) and 14 (steady state) Cohort 3, PK Population

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Mean TBI-223 Plasma Concentration by Treatment and Time Point, 0 to 72 Hours Post-dose

14.2.A.2.1.1	Mean TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population
14.2.A.2.1.2	Mean TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population

14.2.A.2.2.1	Mean TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.A.2.2.2	Mean TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.A.2.3.1	Mean TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population
14.2.A.2.3.2	Mean TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population

14.2.A.3.1-14.2.A.3.3

Mean TBI-223 Plasma Trough Concentration by Treatment and Time Point, Approach to Steady State

14.2.A.3.1	Mean TBI-223 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 1, PK Population
14.2.A.3.2	Mean TBI-223 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 2, PK Population
14.2.A.3.3	Mean TBI-223 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 1 to 14 Cohort 3, PK Population

14.2.B.1.1.1-14.2.B.1.3.2

Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, 0 to 24 Hours Post-dose

14.2.B.1.1.1	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 1, PK Population
14.2.B.1.1.2	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 1, PK Population

14.2.B.1.2.1	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 2, PK Population
14.2.B.1.2.2	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 2, PK Population
14.2.B.1.3.1	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (single dose) and 14 (steady state) Cohort 3, PK Population
14.2.B.1.3.2	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (single dose) and 14 (steady state) Cohort 3, PK Population

14.2.B.2.1.1-14.2.B.2.3.2

Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, 0 to 72 Hours Post-dose

14.2.B.2.1.1	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population
14.2.B.2.1.2	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population
14.2.B.2.2.1	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.B.2.2.2	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.B.2.3.1	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population

14.2.B.2.3.2	Individual Subjects TBI-223 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population

14.2.B.3.1-14.2.B.3.3

Individual Subjects TBI-223 Plasma Trough Concentration by Treatment and Time Point, Approach to Steady State

14.2.B.3.1	Individual Subjects TBI-223 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 1, PK Population
14.2.B.3.2	Individual Subjects TBI-223 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 2, PK Population
14.2.B.3.3	Individual Subjects TBI-223 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 1 to 14 Cohort 3, PK Population

14.2.C.1.1.1-14.2.C.1.3.2

Mean M2 Plasma Concentration by Treatment and Time Point, 0 to 24 Hours Post-dose

14.2.C.1.1.1	Mean M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 1, PK Population
14.2.C.1.1.2	Mean M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 1, PK Population
14.2.C.1.2.1	Mean M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 2, PK Population
14.2.C.1.2.2	Mean M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 2, PK Population
14.2.C.1.3.1	Mean M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (single dose) and 14 (steady state) Cohort 3, PK Population

14.2.C.1.3.2	Mean M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (single dose) and 14 (steady state) Cohort 3, PK Population

14.2.C.2.1.1-14.2.C.2.3.2

Mean M2 Plasma Concentration by Treatment and Time Point, 0 to 72 Hours Post-dose

14.2.C.2.1.1	Mean M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population
14.2.C.2.1.2	Mean M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population
14.2.C.2.2.1	Mean M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.C.2.2.2	Mean M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.C.2.3.1	Mean M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population
14.2.C.2.3.2	Mean M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population

14.2.C.3.1-14.2.C.3.3

Mean M2 Plasma Trough Concentration by Treatment and Time Point, Approach to Steady State

14.2.C.3.1	Mean M2 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 1, PK Population

14.2.C.3.2	Mean M2 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 2, PK Population
14.2.C.3.3	Mean M2 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 1 to 14 Cohort 3, PK Population

14.2.D.1.1.1-14.2.D.1.3.2

Individual Subjects M2 Plasma Concentration by Treatment and Time Point, 0 to 24 Hours Post-dose

14.2.D.1.1.1	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 1, PK Population
14.2.D.1.1.2	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 1, PK Population
14.2.D.1.2.1	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 2, PK Population
14.2.D.1.2.2	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state) Cohort 2, PK Population
14.2.D.1.3.1	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 24 Post-Dose, Days 1 (single dose) and 14 (steady state) Cohort 3, PK Population
14.2.D.1.3.2	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 24 Post-Dose, Days 1 (single dose) and 14 (steady state) Cohort 3, PK Population

14.2.D.2.1.1-14.2.D.2.3.2

Individual Subjects M2 Plasma Concentration by Treatment and Time Point, 0 to 72 Hours Post-dose

14.2.D.2.1.1	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population

14.2.D.2.1.2	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 1, PK Population
14.2.D.2.2.1	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.D.2.2.2	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Days 1 (single dose, fasted) and 17 (steady state, fed) Cohort 2, PK Population
14.2.D.2.3.1	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population
14.2.D.2.3.2	Individual Subjects M2 Plasma Concentration by Treatment and Time Point, Log-linear Scale Hours 0 to 72 Post-Dose, Day 14 (steady state) Cohort 3, PK Population

14.2.D.3.1-14.2.D.3.3

Individual Subjects M2 Plasma Trough Concentration by Treatment and Time Point, Approach to Steady State

14.2.D.3.1	Individual Subjects M2 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 1, PK Population
14.2.D.3.2	Individual Subjects M2 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 4 to 17 Cohort 2, PK Population
14.2.D.3.3	Individual Subjects M2 Plasma Trough Concentrations by Treatment and Time Point, Approach to Steady State, Days 1 to 14 Cohort 3, PK Population

Listings

16.1.7	Subject Enrollment and Randomization
16.2.1.1	Screen Failure
16.2.1.2	Subject Disposition

16.2.2	Protocol Deviations
16.2.3	Population Datasets
16.2.4.1	Demographics and Baseline Characteristics
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16.2.8.4.3	Clinical Laboratory Test Results: Urinalysis
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16.2.8.5	Laboratory Values Outside of Normal Range
16.2.8.6	Vital Signs
16.2.8.7.1	Physical Examinations
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16.2.8.8	12-Lead ECG Results
16.2.9	General Comments

Table 14.1.1: Summary of Subject Disposition

	TBI-223 1800 mg	**TBI-223 2400 mg**	**TBI-223 3000 mg**	**Any TBI-223**	**Pooled Placebo**	**Overall**
Number of Subjects Screened						XX
Number of Subjects Randomized	XX	XX	XX	XX	XX	XX
Number of Subjects in Safety Population, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Subjects in Pharmacokinetic (PK) Population, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Subjects Completing the Study, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Subjects Discontinued, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Reason for Discontinuation, n (%)						
Withdrawal of Informed Consent	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Adverse Event/Serious Adverse Event	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Subject's Request	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Protocol Violation	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Occurrence of one of the safety criteria for exclusion after treatment has been instituted	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Subject is Lost to Follow-up	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Investigator's Judgment	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Other[1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: Denominator for percentages is the number of subjects randomized.
[1] See subject comment for details. <Programming Note: Include this footnote only if applicable. If multiple subjects have the same reason specified as a comment, include a row for that reason.>
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Table 14.1.2: Summary of Subject Demographics and Baseline Characteristics
Safety Population

	TBI-223 1800 mg	**TBI-223 2400 mg**	**TBI-223 3000 mg**	**Any TBI-223**	**Pooled Placebo**	**Overall**
Age (years)						
Mean (SD)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Minimum, Maximum	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Gender, n (%)						
Male	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Female	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Race, n (%)						
White	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Black or African American	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Asian	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
American Indian or Alaskan Native	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Native Hawaiian or Other Pacific Islander	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Other/Multiracial	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Table 14.1.2: Summary of Subject Demographics and Baseline Characteristics
Safety Population

	TBI-223 1800 mg	TBI-223 2400 mg	TBI-223 3000 mg	Any TBI-223	Pooled Placebo	Overall
Ethnicity, n(%)						
Hispanic or Latino	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Hispanic or Latino	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Weight (kg)						
Mean (SD)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Minimum, Maximum	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Height (cm)						
Mean (SD)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Minimum, Maximum	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
BMI (kg/m^2) [1]						
Mean (SD)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)	XX.XX (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Minimum, Maximum	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

[1] Baseline BMI is calculated as baseline weight / baseline height^2.

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Table 14.1.3.1: Summary of Extent of Exposure of TBI-223
Safety Population

	Study Day of Dose for Cohort 1 (1800 mg)/Cohort 2 (2400 mg)	**Study Day of Dose for Cohort 3 (3000 mg)**	**TBI-223 1800 mg (N=XX)**	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Any TBI-223 (N=XX)**
Subjects who Received Treatment, N (%)						
At Least One Dose			XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
All Intended Doses	15 total	14 total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Fasting Dose	Day 1		XX (XX.X)	XX (XX.X)	--	XX (XX.X)
Fed Doses						
Dose 1	Day 4	Day 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 2	Day 5	Day 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 3	Day 6	Day 3	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 4	Day 7	Day 4	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 5	Day 8	Day 5	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 6	Day 9	Day 6	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 7	Day 10	Day 7	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 8	Day 11	Day 8	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 9	Day 12	Day 9	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 10	Day 13	Day 10	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 11	Day 14	Day 11	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 12	Day 15	Day 12	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 13	Day 16	Day 13	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dose 14	Day 17	Day 14	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Total Number of Doses						
N			XX	XX	XX	XX
Mean (SD)			XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median			XX.X	XX.X	XX.X	XX.X
Minimum, Maximum			XX, XX	XX, XX	XX, XX	XX, XX

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Table 14.2.1.X: Summary of Plasma TBI-223 Concentration (ng/mL) by Time Point
[TBI-223 1800mg] [TBI-223 2400mg][TBI-223 3000mg]
Pharmacokinetic (PK) Population

	TBI-223						M2					
Time Point	**N**	**Mean (SD)**	**Geometric Mean (SE)**	**CV (%)**	**Minimum, Maximum**	**Median**	**N**	**Mean (SD)**	**Geometric Mean (SE)**	**CV (%)**	**Minimum, Maximum**	**Median**
Day 1												
Pre-Dose	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
30 Minutes	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
1 Hour	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
2 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
3 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
4 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
5 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
6 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
7 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
8 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
12 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
16 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
20 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
24 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
30 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
36 Hours	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
<etc.>												

Note: Concentrations below the limit of quantitation are imputed as 0.00 in the computation of descriptive statistics. SD = Standard Deviation, SE = Standard Error, CV = Coefficient of Variation.

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Note: Include all measured time points for all cohorts. Label pre-dose time points for Days 5 – 17 (Cohorts 1 and 2) and Days 2-14 (Cohort 3) as C_{trough} (pre-dose).

Table 14.2.2.1.X: Summary of TBI-223 Pharmacokinetic Parameters
[TBI-223 1800mg] [TBI-223 2400mg]
Pharmacokinetic (PK) Population

	Day 1 (fasting)						Day 4 (fed)					
	N	**Mean (SD)**	**Geometric Mean (SE)**	**CV (%)**	**Minimum, Maximum**	**Median**	**N**	**Mean (SD)**	**Geometric Mean (SE)**	**CV (%)**	**Minimum, Maximum**	**Median**
AUC_{0-24} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
AUC_{inf} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
C_{max} (µg/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
T_{max} (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx	xx	xxx (xxx)	--	--	xxx, xxx	xxx
λ_z (/h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx	xx	xxx (xxx)	--	--	xxx, xxx	xxx
$t_{½}$ (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx	xx	xxx (xxx)	--	--	xxx, xxx	xxx
CL/F (L/h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx	xx	xxx (xxx)	--	--	xxx, xxx	xxx
V_Z/F (L)	xx	xxx (xxx)	--	--	xxx, xxx	xxx	xx	xxx (xxx)	--	--	xxx, xxx	xxx

Note: Concentrations below the limit of quantitation are imputed as 0 in the computation of AUC_{0-24}. SD = Standard Deviation, SE = Standard Error, CV = Coefficient of Variation.

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Table 14.2.2.2.X: Summary of TBI-223 Pharmacokinetic Parameters
[TBI-223 1800mg] [TBI-223 2400mg]
[All Subjects][Male Subjects][Female Subjects]
Pharmacokinetic (PK) Population

	N	Mean (SD)	Geometric Mean (SE)	CV (%)	Minimum, Maximum	Median
Day 4 (fed, single-dose)						
AUC_{0-24} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
AUC_{inf} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
C_{max} (µg/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
T_{max} (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
λ_z (/h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
$t_{½}$ (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
Day 17 (fed, steady state)						
AUC_{0-24} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
AUC_{inf} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
C_{max} (µg/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
T_{max} (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
C_{min} (µg/mL)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
T_{min} (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
λ_z (/h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
$t_{½}$ (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
Accumulation Ratio						
C_{max}	xx	xxx (xxx)	--	--	xxx, xxx	xxx
AUC_{0-24}	xx	xxx (xxx)	--	--	xxx, xxx	xxx

Note: Concentrations below the limit of quantitation are imputed as 0 in the computation of AUC_{0-24}. SD = Standard Deviation, SE = Standard Error, CV = Coefficient of Variation.
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Table 14.2.2.2.3: Summary of TBI-223 Pharmacokinetic Parameters
TBI-223 3000mg
[All Subjects][Male Subjects][Female Subjects]
Pharmacokinetic (PK) Population

	N	Mean (SD)	Geometric Mean (SE)	CV (%)	Minimum, Maximum	Median
Day 1 (fed, single-dose)						
AUC_{0-24} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
AUC_{inf} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
C_{max} (µg/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
T_{max} (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
λ_z (/h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
$t_{½}$ (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
CL/F (L/h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
V_Z/F (L)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
Day 14 (fed, steady state)						
AUC_{0-24} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
AUC_{inf} (µg*h/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
C_{max} (µg/mL)	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
T_{max} (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
C_{min} (µg/mL)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
T_{min} (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
λ_z (/h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
$t_{½}$ (h)	xx	xxx (xxx)	--	--	xxx, xxx	xxx
Accumulation Ratio						
C_{max}	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx
AUC_{0-24}	xx	xxx (xxx)	xxx (xxx)	xx.x	xxx, xxx	xxx

Note: Concentrations below the limit of quantitation are imputed as 0.00 in the computation of AUC_{0-24}. SD = Standard Deviation, SE = Standard Error, CV = Coefficient of Variation.
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Table 14.2.3: Summary of TBI-223 Pharmacokinetic Parameters
Food Effect
Pharmacokinetic (PK) Population

	TBI-223 1800 mg (N=xx)	**TBI-223 2400mg (N=xx)**
C_{max} (µg/mL)		
Fasting Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)
Fed Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)
Ratio of Geometric Means	x.xxx	x.xxx
90% Confidence Interval	[x.xxx, x.xxx]	[x.xxx, x.xxx]
AUC_{0-24} (µg.h/mL)		
Fasting Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)
Fed Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)
Ratio of Geometric Means	x.xxx	x.xxx
90% Confidence Interval	[x.xxx, x.xxx]	[x.xxx, x.xxx]
AUC_{inf} (µg.h/mL)		
Fasting Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)
Fed Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)
Ratio of Geometric Means	x.xxx	x.xxx
90% Confidence Interval	[x.xxx, x.xxx]	[x.xxx, x.xxx]
T_{max} (h)		
Fasting Median	x.xx	x.xx
Fed Median	x.xx	x.xx
P value (Wilcoxon Signed Rank test, Fed vs. Fasting)	x.xxx	x.xxx

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Table 14.2.4: Summary of TBI-223 Pharmacokinetic Parameters
Confirmation of Steady State
Pharmacokinetic (PK) Population

	TBI-223 1800 mg (N=xx)	**TBI-223 2400mg (N=xx)**	**TBI-223 3000mg (N=xx)**
P value (study day; slope)	x.xxx	x.xxx	x.xxx
P value (subject-day interaction)	x.xxx	x.xxx	x.xxx

Note: For 1800mg and 2400mg, the analysis includes pre-dose concentrations for Days 10 through 17, and 24h concentration for Day 17; for 3000mg, the analysis includes pre-dose concentrations for Days 7 through 14, and 24h concentration for Day 14.

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Table 14.2.5: Summary of TBI-223 Pharmacokinetic Parameters
Analysis of Gender Differences
Pharmacokinetic (PK) Population

	TBI-223 1800 mg		TBI-223 2400mg		TBI-223 3000mg	
	Male (N=xx)	**Female (N=xx)**	**Male (N=xx)**	**Female (N=xx)**	**Male (N=xx)**	**Female (N=xx)**
Single-Dose, Fed[a]						
C_{max} (µg/mL)						
Arithmetic Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
P value (gender, *t* test)		x.xxx		x.xxx		x.xxx
AUC_{0-24} (µg.h/mL)						
Arithmetic Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
P value (gender, *t* test)		x.xxx		x.xxx		x.xxx

[a] Day 4 for 1800mg and 2400mg, Day 1 for 3000mg.

Table 14.2.5: Summary of TBI-223 Pharmacokinetic Parameters
Analysis of Gender Differences
Pharmacokinetic (PK) Population

	TBI-223 1800 mg		TBI-223 2400mg		TBI-223 3000mg	
	Male (N=xx)	**Female (N=xx)**	**Male (N=xx)**	**Female (N=xx)**	**Male (N=xx)**	**Female (N=xx)**
Steady State, Fed[a]						
C_{max} (µg/mL)						
Arithmetic Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
P value (gender, *t* test)		x.xxx		x.xxx		x.xxx
AUC_{0-24} (µg.h/mL)						
Arithmetic Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
P value (gender, *t* test)		x.xxx		x.xxx		x.xxx

[a] Day 17 for 1800mg and 2400mg, Day 14 for 3000mg.

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Table 14.2.5: Summary of TBI-223 Pharmacokinetic Parameters
Analysis of Gender Differences
Pharmacokinetic (PK) Population

	TBI-223 1800 mg		TBI-223 2400mg	
	Male (N=xx)	**Female (N=xx)**	**Male (N=xx)**	**Female (N=xx)**
Single Dose, Fasting (Day 1)				
C_{max} (µg/mL)				
Arithmetic Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
P value (gender, *t* test)		x.xxx		x.xxx
AUC_{0-24} (µg.h/mL)				
Arithmetic Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
Geometric Mean (SEM)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
P value (gender, *t* test)		x.xxx		x.xxx

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Note: Tables 14.2.6.1.1 through 14.2.9 follow identical layouts to 14.2.2.1.1 through 14.2.5.

Table 14.3.1.1: Overall Summary of Treatment-Emergent Adverse Events by Treatment
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Any TBI-223 (N=XX)**	**Pooled Placebo (N=XX)**
Treatment-Emergent Adverse Events (TEAEs)					
Number of Events	XX	XX	XX	XX	XX
Number of Subjects, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Treatment-Related TEAEs					
Number of Events	XX	XX	XX	XX	XX
Number of Subjects, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Serious TEAEs (All)					
Number of Events	XX	XX	XX	XX	XX
Number of Subjects, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Serious TEAEs (Deaths)					
Number of Events	XX	XX	XX	XX	XX
Number of Subjects, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Treatment-Related Serious TEAEs					
Number of Events	XX	XX	XX	XX	XX
Number of Subjects, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
TEAEs Leading to Study Discontinuation					
Number of Events	XX	XX	XX	XX	XX
Number of Subjects, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: TEAEs include all AEs starting or worsening after the first dosing of the study drug.

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Table 14.3.1.2: Summary of Treatment-Emergent Adverse Events
by Preferred Term in Descending Frequency
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Any TBI-223 (N=XX)**	**Pooled Placebo (N=XX)**
Subjects with Any TEAE, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: TEAEs include all AEs starting or worsening on or after the dosing of the study drug. Counts reflect numbers of subjects reporting one or more adverse events that map to the MedDRA preferred term. Each subject will be counted only once within a preferred term.

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[Programming note: AEs will be presented in descending order of the frequency of PT in the “Any-TBI-223” column.]

Table 14.3.1.3: Summary of Treatment-Related Treatment-Emergent Adverse Events
by Preferred Term in Descending Frequency
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Any TBI-223 (N=XX)**	**Pooled Placebo (N=XX)**
Subjects with Any Treatment-Related TEAE, n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: TEAEs include all AEs starting or worsening on or after the dosing of the study drug. Counts reflect numbers of subjects reporting one or more adverse events that map to the MedDRA preferred term. Each subject will be counted only once within a preferred term.

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[Programming note: AEs will be presented in descending order of the frequency of PT in the "Any-TBI-223" column.]

Table 14.3.1.4: Summary of Treatment-emergent Adverse Events
by System Organ Class and Preferred Term by Maximum Severity
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Any TBI-223 (N=XX)**	**Pooled Placebo (N=XX)**
Subjects with Any TEAE, n (%)					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Potentially Life-Threatening	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<< Adverse Event Body System>>					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Potentially Life-Threatening	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Potentially Life-Threatening	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: TEAEs include all AEs starting or worsening on or after the dosing of the study drug. Counts reflect numbers of subjects reporting one or more adverse events that map to the MedDRA preferred term. Each subject will be counted only once within a system organ class or a preferred term.

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[Programming note: AEs will be presented in alphabetical order of SOC and descending order by the descending frequency of PT in the “Any TBI-223” column]

Table 14.3.1.5: Summary of Treatment-Related Treatment-emergent Adverse Events
by System Organ Class and Preferred Term by Maximum Severity
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Any TBI-223 (N=XX)**	**Pooled Placebo (N=XX)**
Subjects with Any Treatment-Related TEAE, n (%)					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Potentially Life-Threatening	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<< Adverse Event Body System>>					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Potentially Life-Threatening	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Potentially Life-Threatening	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: TEAEs include all AEs starting or worsening on or after the dosing of the study drug. Counts reflect numbers of subjects reporting one or more adverse events that map to the MedDRA preferred term. Each subject will be counted only once within a system organ class or a preferred term.

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Table 14.3.1.6: Summary of Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term by Maximum Causality
Safety Population

	TBI-223 1800mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Any TBI-223 (N=XX)**	**Pooled Placebo (N=XX)**
Subjects with Any TEAE, n (%)					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Unlikely	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Possible	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Probable	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Certain	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<< Adverse Event Body System>>					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Unlikely	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Possible	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Probable	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Certain	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
<<Adverse Event Preferred Term>>					
Total	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Related	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Unlikely	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Possible	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Probable	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Certain	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: TEAEs include all AEs starting or worsening on or after the dosing of the study drug. Counts reflect numbers of subjects reporting one or more adverse events that map to the MedDRA preferred term. Each subject will be counted only once within a system organ class or a preferred term.

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Table 14.3.2.1.X: Summary of Clinical [Hematology][Chemistry][Coagulation]
Absolute Values and Change from Baseline by Treatment and Time Point
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Pooled Placebo (N=XX)**
[Lab Tests Name (Units)]				
Day -1 (Baseline)				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Day 1, 6-7 hours post-dose				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX

Continue for safety labs (hematology and chemistry) and Coagulation at 6-7 hours post-dose on Days 1, 2, 3, 4, 6, 10, 14, 17, and on Days 20 and 26

Note: Baseline is the last available measurement prior to the first dose of the study drug on Day 1. If Day -1 Assessment is missing, use Screening Assessment.
Generated on XX/XX/XX:XXXX by XXX / Uses: XXXX / Reference: Data Listing XXXX

[Programming Note: Summarize all lab tests with continuous results. Page break between lab tests.]

Table 14.3.2.2.X: Summary of Clinical [Hematology][Chemistry][Coagulation]
Categorical Change from Baseline
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Pooled Placebo (N=XX)**
[Lab Tests Name (Units)]				
Day 1				
Number of Subjects Assessed, N (%)	XX	XX	XX	XX
Below Normal –> Below Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Below Normal –> Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Below Normal –> Above Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Normal –> Below Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Normal –> Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Normal –> Above Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Above Normal –> Below Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Above Normal –> Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Above Normal –> Above Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Day 2				
Etc.				
<Programming Note: Continue for Days 3, 4, 6, 10, 14, 17, 20, and 26. Use "—" to indicate not applicable for specific cohorts.>				

Note: Baseline is the last available measurement prior to the first dose of the study drug on Day 1.

Generated on XX/XX/XX:XXXX by XXX / Uses: XXXX / Reference: Data Listing XXXX

[Programming Note: For hematology differential, please include only absolute values (not the % for differentials).]

Table 14.3.2.3.X: Summary of Laboratory Values Outside of Normal Range and Investigator's Assessment
[Hematology][Chemistry][Coagulation]
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Pooled Placebo (N=XX)**
Number of Subjects with Findings, N (%)				
Not clinically significant	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Clinically significant	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
[Lab Tests Name (Units)]				
Number of Subjects with Abnormality, N (%)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Below Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Above Normal	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)

Note: Baseline is the last available measurement prior to the first dose of the study drug on Day 1. This summary includes results from any post-baseline visit.

Generated on XX/XX/XX:XXXX by XXX / Uses: XXXX / Reference: Data Listing XXXX

Table 14.3.2.4.1: Summary of 12-Lead ECG Numeric Results
Absolute Values and Change from Baseline by Treatment and Time Point
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Pooled Placebo (N=XX)**
[Tests Name (Units)]				
Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Day 1 Post-Dose [2]				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX

<Continue for Days 4, 5-10, 12-17, 18-19, 20, 26>

Note: Baseline is the last available measurement prior to the first dose of the study drug on Day 1.

Generated on` XX/XX/XX:XXXX by XXX / Uses: XXXX / Reference: Data Listing XXXX

[Programming note: Summarize all ECG tests with continuous results, including ventricular rate, PR, QRS, QT, QTcF intervals. Page break between ECG tests.]

Table 14.3.2.4.2: Summary of 12-Lead ECG Categorical Analysis
QTcF
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Pooled Placebo (N=XX)**
QTcF (msec)				
Absolute Values [1]				
> 450	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
> 480	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
> 500	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Change from baseline [2]				
> 30	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
> 60	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: Baseline is the last available measurement prior to the first dose of the study drug on Day 1.

[1] Subjects with QTcF absolute values > (450, 480 and 500 msec) at any post dosing time point are included.
[2] Subjects with QTcF change from baseline values > (30 and 60 msec) at any post dosing time point are included.
<Programming Note: Additional QTcF value categories may be added to aid data interpretation.

Generated on XX/XX/XX:XXXX by XXX / Uses: XXXX / Reference: Data Listing XXXX

Table 14.3.2.5: Summary of Vital Signs
Absolute Values and Change from Baseline by Treatment and Time Point
Safety Population

	TBI-223 1800 mg (N=XX)	**TBI-223 2400 mg (N=XX)**	**TBI-223 3000 mg (N=XX)**	**Pooled Placebo (N=XX)**
[Vital Sign Tests Name (Units)]				
Baseline [1]				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Day 1, 1 Hour Post-Dose				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
<Day 2>				
<Day 3>				
etc				

Note: Baseline is the last available measurement prior to the first dose of the study drug on Day 1.

Generated on XX/XX/XX:XXXX by XXX / Uses: XXXX / Reference: Data Listing XXXX

Table 14.3.2.5: Summary of Vital Signs
Absolute Values and Change from Baseline by Treatment and Time Point
Safety Population

<Day 14/Day 17 Pre-Dose>				
Day 14 6 Hours Post-Dose				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
Change from Day 14 Pre-Dose				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX	XX
Minimum, Maximum	XX, XX	XX, XX	XX, XX	XX, XX
<Day 15>				
<Day 16>				
<Day 17>				
<Follow-up Visits>				

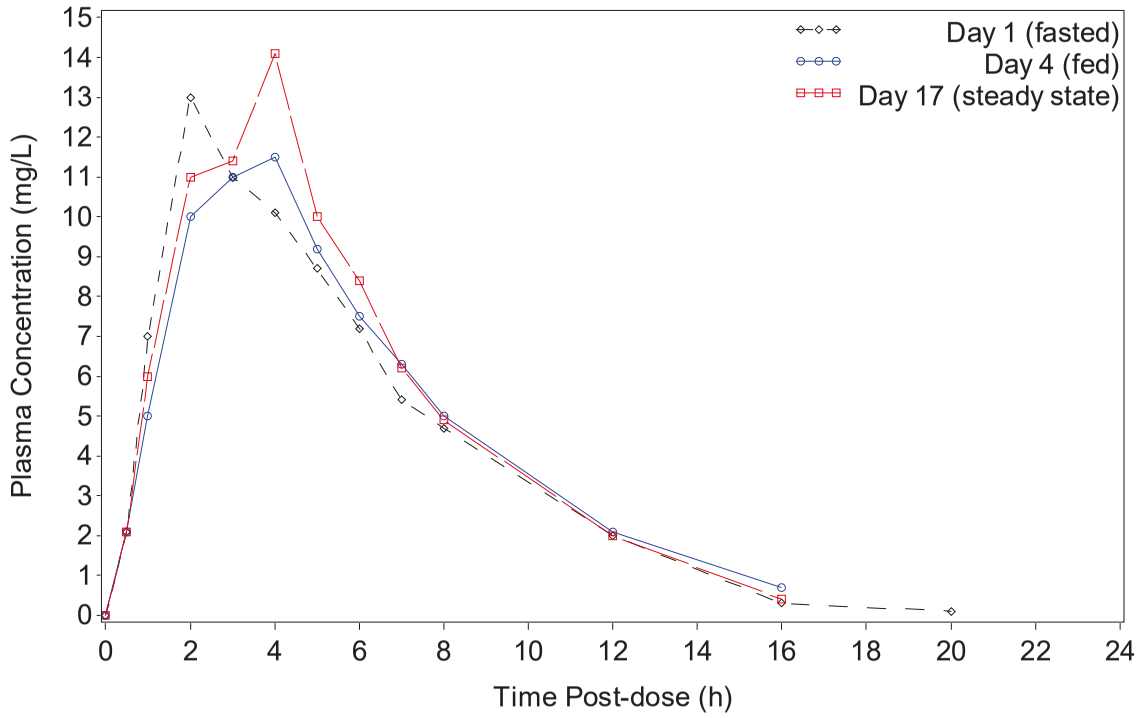
Note: Baseline is the last available measurement prior to the first dose of the study drug on Day 1.

Generated on XX/XX/XX:XXXX by XXX / Uses: XXXX / Reference: Data Listing XXXX

Sample Figure (same layout for all figures)

Global Alliance for TB Drug Development
Protocol Number: TBI-223-CL-002

Figure 14.2.A.1.1.1: Mean TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale
Hours 0 to 24 Post-Dose, Days 1 (fasted), 4 (fed), and 17 (steady state)
Cohort 1, PK Population



Generated on <date-time> by <Program Name> / Uses: <List datasets>

Sample SAS Code (same layout for all figures)

```
DATA BLANK;
       BLANK=" ";
```

```
RUN;

OPTION LS=200 NODATE NONUMBER MISSING=' ';
TITLE1;
ODS RTF FILE="[FILENAME.RTF]" STYLE=STYLES.TEST headery=720 footery=720 nogtitle nogfootnote bodytitle;
ODS LISTING CLOSE;

PROC REPORT DATA=BLANK NOWD SPLIT="|" MISSING NOCENTER
  STYLE(REPORT)={OUTPUTWIDTH=8.75in}
  STYLE(COLUMN HEADER)=[PROTECTSPECIALCHARS=OFF];
  COLUMNS BLANK;
  DEFINE BLANK        / DISPLAY " " ;
COMPUTE BEFORE   _PAGE_ /style=[protectspecialchars=off];
  LINE "\ql\b{Global Alliance for TB Drug Development}\b0\tqr\tx12250\tab{Page 1 of 1}";
  LINE "Protocol Number: TBI-223-CL-002";
  LINE "\par\qc{Figure 14.2.1: Mean TBI-223 Plasma Concentration by Treatment and Time Point, Linear Scale}";
       line "Cohort 1, PK Population";
       LINE "\par\ql{ }\brdrb\brdrs";
ENDCOMP;
RUN;

GOPTIONS RESET=ALL DEVICE=EMF FTEXT="Albany AMT" HSIZE=6 VSIZE=3.75;
AXIS1 LABEL=(ANGLE=90 HEIGHT=2 "Plasma Concentration (mg/L)") ORDER=(0 TO 15 BY 1) VALUE=(HEIGHT=2) MINOR=NONE;
AXIS2 LABEL=(HEIGHT=2 "Time Post-dose (h)") VALUE=(HEIGHT=2) ORDER=(0 TO 24 by 2) MINOR=NONE;
SYMBOL1 VALUE=DIAMOND COLOR="BLACK" LINE=20 INTERPOL=JOIN;
SYMBOL2 VALUE=CIRCLE COLOR="BLUE"   LINE=1  INTERPOL=JOIN;
SYMBOL3 VALUE=SQUARE COLOR="RED"    LINE=5  INTERPOL=JOIN;
LEGEND1 DOWN=3 POSITION=(TOP RIGHT INSIDE) VALUE=(HEIGHT=2 "Day 1 (fasted)" "Day 4 (fed)" "Day 17 (steady state)") MODE=PROTECT
LABEL=NONE;
PROC GPLOT DATA=PLOT;
       PLOT  Y*X=DAY / VAXIS=AXIS1 HAXIS=AXIS2 LEGEND=LEGEND1;
       FORMAT DAY D.;
RUN;

PROC REPORT DATA=BLANK NOWD SPLIT="|" MISSING NOCENTER
  STYLE(REPORT)={OUTPUTWIDTH=8.75in}
  STYLE(COLUMN HEADER)=[PROTECTSPECIALCHARS=OFF];
  COLUMNS BLANK;
  DEFINE BLANK        / DISPLAY " " ;
COMPUTE AFTER /style=[protectspecialchars=off];
    LINE "\ql{ }\brdrt\brdrs{}Generated on <date-time> by <Program Name> / Uses: <List datasets>";
ENDCOMP;
RUN;
```

16.1.7: Subject Enrollment and Randomization

All Subjects

Subject	Date of Informed Consent	Satisfy All I/E Criteria?	Date of Randomization	Randomization Number	Planned Treatment	Actual Treatment
XXX	XXXX-XX-XX	XX	XXXX-XX-XX	XXXXX	XXXX	XXXX
XXX	XXXX-XX-XX	XX	XXXX-XX-XX	XXXXX	XXXX	XXXX
001	2020-06-19	Yes	2020-07-08	0345	TBI-223 1800mg	TBI-223 1800mg

Generated on XX/XX/XX XX:XX by XXXX/ Uses: XXXX

16.2.1.1: Screen Failures

Subject	Date of Informed Consent	Date of Screening	Ethnicity	Gender	Race	Serious Adverse Event Reported?	Inclusion/Exclusion Criteria Not Met	Additional Reason for Screen Failure
XXX	XXXX-XX-XX	XXXX-XX-XX	XXX	XXX	XXX	XXX	XXXX	XXXX
XXX	XXXX-XX-XX	XXXX-XX-XX	XXX	XXX	XXX	XXX	XXXX	XXXX
S002	2020-06-19	2020-06-19	Hispanic or Latino	Female	White	No	Inclusion 3	--

Generated on XX/XX/XX:XXXXXXXX by XXXX/ Uses: XXXX

[Programming Note: Include all additional reasons for screen failure and display format "Other: XXXXXX". XXXX is the detailed reason. Use semi-colon to separate each reason.]

16.2.1.2: Disposition of Subjects

All Randomized Subjects

[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

	Date (Day) of [1]						
Subject	**Screening**	**Randomization**	**First Dose**	**Last Dose**	**Last Visit**	**Last Contact**	**Study Completion Status**
XXX	XXXX-XX-XX(XX)	XXXX-XX-XX(XX)	XXXX-XX-XX(XX) TXX:XX	XXXX-XX-XX(XX) TXX:XX	XXXX-XX-XX(XX)	XXXX-XX-XX(XX)	XXXXX
XXX	XXXX-XX-XX(XX)	XXXX-XX-XX(XX)	XXXX-XX-XX(XX) TXX:XX	XXXX-XX-XX(XX) TXX:XX	XXXX-XX-XX(XX)	XXXX-XX-XX(XX)	XXXXX
0120	2020-06-19 (-10)	2020-06-29 (1)	2020-06-29 (1) T08:30	XXXX-XX-XX(XX) TXX:XX	2020-07-06(8)	XXXX-XX-XX(XX)	Completed

[1] Day is calculated relative to Day 1.

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

[Programming Note: Study completion status will include reason for discontinuation if a subject does not complete the study.]

16.2.2: Protocol Deviation
Safety Population
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Subject	Major or Minor	Visit (Date)	Protocol Deviation	Protocol Deviation Type	Action Taken
XXX	Major	XX (XX-XX-XXXX)	XXXX	XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXX
	Minor	XX (XX-XX-XXXX)	XXXX	XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXX

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

[Programming Note: If site deviation or deviation for SF subjects are also available, include those at the very end of this listing.]

16.2.3: Population Datasets

[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Subject	In Safety Population?	In PK Population?
XXX	Yes	Yes
XXX	No	No

16.2.4.1: Demographics and Baseline Characteristics
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Cohort	Age (years)	Gender	Race	Ethnicity	Weight (kg)	Height (cm)	BMI (kg/m^2) [1]
XXX	TBI-223 1800 mg	XX	Male	XXXX	XX	XXX	XXX	XX.X
XXX	TBI-223 1800 mg	XX	Female	XXXX	XX	XXX	XXX	XX.X

Note: BMI = Body Mass Index
[1] Baseline BMI is calculated as baseline weight / baseline height^2.

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

16.2.4.2: Prior and Concomitant Medication

[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Prior or Concomitant?	WHO Preferred Term (Verbatim Term) / ATC Classification	Indication Dose Unit/Frequency/Route	Start Date (Day)-Stop Date (Day)
XXX	Concomitant	XXXXXX (xxxxx)/ XXXXXX	XXX XX XX/XXX/XXXX	XXXX-XX-XX (XX) – XXXX-XX-XX (XX)
XXX	Concomitant	XXXXXX/ XXXXXX	XXX XX XX/XXX/XXXX	XXXX-XX-XX (XX) – ONGOING

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

[Programming Note: List medication in ascending start date for each subject.]

16.2.4.3: Medical and Surgical History

[[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Diagnosis / Procedure	Start Date (Day)	End Date (Day)	Medication Taken Currently?
XXXX	XXXX	XXXX-XX-XX (XX)	XXXX-XX-XX (XX)	no
XXXX	XXXX	XXXX-XX-XX (XX)	ONGOING	yes

16.2.5.1: Plasma Concentrations
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg]
Safety Population

Subject	Visit	PK Time Point	Dosing Date and Time (Day)	Sample Collection Date and Time (Day)	Elapsed Time (h)	Concentration (ng/mL)	
						TBI-223	M2
XXX	Day 1	Pre-dose	XXXX-XX-XX TXX:XX (XX)	XXXX-XX-XX TXX:XX (XX)	XX,X	XX.X	XX.X
		30 min		XXXX-XX-XX TXX:XX (XX)	XX,X	XX.X	XX.X
		1 hour		XXXX-XX-XX TXX:XX (XX)	XX,X	XX.X	XX.X
	<Etc.>	<Etc.>		XXXX-XX-XX TXX:XX (XX)	XX,X	XX.X	XX.X

16.2.5.2: TBI-223 Pharmacokinetic Parameters
[TBI-223 1800mg][TBI-223 2400mg]

PK Population

Subject	Visit	AUC_{0-24} (µg.h/mL)	AUC_{inf} (µg.h/mL)	C_{max} (µg)	T_{max} (h)	C_{min} (µg)	T_{min} (h)	CL/F (L/h)	V_z/F (L)	RAUC	RC_{max}
XXX	Day 1	XXX	XXX	XXX	XXX	--	--	XXX	XX.XX	--	--
	Day 4	XXX	XXX	XXX	XXX	--	--	XXX	XX.XX	--	--
	Day 17	XXX	--	XXX	XXX	XXX	XXX	--	--	X.XXX	X.XXX

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

16.2.5.2: TBI-223 Pharmacokinetic Parameters
TBI-223 3000mg

PK Population

Subject	Visit	AUC_{0-24} (µg.h/mL)	AUC_{inf} (µg.h/mL)	C_{max} (µg)	T_{max} (h)	C_{min} (µg)	T_{min} (h)	CL/F (L/h)	V_z/F (L)	RAUC	RC_{max}
XXX	Day 1	XXX	XXX	XXX	XXX	--	--	XXX	XX.XX	--	--
	Day 14	XXX	--	XXX	XXX	XXX	XXX	--	--	X.XXX	X.XXX

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

16.2.5.3: TBI-223 Elimination Rate Constant and Half-Life
[TBI-223 1800mg][TBI-223 2400mg]

PK Population

Subject	Visit	Start Time of Elimination Phase (h)	End Time of Elimination Phase (h)	Number of Points Included	λz (h^{-1})	$t_{1/2}$ (h)	R-square
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 4	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 17	xx	xx	x	0.xxx	x.xx	0.xxx
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 4	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 17	xx	xx	x	0.xxx	x.xx	0.xxx

16.2.5.3: TBI-223 Elimination Rate Constant and Half-Life
TBI-223 3000mg

PK Population

Subject	Visit	Start Time of Elimination Phase (h)	End Time of Elimination Phase (h)	Number of Points Included	λz (h^{-1})	$t_{1/2}$ (h)	R-square
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 14	xx	xx	x	0.xxx	x.xx	0.xxx
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 14	xx	xx	x	0.xxx	x.xx	0.xxx

16.2.5.4: M2 Pharmacokinetic Parameters
[TBI-223 1800mg][TBI-223 2400mg]

PK Population

Subject	Visit	AUC_{0-24} (µg.h/mL)	AUC_{inf} (µg.h/mL)	C_{max} (µg)	T_{max} (h)	C_{min} (µg)	T_{min} (h)	CL/F (L/h)	V_z/F (L)	RAUC	RC_{max}
XXX	Day 1	XXX	XXX	XXX	XXX	--	--	XXX	XX.XX	--	--
	Day 4	XXX	XXX	XXX	XXX	--	--	XXX	XX.XX	--	--
	Day 17	XXX	--	XXX	XXX	XXX	XXX	--	--	X.XXX	X.XXX

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

16.2.5.4: M2 Pharmacokinetic Parameters
TBI-223 3000mg

PK Population

Subject	Visit	AUC_{0-24} (µg.h/mL)	AUC_{inf} (µg.h/mL)	C_{max} (µg)	T_{max} (h)	C_{min} (µg)	T_{min} (h)	CL/F (L/h)	V_z/F (L)	RAUC	RC_{max}
XXX	Day 1	XXX	XXX	XXX	XXX	--	--	XXX	XX.XX	--	--
	Day 14	XXX	--	XXX	XXX	XXX	XXX	--	--	X.XXX	X.XXX

Generated on XX/XX/XX:XXXX by XXXX/ Uses: XXXX

16.2.5.5: M2 Elimination Rate Constant and Half-Life
[TBI-223 1800mg][TBI-223 2400mg]

PK Population

Subject	Visit	Start Time of Elimination Phase (h)	End Time of Elimination Phase (h)	Number of Points Included	λz (h^{-1})	$t_{1/2}$ (h)	R-square
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 4	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 17	xx	xx	x	0.xxx	x.xx	0.xxx
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 4	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 17	xx	xx	x	0.xxx	x.xx	0.xxx

16.2.5.5: M2 Elimination Rate Constant and Half-Life
TBI-223 3000mg

PK Population

Subject	Visit	Start Time of Elimination Phase (h)	End Time of Elimination Phase (h)	Number of Points Included	λz (h^{-1})	$t_{1/2}$ (h)	R-square
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 14	xx	xx	x	0.xxx	x.xx	0.xxx
XXX	Day 1	xx	xx	x	0.xxx	x.xx	0.xxx
	Day 14	xx	xx	x	0.xxx	x.xx	0.xxx

16.2.5.6: Fasting and Meals
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

PK Population

Subject	Visit	Fast 10 hours duration prior to dosing	Standard Breakfast 30 min prior to dosing	Breakfast end within 5 min prior to dosing	Fast 4 hour duration post-dosing
XXX	Day 1	Yes	Yes	Yes	Yes
	Etc.	Yes	Yes	Yes	Yes

16.2.7.1: Adverse Events
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	MedDRA Preferred Term (Verbatim Term) / MedDRA SOC Term	Start Date (Day)and Time - End Date (Day) and Time	TEAE? [1] / Severity/ Outcome/ Relationship [2]	Action Taken with Study Product Other Action Taken / Serious (Which Criteria Met)?
XXX	XXXXXXX (XXXXXX)/ XXXXXXXXX	XXXX-XX-XX (XX) TXX:XX – XXXX-XX-XX (XX) TXX:XX	Yes/ Mild/ Recovered/Resolved/ Not Related	Not Applicable / Concomitant Medication / Yes (Hospitalization)
	XXXXXXX (XXXXXX)/ XXXXXXXXX	XXXX-XX-XX (XX) TXX:XX – XXXX-XX-XX (XX) TXX:XX	Yes/ Mild/ Recovered/Resolved/ Possible	Not Applicable / None / No

[1] TEAE is defined as an AE with a start date and time on or after the first dose of any study drugs.
[2] Relationship is determined by the Investigator between an AE and the study drug unless otherwise specified.

Generated on XX/XX/XX:XXXX by XXXX / Uses: XXXX

16.2.7.2: Serious Adverse Events and Adverse Events Leading to Study Discontinuation
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	MedDRA Preferred Term (Verbatim Term) / MedDRA SOC Term	Start Date (Day)and Time - End Date (Day) and Time	TEAE? [1] / Severity/ Outcome/ Relationship [2]	Action Taken with Study Product Other Action Taken / Serious (Which Criteria Met)?
XXX	XXXXXXX (XXXXXX)/ XXXXXXXXX	XXXX-XX-XX (XX) TXX:XX – XXXX-XX-XX (XX) TXX:XX	Yes/ Mild/ Recovered/Resolved/ Not Related	Drug Reduced / Concomitant Medication / Yes (Hospitalization)
	XXXXXXX (XXXXXX)/ XXXXXXXXX	XXXX-XX-XX (XX) TXX:XX – XXXX-XX-XX (XX) TXX:XX	Yes/ Mild/ Recovered/Resolved/ Probable	Drug Withdrawn / Discontinued Study / Yes (Life Threatening)

[1] TEAE is defined as an AE with a start date and time on or after the first dose of any study drugs.
[2] Relationship is determined by the Investigator between an AE and the study drug unless otherwise specified.

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16.2.8.1: Childbearing Potential and Serum Pregnancy Tests
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Childbearing Potential	Visit	Date (Day)	Result
XXX	IUD	Screening	XXXX-XX-XX (XX)	Negative
		Day -2 (Check-In)	XXXX-XX-XX (XX)	Negative

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16.2.8.2: Urine Drug and Alcohol Screenings
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Date (Day)	Urine Drug Screen	Urine Alcohol Screen	Urine Cotinine Screen
XXX	Screening	XXXX-XX-XX (XX)	Negative	Negative	Negative
	Day -2 (Check-In)	XXXX-XX-XX (XX)	Negative	Negative	Negative

16.2.8.3: Clinical Laboratory Tests – Investigator's Assessments
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Date and Time (Day)	Lab Category	Investigator's Assessment
XXX	Screening	XXXX-XX-XXTXX:XX (XX)	Hematology	Normal
		XXXX-XX-XXTXX:XX (XX)	Serum chemistry	Abnormal NCS
		XXXX-XX-XXTXX:XX (XX)	Urinalysis	Normal
		XXXX-XX-XXTXX:XX (XX)	Coagulation	Normal
	Day -1			
		Etc.		

Note: NCS = Not clinically significant. CS = Clinically significant.

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16.2.8.4.X: Clinical Laboratory Test
[Serum Chemistry][Hematology][Urinalysis][Coagulation]
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Date and Time (Day)	Parameter (Unit)	Reference Range	Result / Abnormality	CFBL[1]
XXX	Screening	XXXX-XX-XXTXX:XX (XX)	XXXX	XXXX,XXXX	XXXX	XXX.X
	Day -1	XXXX-XX-XXTXX:XX (XX)			XXXX/**L**	XXX.X
	Day 1	XXXX-XX-XXTXX:XX (XX)			XXXX/**H**	XXX.X
	Etc.					

Note: H = High; L = Low. A = Abnormal, unspecified high or low.
[1] CFBL = Change from Baseline. Baseline value is the last available measurement prior to first dose of study drug.

Generated on XX/XX/XX:XXXX by XXXXX / Uses: XX

[Programming Note: Urinalysis will not have CFBL column. Include all available visits. For out of range results, add a letter (A, H or L) in bold right next the results.]

16.2.8.5: Laboratory Values Outside of Normal Range
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Date and Time (Day)	Category	Parameter (Unit)	Reference Range	Result	Abnormality
XXX	Day -1	XXXX-XX-XXTXX:XX (XX)	Chemistry	XXXX	XXXX,XXXX	XX.XX	Low
	Day -1	XXXX-XX-XXTXX:XX (XX)	Hematology	XXXX	XXXX,XXXX	XX.XX	High

16.2.8.6: Vital Signs

[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Time Point	Date and Time (Day)	Parameter (Unit)	Result	CFBL [1]
XXX	Screening	--	XXXX-XX-XXTXX:XX (XX)	Systolic BP (mmHg)	XXX	--
	Day -2	--	XXXX-XX-XXTXX:XX (XX)	Systolic BP (mmHg)	XXX	--
	Day 1	Pre-dose	XXXX-XX-XXTXX:XX (XX)	Systolic BP (mmHg)	XXX	Baseline
	Day 1	1 Hour Post-dose	XXXX-XX-XXTXX:XX (XX)	Systolic BP (mmHg)	XXX	XXX
	Etc.					

Also include tests: Diastolic BP (mmHg), Pulse Rate (beats/min), Respiration Rate (breaths/min), Temperature (^{o}C), Pulse Oximetry

BP = Systolic Blood Pressure
[1] CFBL = Change from Baseline. Baseline value is the last available measurement prior to first dose of study drug.

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16.2.8.7.1: Physical Examinations
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Date of Test (Day)	Body System	Result	Comment
XXX	Screening	XXX-XX-XX (XX)	All	All Body Systems Normal	--
	Day -1	XXX-XX-XX (XX)	XXX	Abnormal	XXXXX
	Day -1	XXX-XX-XX (XX)	All Other	All Other Body Systems Normal	--
	Etc.				

Note: Body systems examined include Cardiovascular, Respiratory, Gastrointestinal, Musculoskeletal, Skin, Systemic, and Other.

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16.2.8.7.2: Neurological Examinations
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Date of Test (Day)	Nervous System	Findings	Comment
XXX	Screening	XXX-XX-XX (XX)	All	All Nervous Systems Normal	--
	Day -1	XXX-XX-XX (XX)	XXX	Abnormal	XXXXX
	Day -1	XXX-XX-XX (XX)	All Other	All Other Nervous Systems Normal	--

Note: Neurological systems examined include Mental Status: Orientation, Speech, and Memory, Cranial Nerves 2 through 12, Motor System, Sensory System: Face, Neck, Arms, Trunk, and Legs, Reflexes. Coordination: Upper Body and Lower Body, Gait, and Other.

Generated on XX/XX/XX:XXXX by XXXX / Uses: XXXX

16.2.8.8: 12-Lead ECG Results
[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Visit	Date and Time (Day)	Investigator's Assessment	Test (Unit)	Result	CFBL [1]
XXX	Screening	XXXX-XX-XXTXX:XX (XX)	Normal	Heart Rate	XXX	XXX
				PR Interval	XXX	XXX
				Etc.	XXX	XXX
	Day 1 Pre-dose	XXXX-XX-XXTXX:XX (XX)	Normal	Heart Rate	XXX	XXX
				PR Interval	XXX	XXX
				Etc.	XXX	XXX
	Etc.					

[1] CFBL = Change from Baseline. Baseline value is the last available measurement prior to first dose of study drug.

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[Programming Note: Include all visits and all ECG tests collected on the CRF (ventricular rate, PR, QRS, QT, QTcF).]

16.2.9: General Comments

[TBI-223 1800mg][TBI-223 2400mg][TBI-223 3000mg][Pooled Placebo]

Safety Population

Subject	Comment Reference	Comment
XXX	XXXX	XXXXXXXXXXXXXXXXXX
	XXXX	XXXXXXXXXXXXXXXXXX

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Certificate Of Completion

Envelope Id: B5BB91B52BEB41D0993F26E00A6EAA0E
Status: Completed
Subject: Please DocuSign: tbi-223-cl-002-mad-sap-final-2021-03-24 - unsigned.pdf
Source Envelope:
Document Pages: 82
Signatures: 2
Certificate Pages: 5
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Disabled
Time Zone: (UTC-05:00) Eastern Time (US & Canada)

Envelope Originator:
Marie Messina
40 Wall St FL 24
New York, NY 10005
marie.messina@tballiance.org
IP Address: 184.152.37.209

Record Tracking

Status: Original
20 April 2021 | 10:55
Holder: Marie Messina
marie.messina@tballiance.org
Location: DocuSign

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Jerry Nedelman jerry.nedelman@tballiance.org Senior Director, Pharmacometrics Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 7839E5A7-6523-498A-B928-E27ED5F738EA Using IP Address: 71.187.221.226 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I have reviewed this document	Sent: 20 April 2021 | 10:58 Viewed: 20 April 2021 | 11:04 Signed: 20 April 2021 | 11:04
Electronic Record and Signature Disclosure: Accepted: 06 September 2017 | 09:47 ID: 14a4057c-d83c-405f-bceb-b7e7952cc709		
Michael Tuley mtuley@tklresearch.com Michael TKL Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: BE981D7A-3194-4349-9E30-D520D1EBB3FD Using IP Address: 70.36.31.130 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 20 April 2021 | 10:58 Viewed: 20 April 2021 | 11:07 Signed: 20 April 2021 | 11:07
Electronic Record and Signature Disclosure: Accepted: 20 January 2021 | 15:54 ID: 63f91ddf-4564-4029-968b-d91f4c9fbc68		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	20 April 2021 | 10:58
Certified Delivered	Security Checked	20 April 2021 | 11:07
Signing Complete	Security Checked	20 April 2021 | 11:07
Completed	Security Checked	20 April 2021 | 11:07

Payment Events	Status	Timestamps

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Operating Systems:	Windows2000? or WindowsXP?
Browsers (for SENDERS):	Internet Explorer 6.0? or above
Browsers (for SIGNERS):	Internet Explorer 6.0?, Mozilla FireFox 1.0, NetScape 7.2 (or above)
Email:	Access to a valid email account
Screen Resolution:	800 x 600 minimum
Enabled Security Settings:	•Allow per session cookies •Users accessing the internet behind a Proxy Server must enable HTTP 1.1 settings via proxy connection

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