CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN

for

DMID Protocol: 18-0006

Study Title:

A Phase 1, Randomized, Double-Blind, Multi-Site, Single Dose Escalation Study to Evaluate the Safety, Pharmacokinetics, and Immunogenicity of SAR440894 vs Placebo in Healthy Adults

NCT04441905

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DATE: 04-SEP-2024

RESTRICTED

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 18-0006**
Development Phase:	Phase 1
Products:	SAR440894 and Placebo
Form/Route:	Intravenous (IV) Infusion
Indication Studied:	Chikungunya virus (CHIKV)
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health US Department of Health and Human Services
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This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

ADA	Anti-drug Antibody
AE	Adverse Event
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
AP	Alkaline Phosphatase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Classification
AUC	Area Under the Concentration-Time Curve
$AUC_{(0\text{-inf})}$	Area Under the Concentration-Time Curve Extrapolated to Infinity
$AUC_{(0\text{-last})}$	Area Under the Concentration-Time Curve from Time of Dosing to Time of Last Measurable Concentration
BMI	Body Mass Index
BP	Blood Pressure
BQL	Below the Quantification Limit
BUN	Blood Urea Nitrogen
C	Celsius
CAR	Clinical Agent Repository
CHEM	Chemistry
CHIKV	Chikungunya Virus
CI	Confidence Interval
CL	Clearance
cm	Centimeter
C_{max}	Maximum Concentration
COAG	Coagulation
CRF	Case Report Form
CS	Clinically Significant
CSR	Clinical Study Report
CV	Coefficient of Variation
DBP	Diastolic Blood Pressure
DHHS	Department of Health and Human Services
DMID	Division of Microbiology and Infectious Diseases

List of Abbreviations *(continued)*

ECG	Electrocardiogram
eCRF	Electronic Case Report Form
eGFR	Estimated Glomerular Filtration Rate
ET	Early Termination
FDA	Food and Drug Administration
GM	Geometric Mean
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
HCT	Hematocrit
HEM	Hematology
HGB	Hemoglobin
HLGT	High Level Group Term
ICH	International Conference on Harmonisation
IND	Investigational New Drug
IV	Intravenous
IRB	Institutional Review Board
kg	Kilogram
L	Liter
LLN	Lower Limit of Normal
LLOQ	Lower Limit of Quantification
m	Meter
mAb	Monoclonal Antibody
MedDRA	Medical Dictionary for Regulatory Activities
µg	Microgram
mg	Milligram
mL	Milliliter
MM	Medical Monitor
MRSD	Maximum Recommended Starting Dose
N	Number
NCA	Noncompartmental Analysis
NCS	Not Clinically Significant
NHP	Non-human primate

List of Abbreviations *(continued)*

NIAID	National Institutes of Allergy and Infectious Diseases
NIH	National Institutes of Health
NOAEL	No Observed Adverse Effect Level
NSAID	Non-steroidal Anti-inflammatory Drug
ONR	Outside Normal Range
OTC	Over-the-counter
PBPK	Physiological Based Pharmacokinetic
PI	Principal Investigator
PK	Pharmacokinetics
PT	Preferred Term
QNS	Quantity Not Sufficient
QTcF	QT interval corrected for heart rate by Fridericia's cube root correction
RBC	Red Blood Cell
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
SOC	System Organ Class
SRC	Safety Review Committee
SUSAR	Serious and Unexpected Suspected Adverse Reaction
SWFI	Sterile Water for Injection
$t_{1/2}$	Apparent terminal elimination half-life
TEAE	Treatment-emergent Adverse Event
T_{max}	Time of Maximum Concentration
UA	Urinalysis
ULN	Upper Limit of Normal
UP	Unanticipated Problem
V_d	Volume of Distribution
VS	Vital Signs

List of Abbreviations *(continued)*

WBC	White Blood Cells
WHO	World Health Organization
λ_z	Elimination Rate Constant

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1, Randomized, Double-Blind, Multi-Site, Single Dose Escalation Study to Evaluate the Safety, Pharmacokinetics, and Immunogenicity of SAR440894 vs Placebo in Healthy Adults" (Division of Microbiology and Infectious Diseases (DMID) Protocol 18-0006) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports) [1], and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) [2] and Topic E9 (Statistical Principles for Clinical Trials) [3]. The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association [4] and the Royal Statistical Society for statistical practice [5].

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for safety, pharmacokinetics (PK), and immunogenicity outcomes, and (4) a list of proposed tables, figures, and listings. Within the table, figure, and listing mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

This is a Phase 1, randomized, double-blind, placebo-controlled, multi-site, single dose escalation study to evaluate the safety, PK, and immunogenicity of intravenous (IV) SAR440894 in healthy adult participants. Five cohorts of 8 participants each will be enrolled in the study. In each of the 5 cohorts, 6 participants will be randomized to SAR440894, and 2 participants will be randomized to placebo. Each cohort will complete the study approximately 22 weeks (150 days) from randomization through Follow-up, which accounts for the long half-life of SAR440894 and will allow for appropriate characterization of the safety, PK, and immunogenicity of SAR440894.

2.1. Purpose of the Analyses

This SAP describes the safety, PK, and immunogenicity analyses of 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, and 20 mg/kg of SAR440894 that will be included in the CSR. The analyses of safety, PK, and immunogenicity endpoints will be presented in the CSR after completion of the study.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary

- To determine the safety of single ascending IV infusions of SAR440894 when administered in healthy adults.

3.1.2. Secondary

- To determine the PK of single ascending doses of 60-minute IV infusions of SAR440894 in healthy adults.
- To assess the immunogenicity of single ascending doses of 60-minute IV infusions of SAR440894 in healthy adults.

3.2. Endpoints

3.2.1. Primary

- Occurrence of adverse events (AEs) and serious adverse events (SAEs) following the start of study product administration through the final visit (Day 150 [±7]), or Early Termination (ET).
- The occurrence of clinically significant (CS) changes from baseline in vital signs and clinical safety laboratory values following administration of study product through final visit (Day 150 [±7]), or ET.
- The occurrence of CS changes in electrocardiogram (ECG) parameters post administration of study product through the final visit (Day 150 [±7]), or ET.

3.2.2. Secondary

- SAR440894 PK after single ascending doses determined from plasma concentrations pre-dose and from the start of infusion until Day 150 (±7), or ET.
- SAR440894 immunogenicity determined from presence/absence of plasma human anti-drug antibody (ADA) and measurement of concentration from prior to infusion and at selected time points after infusion up to Day 150 (±7) or ET.

3.3. Study Definitions and Derived Variables

Baseline

The baseline value will be the last value obtained prior to start of infusion of study product. In the case of ECG assessments, if triplicate measurements were performed at the last visit prior to study product administration, then baseline will be the mean value of the measurements from that visit. For example, if triplicate ECGs are performed on Day 1 prior to dosing, the baseline ECG value for the purpose of analysis would be the mean value of these measurements.

Treatment Group

Participants will be enrolled and dosed in five dose-ascending cohorts, in which 2 participants will be randomized to placebo and 6 participants will be randomized to SAR440894. The ascending doses of SAR440894 will be 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, and 20 mg/kg. Safety, PK, and immunogenicity results will be presented by treatment group. All participants assigned to placebo will be presented as pooled together for the purposes of these analyses. Treatment groups will be presented in the following order: SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo. Results from participants assigned placebo will not appear in the PK analyses.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase 1, randomized, double-blind, placebo-controlled, multi-site, single dose escalation study to evaluate the safety, PK, and immunogenicity of 5 dose levels of IV SAR440894 vs placebo in healthy adults. An overall schematic of the study design is given in **Figure 1**. The study is expected to enroll approximately 40 participants into 5 cohorts of 8 participants each.

Study enrollment will proceed from Cohort 1 to Cohort 5 starting with the lowest dose and escalating to the next higher dose. In each of the 5 cohorts, participants will be randomized to either SAR440894 (n=6) or placebo (n=2) in an overall 3:1 ratio (**Table 1**). In each cohort, 2 sentinel participants will first be randomized to receive SAR440894 or placebo in a 1:1 ratio. The enrolling site principal investigator(s) (PI(s)) will review safety data through Day 4 to confirm no halting criteria are met. After confirmation that sentinel participant halting rules have not been met, the remaining 6 participants in each cohort will be randomized in a 5:1 ratio to SAR440894 and placebo and dosed in pairs of two at least 24 hours apart. Dosing start times will be staggered by at least 15 minutes between participants. Participants will remain in confinement for at least 72 hours after receiving study product. Thereafter, follow-up in each cohort will occur until Day 150 (±7 days) to account for the long half-life of SAR440894 and allow for appropriate characterization of the PK, safety, and immunogenicity of SAR440894.

Blood (plasma) samples will be collected for measuring SAR440894 concentrations for PK analysis at baseline pre-infusion and for 72 hours following the end of infusion. Additional plasma samples will be collected on Day 7 ± 1, Day 14 ± 2, Day 28 ± 4, Day 56 ± 4, Day 84 ± 7, Day 112 ± 7, Day 150 ± 7, and ET (if needed). Blood (plasma) samples for ADA measurements will be collected for assessing the immunogenicity of SAR440894 at baseline pre-infusion and on Day 56 ± 4, Day 112 ± 7, Day 150 ± 7, and ET. PK and immunogenicity plasma samples will be analyzed by Aptuit (Verona) Srl.

Safety data will be monitored from the time of infusion on Day 1 through confinement on Day 4, as well as at all Follow-up visits on Day 7 ±1, Day 14 ± 2, Day 28 ± 4, Day 56 ± 4, Day 84 ± 7, Day 112 ± 7, Day 150 ± 7, and ET (if needed). This will consist of assessments of treatment-emergent adverse events (TEAEs), vital signs (Screening, Day -1, Day 1 prior to dosing, Day 1 at 15-minute increments after the start of infusion, Day 1 at 1, 2, 4, and 6 hours post-infusion, and post-dose on Days 2, 3, 4, 7 [±1], 14 [±2], 28 [±4], 56 [±4], 84 [±7], 112 [±7], 150 [±7], and ET), symptom-directed physical examination (PE) (Days 1, 2, 3, 7 [±1], 14 [±2], 28 [±4], 56 [±4], 84 [±7], 112 [±7]), clinical laboratory safety tests (Days -1, 2, 3, 4, 7 [±1], 14 [±2], 28 [±4], 56 [±4], 84 [±7], 112 [±7], 150 [±7], and ET), 12-lead ECGs (Screening, Days 1, 4, 150 [±7], and ET), and complete PE at Screening, on Days -1 and 4, and at the last Follow-up visit (Day 150 [±7]) or ET. All laboratory testing for Screening and safety monitoring will be performed at clinical site safety laboratories. TEAEs will be assessed for severity, seriousness, and relatedness to study product. Additionally, SAEs will be evaluated by the Investigational New Drug (IND) Sponsor for whether they meet the criteria of a serious and unexpected suspected adverse reaction (SUSAR). Any unanticipated problems (UPs) will also be reported.

Blinded safety and clinical laboratory data up to the Day 14 visit will be evaluated by the Safety Review Committee (SRC) after each cohort. The safety review will include SAEs, AEs, safety clinical laboratory results, ECGs, and vital signs. The SDCC will notify the SRC and study teams via email if any halting criteria have been potentially met after each cohort. If none of the predefined halting criteria are met, the DMID medical monitor (MM) will provide approval for the study to proceed to the next cohort, or alternatively recommend convening of the Safety Monitoring Committee (SMC). If any of the predefined halting criteria are met, study enrollment and dosing will be stopped until the SMC provides recommendations regarding

continuation of the study. Otherwise, the SMC will meet for an organizational meeting and ad hoc as appropriate.

4.2. Discussion of Study Design, Including the Choice of Control Groups

SAR440894 is a potent, fully human monoclonal antibody (mAb) (IgG1) directed against the viral E2 envelope protein that has profoundly and rapidly reduced circulating and tissue viral levels in CHIKV-infected preclinical models. Due to its expected long terminal elimination half-life (approximately 4 weeks), SAR440894 has the potential for use both as a prophylactic treatment during CHIKV outbreaks and as a targeted therapy to reduce the progression to chronic symptoms in patients with acute CHIKV infections and disabling arthralgia. There are no prior clinical studies completed with SAR440894. The purpose of this single dose-escalation study is to evaluate the safety, PK, and immunogenicity of SAR440894 in healthy adult participants.

Since this is the first clinical study to be completed with SAR440894, 2 sentinel participants will be enrolled and randomized to either SAR440894 or placebo in each cohort and monitored through Day 4 for safety before enrollment of the remaining 6 participants per cohort. In each of the 5 cohorts, 6 participants will be randomized to SAR440894, and 2 participants will be randomized to placebo. There is currently no proven prophylactic or treatment against CHIKV, making placebo the natural choice of control for this study. Enrollment of each cohort will progress sequentially from the lowest dose of SAR440894 to the next highest dose. Doses are selected based on prior mouse and non-human primate (NHP) studies with consideration to the possibility of SAR440894 as both prophylactic treatment and targeted therapy (See **Section 4.4.4** for details concerning dose selection). Follow-up in each cohort will occur until Day 150 (±7 days). This prolonged follow-up period is chosen to account for the long half-life of SAR440894, while allowing for appropriate characterization of the PK, safety, and immunogenicity of SAR440894.

4.3. Selection of Study Population

The study plans to enroll 40 eligible participants. Eligible participants are healthy male and female adults aged 18-45 years inclusive meeting the eligibility criteria. Only participants who meet all inclusion criteria and no exclusion criteria will be eligible for enrollment into the trial. No exemptions are granted on participant inclusion/exclusion criteria in DMID-sponsored studies. Questions about eligibility should be directed toward the DMID medical officer. Eligibility criteria can be found in Section 5.1 of Protocol version 11.0 (v11.0).

4.3.1. Inclusion Criteria

For a list of inclusion criteria, see Section 5.1.1 of Protocol v11.0.

4.3.2. Exclusion Criteria

For a list of exclusion criteria, see Section 5.1.2 of Protocol v11.0.

4.3.3. Participant Withdrawal and Replacement

Participant Withdrawal:

Participants may voluntarily withdraw their consent for study participation at any time without penalty or loss of benefits to which they are otherwise entitled.

An investigator may also withdraw a participant from receiving the study product for any reason. If a participant withdraws or is withdrawn prior to completion of the study, the reason for this decision must be recorded in the case report forms.

A participant may also be discontinued from participation in the study for any of the following reasons:

- Request by the participant to terminate participation in the study
- Inability to collect blood samples or receive study product due to poor venous access or other reasons
- Noncompliance, based on the opinion of the site PI
- Loss to Follow-up
- Request of primary care provider
- At the request of the IRB, DMID, or FDA
- Incarceration
- Participant's well-being, based on the opinion of the site PI
- SMC recommendation
- Death
- Additional information becomes available that makes further participation unsafe
- Participant withdraws informed consent
- Participant no longer meets eligibility criteria

Participant Replacement:

Participants who withdraw prior to receiving study product will be replaced. Up to 1 participant per cohort may withdraw after dosing but before Day 112 without being replaced. Should more than 1 participant from the same cohort withdraw from the study before Day 112, they will be replaced. Any decision to replace a participant who withdraws after receiving study product will be documented in a note to file. Replacement participants will receive the same treatment as the participant being replaced.

Participants who withdraw after receiving study product will be encouraged to continue Follow-up (with participant's consent) for safety and will be asked to complete the ET visit if they do not wish to be followed per protocol. If a participant withdraws following dosing, analyses for safety, PK, and immunogenicity will be completed on blood samples already obtained.

4.4. Treatments

4.4.1. Treatments Administered

In each cohort, participants will be randomized to SAR440894 or placebo. SAR440894 or placebo will be administered as a single IV infusion over 60 minutes (with an acceptable range of 55 to 70 minutes). For each successive treatment cohort, the dose of SAR440894 will be progressively escalated from 0.3 mg/kg in Cohort 1 to 1 mg/kg in Cohort 2 to 3 mg/kg in Cohort 3 to 10 mg/kg in Cohort 4 to 20 mg/kg in Cohort 5.

4.4.2. Identity of Investigational Product(s)

SAR440894

SAR440894 is a fully human mAb (Type IgG1) directed against the E2 envelope protein of CHIKV including mutations in the Fc part that improve binding to FcRn. The drug substance of SAR440894 is produced by cell culture (CHO cells), starting from a cGMP quality cell bank and purified via chromatography steps. SAR440894 is supplied as a lyophilized powder that is to be reconstituted with 2.3 mL sterile water for injection (SWFI). Upon reconstitution, a colorless to slightly brownish/yellowish and clear to slightly opalescent solution is obtained. The formulation is comprised of the following active pharmaceutical ingredient: 10 mM histidine, 8% sucrose, 0.02% polysorbate 80 at a pH of 5.5. Extractable volume is 2 mL at 50 mg/mL (100 mg/vial).

Placebo

Placebo will be supplied as lyophilized 10 mM histidine, 8% sucrose, 0.02% polysorbate 80, pH of 5.5, and is to be reconstituted with 2.3 mL of SWFI (extractable volume 2 mL). The reconstituted product is clear and colorless.

SWFI, USP

The SWFI, USP should be used to reconstitute the SAR440894 product. The SWFI, USP is non-pyrogenic and contains no bacteriostatic, antimicrobial agent, or added buffer.

Each study product will be labeled according to manufacturer and regulatory specifications and include the statement “Caution: New Drug – Limited by Federal Law to Investigational Use.”

4.4.3. Method of Assigning Subjects to Treatment Groups (Randomization)

After informed consent has been obtained and study eligibility has been established, participants will be admitted to the clinical site within approximately 24 hours before dosing. Randomization will occur following admission to the unit and confirmation of eligibility.In each of the 5 planned dosing cohorts, eligible participants will be randomized to SAR440894 or placebo in an overall 3:1 ratio.

In each cohort, the first 2 sentinel participants will be randomized in a 1:1 ratio to SAR440894 and placebo. The remaining 6 participants in each cohort will be randomized in a 5:1 ratio to SAR440894 and placebo after confirmation that the sentinel participant halting rules have not been met. If replacements are needed, replacement participants will receive the same treatment as the originally randomized participant being replaced.

Randomized treatment assignments will be generated by a statistician at the SDCC. Enrollment of participants will be done online using the registration module of Advantage eClinical. The randomization code will be prepared by statisticians at the SDCC and included in the registration module for this trial. Advantage eClinical will assign each participant to a treatment arm after the demographic and eligibility data have been entered into the system. A designated individual at the participating site will be provided with a code list, which will be kept in a secure place, for emergency unblinding purposes. Instructions for use of the registration module are included in the Advantage eClinical User’s Guide. Manual back-up procedures and instructions are provided for use in the event that a participating site temporarily loses access to the Internet or the online enrollment system is unavailable.

4.4.4. Selection of Doses in the Study

A list of planned study product dose by cohort can be found in **Table 1**. In mouse models with early infection, single doses between 0.5 to 12.5 mg/kg administered intraperitoneally demonstrated significant viral load reduction in musculoskeletal tissues and reduction of footpad swelling (ED50 of 0.75 mg/kg) and neutralization of viremia (1 mg/kg dose). In the same mouse model, SAR440894 still induced a significant reduction of the virus in musculoskeletal tissues at a dose of 2.5 mg/kg when administered later after infection (> 72 hours). Using CHIKV-infected NHP models, IV infusion for SAR440894 at dosages of 0.5 mg/kg, 2.5 mg/kg, and 12.5 mg/kg resulted in resolution of viremia at all dosages and absence of replicative virus in joints and tissues at the 2.5 mg/kg and 12.5 mg/kg dosage. Using the mouse and NHP in vivo efficacy models, the predicted effective therapeutic dose is 2.5 mg/kg, and the predicted effective prophylactic dose is 1 mg/kg.

To determine the starting doses for the study, two approaches were used (physiological based pharmacokinetic [PBPK] modeling and single species allometry). The maximum recommended starting dose (MRSD) was chosen to give a target plasma area underneath the plasma concentration versus time curve (AUC) in humans that is 1/10th the exposure level at the no observed adverse effect level (NOAEL) from toxicity studies in NHPs. Both approaches were also used to predict the clearance and dose that would result in the same target exposure level in CHIKV infected individuals. A PBPK model for SAR440894 was constructed using the Simcyp minimal PBPK model for mAbs with 1:1 FcRn binding and used the measured FcRn binding affinity as a model input. The resulting model for NHPs adequately captured the preclinical half-life and clearance with predicted values within 2-fold of the observed values. The predicted MRSD based on the human PBPK model was 0.83 mg/kg. The MRSD was also predicted using single species allometry using NHP data and allometric exponents of 0.5, 0.8, 0.9 and 1.1. The predicted MRSD was 0.29-1.79 mg/kg and the results from the PBPK model fall within this range. In totality, these results support a conservative MRSD of 0.29 mg/kg.

The remaining doses were chosen to further allow for accurate characterization of PK and safety while balancing the public health need to advance the development of this product by reducing the overall study timeline.

4.4.5. Selection and Timing of Dose for Each Subject

Study product for each participant will be assigned by randomization. All participants are scheduled to receive study product during one 60-minute (55 to 70 minutes) infusion on Day 1.

4.4.6. Blinding

All study personnel, including the sponsor, site investigators, study personnel involved in study conduct, and participants will remain blinded to study product assignment until the study is completed and the database is locked, with the exception of the SDCC and pharmacist to prepare drug and monitor drug accountability during the study, and cases in which unblinding is required due to a safety issue. To maintain study blinding, study product preparation will be performed by an unblinded site pharmacist (or qualified unblinded personnel not involved with study procedures or evaluations, at the study site). Blinding of bioanalytical staff will be achieved through use of the SDCC GlobalTrace electronic specimen tracking system in combination with unique sample barcodes. The system provides all trial specimens with a masked label (barcode) to blind both the DMID Clinical Agent Repository (CAR) and the laboratories that receive trial specimens. The SMC may receive data in aggregate and presented by cohort. The SMC will review grouped (by treatment) and unblinded data in closed session only.

If unblinding is necessary to maintain participant safety, an unblinded statistician may be engaged to confirm if any of the impacted participants were administered SAR440894. In the case of a medical emergency requiring the site PI to know the identity of the study product the site PI is strongly advised to discuss options with the DMID MM or appropriate sponsor study personnel prior to any unblinding. As soon as possible and without revealing the participant's study product assignment (unless important to the safety of participants remaining in the study), the PI must notify the sponsor within 24 hours if the blind is broken for any reason and the PI was unable to contact the sponsor before unblinding. The site will record unblinding as a protocol deviation and document the date and reason for revealing the blinded treatment assignment for that participant.

4.4.7. Prior and Concomitant Therapy

Concomitant medications will include all current medications and medications taken in the 45 days before study treatment administration through the last study visit. Administration of any medications, therapies, or vaccines will be recorded on the appropriate data collection form.

All over-the-counter (OTC) medications or herbal, nutritional, and dietary supplements within 7 days and selected prescription medications within 14 days before study product administration are prohibited per exclusion criteria. Influenza vaccine and COVID-19 vaccine are permitted if given more than 45 days before study product administration or after Day 56. No other vaccines are permitted within 45 days of study product administration or during the duration of the study. Concurrent therapy with any prescription or OTC medication (except for acetaminophen or non-steroidal anti-inflammatory drugs (NSAID) in the case of necessary treatment of AEs) during the course of the protocol after randomization should be reviewed by the site PI before study product infusion, unless appropriate medical care necessitates that therapy should begin before the site PI can be consulted. Nonprescription systemic drugs may be used after Day 28 while prescription drugs (excluding contraceptives in females) may be used after Day 56.

4.4.8. Treatment Compliance

Since participants will be directly observed at the time of dosing by a blinded member of the clinical research team who is trained and delegated to administer the study product, participant compliance is not expected to be an issue. Treatment compliance will be documented in the electronic case report form (eCRF) by recording the date, start time, stop time, and whether the dose of study product was completely infused.

4.5. Safety, Pharmacokinetics, and Immunogenicity Variables

The following section describes the safety, PK, and immunogenicity endpoints of the study. As this study is a Phase 1 clinical trial in healthy adult participants, there will be no assessment of drug efficacy. For a detailed schedule of study procedures refer to **Table 2**.

4.5.1. Safety Variables

The following safety endpoints will be assessed:

- Chemistry (CHEM), Hematology (HEM), Urinalysis (UA), and Coagulation (COAG) clinical laboratory result safety parameters will be collected according to the schedule of study procedures in **Table 2**. The following parameters will be measured:
  - CHEM parameters: alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, total bilirubin, sodium, potassium, bicarbonate, glucose, blood urea nitrogen

(BUN), calcium, alkaline phosphatase (AP), direct bilirubin, albumin, total protein, estimated glomerular filtration rate (eGFR), and Cystatin-C.

- HEM parameters: hemoglobin (HGB), platelet count, white blood cell (WBC) count, hematocrit (HCT), red blood cell (RBC) count, basophil count, eosinophil count, lymphocyte count, monocyte count, and neutrophil count.
- COAG parameters: activated partial thromboplastin time (APTT), prothrombin time (PT), and international normalized ratio (INR).
- UA parameters: protein, occult blood, ketones, leukocyte esterase, glucose, bilirubin, nitrites, urobilinogen, WBC, and urine RBC.
  - UA will first be performed by urine dipstick testing. If any abnormal value is observed on the urine dipstick test, then urine microscopy will be performed, and the results will supersede those of the dipstick UA.

- Vital signs (VS) parameters will be collected according to the schedule in **Table 2**. The following parameters will be measured:
  - Resting (measured after lying supine for at least 5 minutes) temperature, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and respiratory rate
- ECG parameters will be collected according to the schedule in **Table 2**. The following parameters will be measured:
  - PR interval, QRS duration, QT interval, QT corrected for heart rate by Fridericia's cube root (QTcF) correction, RR interval, and ventricular rate.
    - Triplicate ECGs with 10-second rhythm strips will be obtained within a 60-minute period prior to dosing and within approximately 15 minutes after dosing is complete, separated by at least 1 minute.
    - Single, standard 12-lead safety ECGs will also be obtained.
    - If any significant changes are observed, triplicate ECG tracings, approximately 2 minutes apart, should be recorded and repeated hourly until cessation of the abnormality. Significant changes are defined as
      - Any significant change in rate or rhythm as determined by the site PI
      - QTcF interval of greater than 450 msec (male) or greater than 470 msec (female)
      - Increase from the QTcF baseline (see **Section 3.3** for definition of baseline) greater than 50 msec until the change resolves.
    - During the study, from 30 minutes before the administration of study product until approximately 4 hours post dose, continuous 12-lead ECG remote telemetry monitoring will be conducted to assess for acute changes. If a CS change occurs, the monitoring will be continued until it has resolved and deemed safe to discontinue monitoring by the site PI or designee.

All ECG recordings will be taken before obtaining any blood sample. Safety ECGs will be signed and dated by the reader, who will provide a global interpretation using the categories of Normal, Abnormal – not clinically significant (NCS), or Abnormal –CS.

- Physical exams will be performed by the qualified investigator or sub-investigator listed on the Form FDA 1572:
  - Complete physical exams will be conducted according to the schedule in **Table 2** and include the following parameters:
    - general appearance, head, ears, external examination of eyes, nose, throat, dentition, thyroid, chest (heart, lungs), abdomen, skin, neurological, extremities, back, neck, musculoskeletal, and lymph nodes.
  - A symptom-directed physical examination will be performed according to the schedule in **Table 2** for the assessment of TEAEs. Symptom-directed physical examinations following infusion will be conducted only if a participant endorses a symptom at the discretion of the PI.

The type, incidence, relatedness, and severity of TEAEs and SAEs will be recorded from the start of infusion of the study product on Day 1through the final visit on Day 150 (± 7) or ET on the appropriate data collection form and eCRF. SAEs will additionally be evaluated for whether they meet the definition of a SUSAR. UPs will also be recorded on the appropriate data collection form and eCRF within 7 calendar days of an investigator becoming aware of the actual or suspected UP.

4.5.2. Pharmacokinetics Variables

SAR440894 plasma concentrations will be determined using a validated enzyme-linked immunosorbent assay. PK samples will be analyzed by Aptuit (Verona) Srl. PK sample collections will be performed at the following time points: Baseline pre-infusion (60 to 0 minutes prior to start of infusion), at the completion of the infusion, and at (relative to the end of the infusion), 1, 4, 8, 12, 24, 48, and 72 hours, and on Day 7 ± 1, Day 14 ± 2, Day 28 ± 4, Day 56 ± 4, Day 84 ± 7, Day 112 ± 7, Day 150 ± 7, and ET (if needed). For blood sample collection, there will be an acceptable window of ±10 minutes in the first 8 hours after dosing and ±30 minutes between 9 and 72 hours. PK samples at Follow-up visits will be collected during the designated Follow-up window. The “end of infusion” sample should be obtained within 5 minutes of the end of the infusion.

4.5.3. Immunogenicity Variables

ADA in K3EDTA plasma will be assessed by using validated bridging electrochemiluminescence assays for Screening, confirmation, and titration. Immunogenicity samples for ADAs will be analyzed by Aptuit (Verona) Srl. Plasma samples for ADA measurements will be collected pre-infusion (60 to 0 minutes prior to start of infusion), Day 56 ± 4, Day 112 ± 7, Day 150 ± 7, and ET (if necessary).

For immunogenicity assays, a positive result will be defined as a positive screening assay followed by a positive confirmatory assay. A negative result will be defined as a negative screening assay or a positive screening assay followed by a negative confirmatory assay. Treatment-induced ADA is defined as a negative result at baseline and a positive result post-dose. Treatment-boosted ADA is defined as a positive result at both baseline and post-dose, with a 4-fold increase to titer. Pre-existing ADA is defined as a positive result at both baseline and post-dose, but without meeting the definition of treatment-boosted ADA.

5. SAMPLE SIZE CONSIDERATIONS

No formal sample-size calculations based on testing a statistical hypothesis were performed. This study plans to randomize 40 participants. The number of participants was selected to allow sufficient evaluation of safety, and PK of the various single dose regimens to be administered in this study and is consistent with standards of practice for Phase 1 studies.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Unless otherwise specified, continuous variables will be summarized by the following descriptive statistics: the number of participants with non-missing data included in the analysis (n), mean, standard deviation (SD), median, minimum value (min), and maximum value (max). Summary statistics for discrete data will include frequencies and proportions and may include confidence intervals (CIs) for the proportion. When 95% CIs are given for a proportion, exact (Clopper-Pearson) CIs will be used, unless otherwise specified.

All randomized participants will be included in summaries of participant demographics. The Safety Population will be used for summaries of safety endpoints, the PK Population will be used for summaries of PK endpoints, and the Immunogenicity Population or the Pharmacokinetics – Immunogenicity Subset Population will be used for summaries of immunogenicity endpoints. Denominators for clinical, clinical laboratory, VS, and ECG results at planned study time points will be the number of participants in the Safety Population with available results at the specified time point for that parameter. Denominators for the conceptual "Maximum Severity Post Baseline" time point for clinical, clinical laboratory, VS, and ECG results will be the number of participants with an observed result for the parameter obtained post-dose. Unless otherwise specified, denominators for all other safety endpoints will be the number of participants in the Safety Population. All tables will be annotated with the total population size relevant to that table/group, including any missing observations.

The sort order for listings is indicated in the implementation note for each listing shell. The sort order of treatment groups is given in **Section 3**. The sort order of clinical laboratory tests, VS, and ECG parameters is described in **Section 9**.

6.2. Timing of Analyses

A final CSR will be prepared after all safety, PK, and immunogenicity data are available following database lock.

Safety data will be reviewed in real time by the site PI(s) to evaluate whether cohort dose escalation halting rules or study halting criteria have been met, and findings will be shared with the DMID MM and Evotec medical officer. Blinded safety and clinical laboratory data up to the Day 14 visit will be evaluated by the SRC after each cohort. Interim cumulative safety data to determine escalation to higher dose will be presented to the SRC after completion of Cohort 1. After each additional cohort, the SRC will review blinded safety and clinical laboratory data through Day 14 via study web reports to determine escalation to a higher dose.

The SMC may be convened ad hoc at the recommendation of the SRC in response to a safety issue. An end of study summary of summary of final cumulative safety data will be provided for the SMC to review will be provided for the SMC to review once final safety data are once final safety data are available after database lock.

6.3. Analysis Populations

All analysis populations to be used in the final analysis are described in this section. A tabular listing of all randomized and enrolled participants excluded from an analysis population (Safety Population, PK Population, Immunogenicity Population, or Pharmacokinetics – Immunogenicity Subset Population) will be included in the CSR (**Listing 5**). Reasons for exclusion from analysis populations will be summarized in **Table 8**.

6.3.1. Safety Population

The Safety Population will include all participants who receive any amount of study product.

6.3.2. Pharmacokinetics Population

The PK Population will include all participants who received a complete dose of SAR440894 and have at least one quantifiable post-dose plasma drug concentration record.

6.3.3. Immunogenicity Population

The Immunogenicity Population will include all participants who receive any amount of study product and contribute at least one post-infusion plasma sample for immunogenicity testing for which valid results are reported.

6.3.4. Pharmacokinetics – Immunogenicity Subset Population

The Pharmacokinetics – Immunogenicity Subset Population will include all participants who received a complete dose of SAR440894, have sufficient data to permit estimation of PK parameters, and contribute at least one post-infusion plasma sample for immunogenicity testing for which valid results are reported.

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup analyses, and no formal subgroup analyses will be performed.

6.5. Missing Data

All attempts will be made to collect all data per protocol. No imputation will be performed for missing values.

6.6. Interim Analyses and Data Monitoring

Blinded combined safety data will be reviewed by the SRC after each cohort. Safety data may include, but is not limited to, vital signs, safety laboratory assessments, AEs, physical exam findings, and any noted trends through Day 14 for current cohort. The site PI(s) will also review the data in real time to assess whether any cohort dose escalation halting rules or study halting criteria have been met.

An ad hoc SMC meeting may be convened at any point throughout the study in response to a safety issue at the recommendation of the SRC.

6.7. Multicenter Studies

Safety data will be presented according to whether participants enrolled prior to or under Protocol v11.0. For all participants enrolled prior to Protocol v11.0, AEs will be assessed by the investigator using a protocol-defined grading system (see **Table 4**) using the following categories: Mild (Grade 1), Moderate (Grade 2), and Severe (Grade 3). For participants who screen and enroll with Protocol Version 11.0, AEs will be assessed by the investigator using the NCI CTCAE, Version 5.0 – November 2017 [**6**] with the following categories: Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe), Grade 4 (Life-threatening), and Grade 5 (Death).

Likewise, clinical safety laboratory evaluations and vital signs will be assessed using a protocol-defined grading system provided in **Table 5** and **Table 6** for participants enrolled prior to Protocol v11.0. For

participants enrolled under Protocol v11.0, clinical safety laboratory evaluations and vital signs will be assessed by the investigator using the NCI CTCAE, Version 5.0 – November 2017 [6]. Additionally, prior to Protocol v11.0, all abnormal laboratory and vital signs findings were defined as AEs. However, with Protocol v11.0, the language was amended to state that only CS abnormal laboratory or vital signs findings will be defined as AEs. After discussion with DMID, for participants enrolled under Protocol v11.0, it was decided to also include related abnormal laboratory findings of any clinical significance as AEs. This will potentially result in differences in the number of clinical laboratory and vital signs AEs reported across treatment groups, depending on which protocol version the participant was enrolled under.

Given the timing of the finalization of Protocol v11.0, each site will adhere to only one of these toxicity grading methods for AEs, clinical laboratory evaluations, and vital signs. Safety data will otherwise be pooled across clinical sites.

All other data will be pooled across all clinical sites. Center effects are not otherwise anticipated because the sites are using standardized procedures for study product administration, and the study relies on central laboratories for the assessment of PK and immunogenicity endpoints.

6.8. Multiple Comparisons/Multiplicity

The analysis of the primary endpoint is descriptive and no formal hypothesis tests are planned for this study. Therefore, no adjustments for multiple testing are planned.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Screened participants who were ineligible for enrollment in the study (screen failures) or eligible but not enrolled will be summarized by inclusion and exclusion criteria (**Table 10**). Enrolled participants who were ineligible for inclusion in analysis populations will be summarized by reason for participant exclusion and treatment group (**Table 8**). Individual listings of participants who were excluded from the Safety Population, the PK Population, the Immunogenicity Population, or the Pharmacokinetics – Immunogenicity Subset Population will be listed (**Listing 5**).

Participant disposition will be summarized in **Table 7**, displaying the number of participants who were screened, enrolled and randomized, received study product, had at least one quantifiable post-dosing plasma drug concentration measured, completed all planned PK blood draws, had at least one pre-infusion immunogenicity blood draw with valid results, had at least one post-infusion immunogenicity blood draw with valid results, completed all planned immunogenicity blood draws, completed final study visit, and terminated early. Participants who discontinued dosing or terminated early from the study will be listed (**Listing 2**). A flowchart displaying the disposition of study participants will be included (**Figure 2**). This figure will present the number of participants screened, enrolled, lost to follow-up, and analyzed by treatment group.

7.2. Protocol Deviations

A summary of participant-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and treatment group for all participants **(Table 3**). This table will provide the number of participants and the number of deviations for each deviation and deviation type. All participant-specific protocol deviations and non-participant-specific protocol deviations will be listed in **Listing 3** and **Listing 4**, respectively. All protocol deviations will be classified as either a major or minor deviation and summarized accordingly. As the question of a major or minor deviation wasn't included on the protocol deviation CRFs, the following process will be used to classify the deviations: (1) Prior to database lock, Emmes will generate a blinded spreadsheet of all protocol deviations and will assign major/minor according to the list in **Appendix 4**; (2) DMID will review the list and confirm their agreement or not; (3) Once the classifications are completed and finalized, Emmes will incorporate this spreadsheet into their programming.

8. EFFICACY EVALUATION

There are no efficacy endpoints for this trial.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Summaries of sex, ethnicity, and race will be presented by treatment group (**Table 13**) and by site (**Table 11**). Ethnicity is categorized as Hispanic or Latino, or Not Hispanic or Latino, Unknown, or Not Reported. In accordance with NIH reporting policy, participants may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option. Summaries of age, height, weight, and body mass index (BMI) at Screening will be presented by treatment group (**Table 14**) and by site (**Table 12**).

Individual participant listings (**Appendix 3**) will be presented for all demographics and baseline characteristics (**Listing 6**).

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past pre-existing medical conditions will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®) with MedDRA dictionary version 24.1 or higher. Summaries of participants' pre-existing and concurrent medical conditions by MedDRA System Organ Class (SOC) will be presented by treatment group (**Table 15**). Individual participant listings will be presented for all pre-existing or concurrent medical conditions (**Listing 7**).

9.1.2. Prior and Concomitant Medications

All medications will be coded to the Anatomical Therapeutic Classification (ATC) using the current version of the WHO Drug Dictionary. The use of concomitant medications taken during the study in the 45 days prior to study treatment administration through the last study visit will be summarized by treatment group, ATC 1, and ATC 2 (**Table 223**). Individual participant listings will be presented for all concomitant medications (**Listing 27**).

9.2. Measurements of Treatment Compliance

The dates of study product administration will be summarized by period and during the entire enrollment period in **Table 9** by site and treatment group. Date and time of study product administration, along with information on whether the participant was dosed according to protocol will be included in **Listing 8**. A listing of infusion interruptions will be presented in **Listing 9**.

9.3. Adverse Events

An AE that occurs during or after the first study product infusion and through the final visit is defined as a TEAE. Only TEAEs will be documented as AEs in this study. AEs will be presented separately for participants who enrolled prior to Protocol v11.0 and participants who enrolled under Protocol v11.0.

Overall summaries of TEAEs will be given in **Table 40** and **Table 41** for participants enrolled before Protocol v11.0 and for participants enrolled under Protocol v11.0, respectively. These tables will include the number of participants with at least one AE, number of participants with at least one related AE, number of participants with at least one SAE, and the number of participants with laboratory abnormalities.

All TEAEs will be presented for participants enrolled before Protocol v11.0 in **Listing 13** and for participants enrolled under Protocol v11.0 in **Listing 14**. Participant listings of non-serious AEs of moderate or greater severity will also be reported separately for participants enrolled prior to Protocol v11.0 (**Table 54**) and for

participants enrolled under Protocol v11.0 (**Table 55**). Individual listings of TEAEs leading to study product discontinuation will be presented for participants enrolled prior to Protocol v11.0 (**Table 56**) and for participants enrolled under Protocol v11.0 (**Table 57**).

The following summaries for TEAEs will be presented by treatment group, MedDRA System Organ Class (SOC), High Level Group Term (HLGT) and Preferred Term (PT):

- The number of TEAEs and number and proportion of participants reporting a TEAE will be presented for participants enrolled before Protocol v11.0 (**Table 42**) and for participants enrolled under Protocol v11.0 (**Table 43**). The exact Clopper-Pearson 95% CI for the proportion of participants experiencing each SOC/HLGT/PT will also be presented.
- The number and proportion of participants reporting a TEAE will be presented by treatment group, SOC, HLGT, PT, maximum severity, and relationship to study product for participants enrolled before Protocol v11.0 (**Table 44**) and for participants enrolled under Protocol v11.0 (**Table 45**). Participants will only be counted once per PT and highest severity but may be counted for any relationship to study treatment.
- The number and proportion of participants reporting a TEAE will also be presented by treatment group, SOC, HLGT, PT, and whether or not they resulted in alteration of administration of or discontinuation of study product for participants enrolled before Protocol v11.0 (**Table 46**) and for participants enrolled under Protocol v11.0 (**Table 47**).
- The number and proportion of participants reporting a TEAE leading to discontinuation of study product will be presented by treatment group, SOC, HLGT, PT, and relationship to study product for participants enrolled before Protocol v11.0 **(Table 50**) and for participants enrolled under Protocol v11.0 (**Table 51**). Participants will only be counted once per PT but may be counted for any relationship to study treatment.

Summaries of TEAEs will be presented graphically in bar charts by treatment group and SOC. For summaries of proportions of participants enrolled before Protocol v11.0 reporting a TEAE, denominators will be the number of participants in the Safety Population enrolled before Protocol v11.0 for each treatment group. For summaries of proportions of participants enrolled under Protocol v11.0 reporting a TEAE, denominators will be the number of participants in the Safety Population enrolled under Protocol v11.0 for each treatment group.

- The total number of related TEAEs reported will be presented by severity for participants enrolled before Protocol v11.0 (**Figure 13**) and for participants enrolled under Protocol v11.0 (**Figure 14**).
- The proportion of participants reporting a related TEAE will be presented by the maximum severity
  reported per SOC for participants enrolled before Protocol v11.0 (**Figure 15**) and for participants enrolled under Protocol v11.0 (**Figure 16**).

9.4. Deaths, Serious Adverse Events and Other Significant Adverse Events

The number and proportion of participants reporting an SAE will be presented by treatment group, MedDRA SOC, HLGT, PT, and relationship to study product for participants enrolled before Protocol v11.0 (**Table 48**) and for participants enrolled under Protocol v11.0 (**Table 49**).

Individual data listings of deaths and other SAEs will be provided for participants enrolled prior to Protocol v11.0 (**Table 52**) and for participants enrolled under Protocol v11.0 (**Table 53**). These listings will include participant ID, treatment group, AE description, SOC, HLGT, PT, duration of AE, reason reported as an SAE,

severity, relationship to treatment, alternate etiology if not related, action taken with study treatment, whether the participant discontinued due to the AE, and AE outcome.

Individual listings of SUSARs (**Table 58** and **Table 59**) and UPs (**Table 60** and **Table 61**) will also be presented for participants enrolled prior to Protocol v11.0 and for participants enrolled under Protocol v11.0, respectively. These listings will include participant ID, treatment group, AE description, SOC, HLGT, PT, duration of AE, severity, relationship to treatment, alternate etiology if not related, action taken with study treatment, whether the participant discontinued due to the AE, and AE outcome.

9.5. Pregnancies

For any participants in the Safety Population who become pregnant during the study, every attempt will be made to follow these participants until the immediate postnatal period (6 weeks) or until termination or loss of the pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. Individual data listings of pregnancy reports will be provided if a pregnancy occurs post dosing:

- Maternal information will be presented in **Listing 28**.
- Gravida and para information will be presented in **Listing 29**.
- Live birth outcomes will be presented in **Listing 30**, and still birth outcomes will be presented in **Listing 31**.
- Spontaneous, elective, or therapeutic abortion outcomes will be presented in **Listing 32**.

9.6. Clinical Laboratory Evaluations

Descriptive statistics for clinical laboratory test results including changes from baseline will be presented by time point and treatment group. Baseline is defined in **Section 3.3**. Laboratory results obtained after start of dosing will be graded according to toxicity grading criteria given in **Table 5** and **Table 6** for participants who screened and enrolled prior to Protocol v11.0 and according to NCI CTCAE, Version 5.0 – November 2017 for participants who screen and enroll with Protocol v11.0. Note there are two instances in which the NCI CTCAE, Version 5.0 will not be used as implied: (1) eGFR toxicity will be assessed via chronic kidney disease, not acute kidney injury; and (2) calcium (corrected for albumin) will not be used and general grading (CTCAE term Investigations - Other) will be used instead. Laboratory results will be summarized by toxicity grade separately for participants who enrolled prior to Protocol v11.0 and participants who enrolled under Protocol v11.0.

Laboratory results that meet grading critera per the toxicity table but fall within the specific site's reference range may be recorded in the database as normal and will only be reported as an AE if deemed related or clinically significant per the site PI. Any laboratory results that meet this criteria will be described in the CSR.

All safety laboratory results, change from baseline, and severity with applicable references ranges will be listed for each parameter by treatment group and time point. Unscheduled clinical laboratory evaluations will be included in listings of all clinical laboratory results but excluded from tabular and graphical summaries by time point, except when calculating the maximum severity post baseline. Abnormal laboratory results will also be presented. Abnormal laboratory results that do not have toxicity grading ranges defined will not have severity indicated in tables and listings except as “ONR” (outside of normal range). Abnormal laboratory results for parameters with defined toxicity grading ranges that are outside of the normal range but not at least mild in severity will have ONR as the severity included after the result.

The sort order for chemistry parameters will be as follows: sodium, potassium, bicarbonate, glucose, blood urea nitrogen, creatinine, eGFR, calcium, albumin, total protein, AP, AST, ALT, direct bilirubin, total bilirubin, and cystatin-C.

The sort order for hematology parameters will be as follows: hemoglobin, WBC, lymphocytes, neutrophils, eosinophils, platelets, hematocrit, RBC, basophils, and monocytes.

The sort order for coagulation parameters will be as follows: APTT, prothrombin time, and INR.

The sort order for urinalysis parameters will be as follows: urine protein, urine glucose, bilirubin, nitrite, occult blood, urine WBC, urine RBC, urobilinogen, ketones, and leukocyte esterase.

- All chemistry results, including at unscheduled visits, will be presented in **Listing 15**. Abnormal chemistry results, including ONR and Grade 1 or higher results, will be presented in **Table 62** for participants enrolled prior to Protocol v11.0 and in **Table 63** for participants who enrolled under Protocol v11.0.
- All hematology results, including at unscheduled visits, will be presented in **Listing 16**. Abnormal hematology results, including ONR and Grade 1 or higher results, will be presented in **Table 64** for participants enrolled prior to Protocol v11.0 and in **Table 65** for participants who enrolled under Protocol v11.0.
- All coagulation results, including at unscheduled visits, will be presented in **Listing 17**. Abnormal coagulation results, including ONR and Grade 1 or higher results, will be presented in **Table 66** for participants enrolled prior to Protocol v11.0 and in **Table 67** for participants who enrolled under Protocol v11.0.
- All urinalysis results, including at unscheduled visits, will be presented in **Listing 18**. Abnormal urinalysis results, including ONR and Grade 1 or higher results, will be presented in **Table 68** for participants enrolled prior to Protocol v11.0 and in **Table 69** for participants who enrolled under Protocol v11.0.

All screening results will be listed for each participant by treatment group and visit. Serology results will be presented in **Listing 19**, serum ß-hCG and FSH pregnancy testing results will be given in **Listing 20**, and urine toxicology and alcohol results will be presented in **Listing 21**.

The distribution of laboratory results will be presented by severity, treatment group, and time point.

Chemistry

- Proportions of participants with mild, moderate, and severe results for any chemistry parameter will be presented for participants who enrolled prior to Protocol v11.0 in **Table 70** by treatment group, severity at baseline, time point, and severity across all graded chemistry parameters. Proportions of participants with results that are mild, moderate, severe, life-threatening, or result in death for any chemistry parameter will be presented for participants who enrolled under Protocol v11.0 in **Table 71** by treatment group, severity at baseline, time point, and severity across all graded chemistry parameters.
- Proportions of participants with graded abnormal results will be presented by treatment group, severity at baseline, time point, and severity separately for participants enrolled prior to Protocol v11.0 and for participants enrolled under Protocol v11.0 for chemistry parameters beginning in **Table 72** and continuing through **Table 101**. Chemistry parameters with separate high and low toxicity ranges will be summarized by severity with high and low ranges indicated. The

proportions of participants with ONR results will be presented by treatment group, severity at baseline, time point, and severity for chemistry parameters that do not have toxicity grading ranges defined in **Table 102** and **Table 103**.

- Proportions of participants with graded CS chemistry results post-baseline will be presented by parameter, treatment group, and maximum severity of all CS results post-baseline for participants enrolled prior to Protocol v11.0 in **Table 120** and for participants enrolled under Protocol v11.0 in **Table 121**. The proportions of participants with CS ONR chemistry results post-baseline will also be presented by parameter, treatment group, and maximum severity of all CS results for parameters that do not have toxicity grading ranges defined in **Table 122** for participants enrolled prior to Protocol v11.0 and in **Table 123** for participants enrolled under Protocol v11.0.

Hematology

- Proportions of participants with mild, moderate, and severe results for any hematology parameter will be presented for participants who enrolled prior to Protocol v11.0 in **Table 124** by treatment group severity at baseline, time point, and maximum severity across all graded chemistry parameters. Proportions of participants with results that are mild, moderate, severe, life-threatening, or result in death for any hematology parameter will be presented for participants who enrolled under Protocol v11.0 in **Table 125** by treatment group, severity at baseline, time point, and maximum severity across all graded chemistry parameters.
- Proportions of participants with graded abnormal results will be presented by treatment group, severity at baseline, time point, and severity separately for participants enrolled prior to Protocol v11.0 and for participants enrolled under Protocol v11.0 for hematology parameters beginning in **Table 126** through **Table 137**. Hematology parameters with separate high and low toxicity ranges will be summarized by maximum severity with high and low ranges indicated. The proportions of participants with ONR results will be presented by treatment group, severity at baseline, time point, and severity for hematology parameters that do not have toxicity grading ranges defined in **Table 138** through **Table 145**.
- Proportions of participants with graded CS hematology results post-baseline will be presented by parameter, treatment group, and maximum severity of all CS results post-baseline for participants enrolled prior to Protocol v11.0 in **Table 156** and for participants enrolled under Protocol v11.0 in **Table 157**. The proportions of participants with CS ONR hematology results post-baseline will also be presented by parameter, treatment group, and maximum severity of all CS results for parameters that do not have toxicity grading ranges defined in **Table 158** for participants enrolled prior to Protocol v11.0 and in **Table 159** for participants enrolled under Protocol v11.0.

Coagulation

- Proportions of participants with mild, moderate, and severe results for any coagulation parameter will be presented for participants who enrolled prior to Protocol v11.0 in **Table 160** by treatment group, severity at baseline, time point, and maximum severity across all graded chemistry parameters. Proportions of participants with results that are mild, moderate, severe, life-threatening, or result in death for any coagulation parameter will be presented for participants who enrolled under Protocol v11.0 in **Table 161** by treatment group, severity at baseline, time point, and maximum severity across all graded chemistry parameters.

- Proportions of participants with graded abnormal results will be presented by treatment group, severity at baseline, time point, and severity separately for participants enrolled prior to Protocol v11.0 and for participants enrolled under Protocol v11.0 for coagulation parameters beginning in **Table 162** through **Table 167**.
- Proportions of participants with graded clinically significant coagulation results post-baseline will be presented by parameter, treatment group, and maximum severity post-baseline for participants enrolled prior to Protocol v11.0 in **Table 171** and for participants enrolled under Protocol v11.0 in **Table 172**.

Urinalysis

- Proportions of participants with mild, moderate, and severe results for any urinalysis parameter will be presented for participants who enrolled prior to Protocol v11.0 in **Table 173** by treatment group, severity at baseline, time point, and maximum severity across all graded chemistry parameters. Proportions of participants with results that are mild, moderate, severe, life-threatening, or result in death for any urinalysis parameter will be presented for participants who enrolled under Protocol v11.0 in **Table 174** by treatment group, severity at baseline, time point, and maximum severity across all graded chemistry parameters.
- Proportions of participants with graded abnormal results will be presented by treatment group, severity at baseline, time point, and severity separately for participants enrolled prior to Protocol v11.0 and for participants enrolled under Protocol v11.0 for urinalysis parameters beginning in **Table 175** through **Table 190**. The proportions of participants with ONR results will be presented by treatment group, severity at baseline, time point, and severity for urinalysis parameters that do not have toxicity grading ranges defined in **Table 191** through **Table 194**.
- Proportions of participants with graded CS urinalysis results post-baseline will be presented by parameter, treatment group, and maximum severity of all CS results post-baseline for participants enrolled prior to Protocol v11.0 in **Table 198** and for participants enrolled under Protocol v11.0 in **Table 199**. The proportions of participants with CS ONR urinalysis results post-baseline will also be presented by parameter, treatment group, and maximum severity of all CS results for parameters that do not have toxicity grading ranges defined in **Table 200** for participants enrolled prior to Protocol v11.0 and in **Table 201** for participants enrolled under Protocol v11.0.

Descriptive statistics for each continuous laboratory parameter and its change from baseline, including mean, SD, median, min, and max, will be presented together for all participants by treatment group and planned time point.

- Descriptive statistics for each continuous chemistry parameter and its change from baseline will be presented by treatment group and planned time point in **Table 104** through **Table 119**.
- Descriptive statistics for each continuous hematology parameter and its change from baseline will be presented by treatment group and planned time point in **Table 146** through **Table 155**.
- Descriptive statistics for each continuous coagulation parameter and its change from baseline will be presented by treatment group and planned time point in **Table 168** through **Table 170**.
- Descriptive statistics for each continuous urinalysis parameter and its change from baseline will be presented by treatment group and planned time point in **Table 195** through **Table 196**.

Mean change from baseline with bars representing ±1 SD will also be presented for each continuous laboratory parameter by treatment group and time point in the following figures.

- Mean change from baseline will be presented for continuous chemistry parameters in **Figure 17** through **Figure 32**.
- Mean change from baseline will be presented for continuous hematology parameters in **Figure 33** through **Figure 41**.
- Mean change from baseline will be presented for continuous coagulation parameters in **Figure 42** through **Figure 44**.
- Mean change from baseline will be presented for continuous urinalysis parameters in **Figure 45** and **Figure 46**.

9.7. Vital Signs and Physical Evaluations

Vital signs will include systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, and temperature. Vital signs will be assessed according to the schedule detailed in **Section 4.1** and **Table 2**. Baseline will be defined for vital sign assessments according to the definition given in **Section 3.3**. Clinical significance for post-baseline vital signs will be determined by the site PI with consideration to persistence, association with clinical symptoms, and impact to participant safety. For participants who screened and enrolled prior to Protocol v11.0, clinically significant vital signs will be determined by a blinded review from the site PI of all vital sign AEs reported. For participants who screened and enrolled with Protocol v11.0, clinically significant vital signs will include all abnormal vital signs results reported as AEs.

Toxicity grading criteria for vital signs results can be found in **Table 5** and **Table 6** for participants who screened and enrolled prior to Protocol v11.0. Vital signs results post-dosing for participants who screened and enrolled with Protocol v11.0 will be graded according to NCI CTCAE, Version 5.0 – November 2017. The distribution of vital signs results will be presented by severity, treatment group, and time point.

The sort order for vital signs assessments will be as follows: SBP, DBP, heart rate, respiratory rate, and temperature.

- Proportions of participants with mild, moderate, and severe results for any vital sign assessment will be presented for participants who enrolled prior to Protocol v11.0 in **Table 202** by treatment group, time point, and maximum severity. Proportions of participants with results that are mild, moderate, severe, life-threatening, or result in death for any vital sign assessment will be presented for participants who enrolled under Protocol v11.0 in **Table 203** by treatment group, time point, and maximum severity.
- Proportions of participants with graded abnormal vital signs results will be presented by treatment group, time point, and maximum severity separately for participants enrolled prior to Protocol v11.0 and for participants enrolled under Protocol v11.0 for vital sign parameters beginning in **Table 204** through **Table 213**. Vital sign parameters with separate high and low toxicity ranges will be summarized by maximum severity for both high and low ranges.
- Proportions of participants with clinically significant vital signs results post-baseline will be presented by parameter, treatment group, and maximum severity post-baseline for participants enrolled prior to Protocol v11.0 in **Table 219** and for participants enrolled under Protocol v11.0 in **Table 220**.

Descriptive statistics for each vital sign parameter and its change from baseline, including mean, SD, median, min, and max, will be presented by treatment group and planned time point in **Table 214** through **Table 218**. Mean change from baseline will also be presented with bars representing ±1 SD for each vital sign parameter by treatment group and planned time point in **Figure 47** through **Figure 51**.

All vital sign measurements, including height, weight, and BMI, will be listed by treatment group and time point with severity, applicable reference ranges, and change from baseline in **Listing 22**. Unscheduled vital signs measurements will be included in the listing but will otherwise be excluded from tabular and graphical summaries by time point, except when calculating the maximum severity post baseline.

Complete physical examinations and symptom-directed physical examinations will be performed according to the scheduled given in **Section 14** and **Table 2**. All physical examination findings, whether from exams performed at scheduled or unscheduled time points, will be listed in **Listing 23** by treatment group and time point with body system and whether the finding was reported as an AE.

9.8. Electrocardiograms

Standard 12-lead ECGs will be performed at Screening (in triplicate), Day 1 prior to dosing, Day 4, final study visit (Day 150), and ET visits. Unscheduled 12-lead ECG measurements will be listed but excluded from tabular and graphical summaries by time point. Individual ECG measurements, overall interpretations, and abnormal findings will be presented in **Listing 24**, **Listing 25**, and **Listing 26**, respectively.

Clinical significance for post-dose ECGs will be determined by the site PI with consideration to persistence, association with clinical symptoms, and impact to participant safety. For all participants, clinically significant ECG parameters will include any results meeting toxicity grading criteria (using **Table 4** for participants who screened and enrolled prior to Protocol v11.0 or NCI CTCAE, Version 5.0 for participants who screened and enrolled with Protocol v11.0) who had an overall ECG interpretation of abnormal, clinically significant.

The sort order for ECG parameters will be as follows: PR interval, QRS duration, QT interval, QTcF correction, RR interval, and ventricular rate.

12-lead standard ECG results will be summarized in the following tables and figures:

- Change in overall interpretations of post-dose 12-lead standard ECG results from baseline will be summarized by treatment group and time point in **Table 221**.
- Descriptive statistics for each ECG parameter and its change from baseline, including mean, SD, median, min, and max, will be presented by treatment group and planned time point in **Table 222**.
- Mean change from baseline of ECG parameters will also be presented with bars representing ±1 SD by treatment group and planned time point beginning in **Figure 52** and continuing through **Figure 57**.

10. PHARMACOKINETICS

10.1. Graphical and Tabular Summaries of Pharmacokinetic Profiles

The PK Population will be used when summarizing plasma PK concentrations. Participants enrolled who did not complete dosing will not be included in the PK analysis but will have concentration and PK parameters included in listings as appropriate.

Concentrations below the limit of quantification (BQL) collected before the first measurable concentration above the lower limit of quantification (LLOQ) will be treated as zero (0) for plotting and all calculations (including noncompartmental analysis [NCA]) and summary statistics. All other BQL values observed after the first measurable concentration will be treated as missing. There will be no imputation of missing concentrations. The geometric mean (GM) of concentrations will be treated as missing for sets of data points containing a BQL value.

Collection of plasma samples outside of the protocol-defined time window for the time point will not result in exclusion of the sample results from NCA. Plasma samples collected out of window will be evaluated on a case-by-case basis. Results from PK samples that were collected substantially outside of the protocol-defined time window will be excluded from concentration summary statistics by nominal time points and plots of mean concentration by nominal time point. Substantially out of window samples are defined as samples that were collected outside twice the size of the protocol required window, and are as follows: >10 minutes after the completion of the infusion; ±20 minutes in the first 8 hours after dosing; ±1 hour between 9 and 72 hours after dosing; ±2 days on Day 7; ±4 days on Day 14; ±8 days on Day 28 and Day 56; and ±14 days on Day 84, Day 112, and Day 150.

If the exact time of the PK sample collection is not recorded, then the collection time will be imputed as the planned time for analysis if it is not known that the sample was collected outside of the protocol-defined time window. If the exact collection time is not known, but it is known that the sample was collected outside of the protocol-defined time window, then the time point may be excluded from analysis at the discretion of the PK analyst. Rationale for excluding results from analysis will be described in the CSR. Results from samples with imputed collection times will be indicated in listings of PK sample concentrations.

The bioanalytical lab will report plasma concentrations in units of µg/mL. Plasma drug concentrations will be summarized and listed by participant in **Listing 10**. This listing will include separate columns for concentrations reported by the lab and concentrations used for analysis. The lab reported concentrations may include codes, such as: “BQL” or “QNS” (Quantity not Sufficient), while the analysis concentrations will contain numeric data only, including imputed values such as 0 for pre-dose time points and BQL samples prior to the first quantifiable sample. It will also indicate the nominal time (i.e., the planned time) and actual post dose time in hours associated with the sample and will note sample times which were collected out of window, substantially out of window, or imputed.

Individual concentrations will be presented in tables and figures by dose group and nominal time point:

- The GM and coefficient of variation as a percent (CV%) of individual concentrations in plasma will be presented tabularly by Treatment Group (**Table 16** for sampling times between 0 and 72 hours post dose and **Table 17** for sampling times between Day 7 and Day 150).
- Individual concentrations in plasma and summary statistics, including mean, SD, min, max, GM, and CV%, will be presented tabularly for each Treatment Group beginning at **Table 18** and continuing through **Table 27**.

- Individual concentration profiles in plasma will be presented graphically by Treatment Group for 0 to 72 hours post dose and across all post dose sampling time points in **Figure 3** and **Figure 4**, respectively.
- Semi-log individual concentration profiles in plasma will be presented graphically by Treatment Group for 0 to 72 hours post dose and across all sampling time points in **Figure 5** and **Figure 6**, respectively.
- Mean concentration profiles in plasma with error bars presenting ±1 SD around each time point will be presented graphically by Treatment Group for 0 to 72 hours post dose and across all post dose sampling time points in **Figure 7** and **Figure 8**, respectively.
- Semi-log mean concentration profiles in plasma with error bars presenting ±1 SD around each time point will be presented graphically by Treatment Group for 0 to 72 hours post dose and across all post dose sampling time points in **Figure 9** and **Figure 10**, respectively.

The CV% will be calculated using the method for log-normally distributed data:

$$CV\% = \sqrt{\exp(s^2) - 1} \times 100\%,$$

where s^2 is the variable of the natural log-transformed data.

10.2. Noncompartmental Analysis

PK parameters from plasma PK data will be estimated through NCA using version 8.3.4 or higher of Phoenix WinNonlin®. Actual post dose times will be used for the estimate of PK parameters instead of nominal time. In the case of imputed sample collection times, the imputed time will be included in the NCA. Any outlier identified in the PK analysis will be discussed in the CSR. Outliers will not be excluded from the PK analysis.

Individual plasma PK parameter estimates will be listed (**Listing 11**). PK parameters will be summarized and presented tabularly for all Treatment Groups (**Table 28**). Detailed summary statistics of each PK parameter will be presented tabularly for each Treatment Group (beginning at **Table 29** and continuing through **Table 33**). Summary statistics will include mean, SD, min, max, GM, and CV%.

Phoenix WinNonlin NCA will use the following settings to compute parameters from plasma PK data:

- Linear Up Log Down calculation method
- Uniform weighting
- IV infusion
- Lambda Z Acceptance Criteria
  - Rsq_adjusted ≥ 0.90
  - Include at least 3 time points after T_{max}

If an insufficient number of participants meet the Lambda Z Acceptance Criteria for computing plasma PK parameters, then relaxed criteria may be used and will be described in the CSR.

C_{max}

C_{max} is defined as the maximum concentration observed over all PK sample concentrations. It will be obtained from the **Cmax** parameter calculated by WinNonlin. If there are no measurable concentrations in the

participant's PK profile, then C_{max} will be missing for that participant. C_{max} will be reported in units of µg/mL. The dose-normalized parameter C_{max}/Dose will also be reported from the **Cmax_D** parameter calculated by WinNonlin with units (µg/mL)/(mg/kg).

C_{min}

C_{min} is defined as the minimum concentration observed over all PK sample concentrations. It will be obtained from the **Cmin** parameter calculated by WinNonlin. If there are no measurable concentrations in the participant's PK profile, then C_{min} will be missing for that participant. C_{min} will be reported in units of µg/mL.

T_{max}

T_{max} is defined as the time at which the C_{max} occurs. It will be obtained from the **Tmax** parameter calculated by WinNonlin. If there is no measurement C_{max} in the participant's PK profile, then T_{max} will be missing for that participant. T_{max} will be reported in units of h.

λz

The terminal phase elimination rate constant (λz) is defined as the first-order rate constant describing the rate of decrease of drug concentration in the terminal phase (defined as the terminal region of the PK curve where drug follows first-order elimination kinetics). λz will be computed as the slope of the terminal region consisting of ≥ 3 successive points in the plot of the log-transformed concentration versus time. λz will be estimated using uniform weighting.

Time points used in the estimation of λz will be initially selected using the WinNonlin automatic algorithm. Manually chosen time points may be used at the discretion of the PK analyst after examination of the automatically chosen points in the context of the semi-log profile to improve estimation of λz on a case-by-case basis. The set of points chosen must satisfy the Lambda Z Acceptance Criteria, described above. Otherwise, the elimination rate constant and all derived parameters (apparent terminal elimination half-life [$t_{½}$], AUC Extrapolated to Infinity [$AUC_{(0-\infty)}$], clearance [CL], and volume of distribution [V_d]) will be treated as missing.

Drug concentrations used to calculate λz will be indicated in **Listing 10**. This parameter will be obtained from the **Lambda_z** parameter calculated by WinNonlin. λz will be reported in units of 1/h.

$t_{½}$

The $t_{½}$ is defined as the time required for the drug or metabolite concentration to decrease by a factor of one-half in the terminal phase. The $t_{½}$ can be estimated as ln(2)/λz. It will be obtained from the **HL_Lambda_z** parameter calculated by WinNonlin. Half-life will be reported in units of h. If the Lambda Z Acceptance Criteria is not met, $t_{½}$ will be treated as missing.

AUC

$AUC_{(0-last)}$ is defined as the area under the concentration-time curve from dosing (time 0) to the time of the last measured concentration. $AUC_{(0-last)}$ will be estimated using the Linear Up Log Down calculation method and obtained from the **AUClast** parameter calculated by WinNonlin.

$AUC_{(0-inf)}$ is defined as the total area under the concentration-time curve from dosing (time 0) taken to the limit as the end time becomes arbitrarily large. $AUC_{(0-inf)}$ can be calculated by adding $AUC_{(0-last)}$ to an extrapolated value equal to the last measured concentration greater than the LLOQ divided by λz:

$$AUC_{(0\text{-inf})} = AUC_{(0\text{-last})} + \frac{C_{last}}{\lambda z},$$

where C_{last} is the last measured concentration ≥ LLOQ. $AUC_{(0\text{-inf})}$ will be obtained from the **AUCINF_obs** parameter calculated by WinNonlin®. If the Lambda Z Acceptance Criteria are not met, $AUC_{(0\text{-inf})}$ will be treated as missing.

$\%AUC_{ex}$ is defined as percentage of $AUC_{(0\text{-inf})}$ obtained by extrapolation from time of the last measured concentration to infinity. $\%AUC_{ex}$ can be calculated by dividing AUC from time of the last measured concentration to infinity by $AUC_{(0\text{-inf})}$:

$$\%AUC_{ex} = \frac{AUC_{(0-\text{inf})} - AUC_{(0-\text{last})}}{AUC_{(0-\text{inf})}}.$$

If $\%AUC_{ex}$ is >20% or the Lambda Z Acceptance Criteria is not met, the estimated $AUC_{(0\text{-inf})}$ will be excluded from statistical summaries of PK parameter estimates and downstream calculations. $\%AUC_{ex}$ will be obtained from the **AUC_%Extrap_obs** parameter calculated by WinNonlin.

All AUCs will be reported in units of µg*h/mL. The dose-normalized parameter $AUC_{(0\text{-last})}$/Dose will also be reported from the **AUClast_D** parameter calculated by WinNonlin with units (µg*h/mL)/(mg/kg).

CL

Clearance (CL) is defined as the volume of plasma completely cleared of drug per unit time and is estimated in trials of an IV-administered drug as the dose divided by the $AUC_{(0\text{-}\infty)}$. It will be obtained from the **CL_obs** parameter calculated by WinNonlin. If $\%AUC_{ex}$ is >20% or the Lambda Z Acceptance Criteria are not met, the estimated CL value will be flagged when listed in the report and will be excluded from statistical summaries of parameter estimates and downstream calculations. CL will be reported in units of L/h/kg.

V_d

Volume of distribution (V_d) central is estimated in trials of an IV-administered drug as CL divided by λz. It will be obtained from the **Vz_obs** parameter calculated in WinNonlin. If $\%AUC_{ex}$ is >20% or the Lambda Z Acceptance Criteria is not met, the estimated V_d value will be flagged when listed in the report and will be excluded from statistical summaries of parameter estimates and downstream calculations. V_d will be reported in units of L/kg.

11. IMMUNOGENICITY

Plasma samples for ADA measurements will be collected pre-infusion (60 to 0 minutes prior to start of infusion), Day 56 ± 4, Day 112 ± 7, Day 150 ± 7, and ET. For immunogenicity assays, baseline will be defined as the pre-infusion ADA measurement collected on Day 1. Unless otherwise specified, the immunogenicity population will be used when summarizing ADA results.

Positive and negative results for immunogenicity assays will be defined as described in **Section 4.5.3**. ADA titers may be determined in the case of positive ADA results. Positive post-dose ADA results for participants with baseline ADA results will be further defined as treatment-induced ADA, treatment-boosted ADA, or pre-existing ADA, with the definitions of these provided in **Section 4.5.3**.

The proportion of participants with a positive screening assay will be summarized by dose group and time point in **Table 34**. The proportion of participants with negative, treatment-induced, treatment-boosted, and pre-existing ADA results will be summarized by dose group and post-dose time point in **Table 35**. The incidence of ADA, defined as either treatment-induced or treatment-boosted ADA at any time point, will be summarized by dose group in **Table 36**.

Reverse cumulative distribution (RCD) curves will be presented for post-dose ADA titers by dose group and time point in **Figure 11**.

If positive ADA results are ascertained and ADA titers are determined, summary statistics of ADA titers including mean titer, SD, median titer, min titer, max titer, geometric mean titer (GMT), geometric mean fold rise (GMFR) from baseline, and percent of participants with at least a 4-fold rise in titer from baseline will be presented by dose group and time point in **Table 37**. GMT, GMFR, and percent of participants with at least a 4-fold rise in titer from baseline will be presented with corresponding 95% confidence intervals. ADA GMTs will also be presented in **Figure 12** by dose group and time point.

Individual ADA assay results will be presented in **Listing 12**.

11.1. ADA-Clearance Analysis

If five or more participants have positive ADA results, the effect of ADA incidence on the clearance of SAR440894 will be explored. The pharmacokinetics – immunogenicity subgroup population will be used for this analysis.

An analysis of variance (ANOVA) model will be fit to assess the effect of ADA on the clearance of SAR440894. The mixed effects model for the ANOVA analysis of the effect of ADA incidence on clearance of SAR440894 may be specified:

$$CL_{ijk} = \mu + a_{i(jk)} + \gamma_j + \beta_k + \epsilon_{ijk},$$

where CL represents clearance, μ is the overall mean of clearance, $a_{i(jk)}$ $(i = 1, \ldots, n_k)$ is a random participant-specific intercept where there are n_k participants in the kth dose group in the pharmacokinetics – immunogenicity subset population with estimable clearance, γ_j $(j = 1,2)$ represents the fixed ADA effect, β_k $(k = 1, \ldots, 5)$ represents the fixed effect of dose group on clearance, and the errors ϵ_{ijk} are assumed independent and identically distributed from the standard normal distribution. For this analysis, ADA will be defined as positive if a participant experiences either treatment-induced or treatment-boosted ADA at any time point, and ADA will be defined as negative if a participant does not experience treatment-induced or treatment-boosted ADA during the study period. Negative will be treated as the reference category. For this model, only participants in the pharmacokinetics-immunogenicity subgroup population with ADA results at

baseline will be included. Additionally, the association between dose group and clearance will be assessed, and dose group (β_k) will only be included in the model if related to clearance.

The effect of ADA titers on clearance will additionally be explored via an analysis of covariance (ANCOVA) model, given:

$$CL_{ik} = \mu + a_{i(k)} + \gamma T_{ik} + \beta_k + \epsilon_{ik},$$

where CL represents clearance, μ is the overall mean of clearance, $a_{i(k)}$ $(i = 1, \dots, n_k)$ is a random participant-specific intercept where there are n_k participants in the kth dose group in the pharmacokinetics – immunogenicity subset population with estimable clearance, T_{ik} represents the value of the ADA titer for the ith participant in the kth dose group, and γ represents the change in clearance for a 1-unit increase in ADA titer, β_k $(k = 1, \dots, 5)$ represents the fixed effect of dose group on clearance, and the errors ϵ_{ik} are assumed independent and identically distributed from the standard normal distribution. Again, dose group (β_k) will only be included in the model if related to clearance.

For each mixed effects model, either clearance or log-transformed clearance, $\log(CL)$, will be used as the response. Whether clearance or log-transformed clearance will be included in the model will be determined after assessing normality and homogeneity of variance using Q-Q plots and plots of residuals against predicted values. The final models used will be stated in the CSR.

For the analysis of the effect of ADA incidence on clearance, the mean clearance will be presented for each ADA result along with the difference in mean clearance between positive and negative ADA, with 95% confidence intervals in **Table 38**. For the analysis of the effect of ADA titers on clearance, the ADA effect parameter estimates, $\hat{\gamma}$, will be presented with corresponding standard error and 95% confidence interval in **Table 39**. If the mixed effects models are fit on the log-transformed clearance, statistics and parameter estimates and 95% confidence intervals will be provided after their transformation from the log-transformed analysis back to the original scale for clearance.

The following pseudocode will be used to perform the ANOVA analysis for the effect of ADA incidence on clearance:

```
/* Fit Treatment Group-Specific Mixed-Effects ANOVA model */
proc mixed data=ada_clearance plots=studentpanel(marginal unpack);
class subjid ada(ref='Negative') trtn(ref='1');
model clearance = ada trt/ ddfm=kr2;
random intercept / subject=subjid;
estimate 'ADA Effect' ada 1 -1 / cl alpha=0.05; *use estimate statement to output mean difference;
ods output estimates=estimate_param; *output ADA mean difference estimate and CI;
run;

/* If Diagnostics Indicate Log-transformed Clearance is More Appropriate*/
/* Fit Treatment Group-Specific Mixed-Effects ANOVA model for log-transformed clearance */
proc mixed data=ada_clearance plots=studentpanel(marginal unpack);
class subjid ada(ref='Negative') trt(ref='1');
model logclearance = ada trt / ddfm=kr2;
random intercept / subject=subjid;
estimate 'ADA Effect' ada 1 -1 / cl alpha=0.05; *use estimate statement to output log-transformed mean difference;
ods output estimates=estimate_logparam; *output log-transformed mean difference and CI;
run;

/* Transform mean difference estimate and CI limits to original scale (similar for mean clearance) */
```

```
data estimate_logparam; set estimate_logparam;
OG_est=exp(estimate);
OG_lower=exp(lower);
OG_upper=exp(upper);
run;
```

The following pseudocode will be used to perform the ANCOVA analysis for the effect of ADA titer on clearance:

```
/* Fit Treatment Group-Specific Mixed-Effects ANCOVA model */
proc mixed data=ada_clearance plots=studentpanel(marginal unpack);
class subjid  trt(ref='1');
model clearance = ada trt/ ddfm=kr2;
random intercept / subject=subjid;
estimate 'ADA Effect' ada 1 -1 / cl alpha=0.05; *use estimate statement to output ADA parameter estimate;
ods output estimates=estimate_param; *output ADA parameter estimate and CI;
run;

/* If Diagnostics Indicate Log-transformed Clearance is More Appropriate*/
/* Fit Treatment Group-Specific Mixed-Effects ANCOVA model for log-transformed clearance */
proc mixed data=ada_clearance plots=studentpanel(marginal unpack);
class subjid trt(ref='1');
model logclearance = ada trt / ddfm=kr2;
random intercept / subject=subjid;
estimate 'ADA Effect' ada 1 -1 / cl alpha=0.05; *use estimate statement to output log-transformed ADA parameter
estimate;
ods output estimates=estimate_logparam; *output log-transformed ADA parameter estimate and CI;
run;

/* Transform parameter estimate and CI limits to original scale */
data estimate_logparam; set estimate_logparam;
OG_est=exp(estimate);
OG_lower=exp(lower);
OG_upper=exp(upper);
run;
```

12. OTHER ANALYSES

Not applicable.

13. REPORTING CONVENTIONS

The mean, SD, and other statistics will be reported to 1 decimal place greater than the original data. The min and max will use the same number of decimal places as the original data. Proportions will be presented to 2 decimal places; values greater than zero but <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than zero but < 1% will be presented as "<1"; values greater than 99% but less than 100% will be reported as ">99". Estimated parameters not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

For PK parameters, AUCs will be reported using 3 significant digits. $t_{½}$, T_{max}, CL, and V_d values will be reported using 2 significant digits. λz values will be reported to 3 significant digits. C_{max} will be reported with the same number of significant digits as the measurement.

14. TECHNICAL DETAILS

SAS version 9.4 or above and R versions 3.2 or above will be used to generate tables, figures, and listings. PK parameters will be estimated through NCA using Phoenix® WinNonlin version 8.3.4 or later.

15. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

The following changes will be made in the final analysis:

- Protocol v11.0 states that creatinine clearance will be calculated and reported. However, in discussion with the study team, it was decided this parameter did not need to be included in the analysis and summaries, since eGFR is being collected and reported.
- Protocol v11.0 states that only CS abnormal laboratory findings will be reported as AEs. In discussion with the study team, it was decided related abnormal laboratory findings of any clinical significance will also be reported as AEs.

16. REFERENCES

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6. National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE); Version 5.0, 27 November 2017.

17. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3.

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9.1 Overall Study Design and Plan Description

Table 1: Single Ascending Dose Cohorts and Dose Regimens

Cohort	Dose	Number of Subjects	
		SAR440894	Placebo
1	0.3 mg/kg	6	2
2	1 mg/kg	6	2
3	3 mg/kg	6	2
4	10 mg/kg	6	2
5	20 mg/kg	6	2
Total Number of Subjects		30	10
		40	

9.5.1 Pharmacokinetic, Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures

Study Visit	**Screening[1]**	**Admit to Unit**	**Confinement and Infusion**			**Discharge from Unit**	**Follow-Up Visits**						**Final Visit**	**Early Term**	**Unscheduled Visit**
Study Day ±Window	**-45 to -2**	**-1**	**1**	**2**	**3**	**4**	**7 ±1**	**14 ±2**	**28 ±4**	**56 ±4**	**84 ±7**	**112 ±7**	**150 ±7**	**NA**	
Obtain informed consent	X														
Record demographics	X														
Review inclusion/ exclusion criteria	X	X													
Review medical history	X	X	X[12]												X
Review concomitant medications[2]	X	X	X[12]	X	X	X	X	X	X	X	X	X	X	X	X
Review contraception/ menses	X	X	X			X	X	X	X	X	X	X	X	X	
Height/weight/BMI	X	X[16]													
Perform complete physical examination[3]	X	X				X							X	X	
Perform symptom-directed physical examination			X[12,13]	X[13]	X[13]		X	X	X	X	X	X			X
Obtain vital signs[4]	X	X	X[12,14]	X[4]	X[4]	X	X	X	X	X	X	X	X	X	X
Obtain Screening labs[5]	X														
Obtain clinical safety labs[6]		X		X	X	X	X	X	X	X	X	X	X	X	
Renal injury biomarker (serum cystatin-C)		X		X	X	X	X	X	X	X	X	X	X	X	
Serum β-hCG[7]	X	X													
Urine pregnancy test									X		X		X	X	
Urine dipstick[8]	X	X		X	X	X	X	X	X	X	X	X	X	X	

Table 2: Schedule of Study Procedures *(continued)*

Study Visit	Screening[1]	Admit to Unit	Confinement and Infusion			Discharge from Unit	Follow-Up Visits						Final Visit	Early Term	Unscheduled Visit
Study Day ±Window	**-45 to -2**	**-1**	**1**	**2**	**3**	**4**	**7 ±1**	**14 ±2**	**28 ±4**	**56 ±4**	**84 ±7**	**112 ±7**	**150 ±7**	**NA**	
Urine toxicology	X	X													
Breathalyzer	X	X													
Immunogenicity (ADA)			X[12]							X		X	X	X	
Hypersensitivity panel			X[12,15]											X[15]	
12-lead ECG[9]	X		X			X							X	X	
Viral serology[10]	X														
Obtain PK samples[11]			X	X	X	X	X	X	X	X	X	X	X	X	
Randomization		X													
Study product administration			X												
Counsel on the avoidance of pregnancy and prohibited medications/ substances	X					X	X	X	X	X	X	X		X	
Counsel on avoidance of vaccines						X	X	X	X	X					
AE review			X	X	X	X	X	X	X	X	X	X	X	X	
SAE review			X	X	X	X	X	X	X	X	X	X	X	X	

1. Screening will be completed within 45 days prior to administration of study product and may require more than one visit.
2. Concomitant medications including all of the following: prescription drugs, over-the–counter drugs, herbs, vitamins, nutritional supplements, illicit and recreational substance use, vaccines, birth control information.
3. Complete physical examination includes general appearance, head, ears, eyes, nose, throat, dentition, thyroid, chest (heart, lungs), abdomen, skin, neurological, extremities, back, neck, musculoskeletal, lymph nodes.
4. Vital signs include supine diastolic and systolic BP, heart rate, respiratory rate and oral temperature. Vital signs will be collected in singlicate unless part of AE/SAE assessment. If AE/SAE involving BP or heart rate occurs, vital signs will be collected in triplicate from the same arm at least 5 minutes apart. At Screening and on Days -1, 2, 3, and all Follow up visits, measure vital signs prior to blood collection.
5. Screening laboratory tests are outlined in Table 7-1 and Section 6.2 of the protocol.
6. Clinical safety laboratory tests are outlined in Table 7-1, Section 6.3, and Section 6.4 of the protocol.
7. A serum pregnancy test will be obtained for all women of reproductive capacity at Screening and within approximately 24 hours before study product administration. Results must be confirmed as negative before study product infusion begins. An FSH level will be checked in female participants reporting postmenopausal status.

Table 2: Schedule of Study Procedures *(continued)*

8. A urine dipstick will be done to evaluate for presence of protein, glucose, or blood in urine. If dipstick is abnormal, a complete urinalysis with microscopy will be performed.
9. A 12-lead ECG will be done during Screening (triplicate), within 60-minutes prior to dosing (triplicate), at the end of the infusion of the study product +15 minutes (triplicate, ±5 minutes), and prior to discharge (triplicate). Continuous remote telemetry monitoring will be conducted from 30 minutes prior to study product administration to approximately 4 hours post dose.
10. Viral serology includes CHIKV antibody, HIV antibody, HB surface antigen and antibody to HCV.
11. Plasma PK samples will be taken at the following times with an acceptable window of 60-minutes prior to dosing; ±10 minutes in the first 8 hours after dosing; and ±30 minutes between 9 and 72 hours: within 5 minutes of the completion of the infusion, and at: 1, 4, 8, 12, 24, 48, and 72 hours relative to the end of the infusion time, and on Day 7 ±1, Day 14 ±2, Day 28 ±4, Day 56 ±4, Day 84 ±7, Day 112 ±7, Day 150 ±7, and ET (if needed). PK samples at Follow-up visits will be collected during the designated Follow-up window.
12. Occurs prior to dosing on Day 1 and is considered to be the baseline sample.
13. A symptom-directed physical exam will be performed prior to infusion and after (as needed) to assess potential/active AEs and signs and symptoms of infusion reactions.
14. Vital signs will be checked within a 60-minute period prior to dosing and every 15 minutes (±5 minutes) during the infusion. After the infusion, vital signs will be taken at the following time points: 1, 2, 4, and 6 hours with an acceptable window of ±5 minutes for each time point.
15. Draw 12 mL prior to dosing. If a subject develops anaphylaxis or anaphylactoid reaction, three additional 12 mL samples will be collected: during onset, 2 or more hours after onset, and after resolution of symptoms.
16. Measure only weight on Day -1. Day -1 weight will be used for dose calculations.

10.2 Protocol Deviations

Table 3: Distribution of Protocol Deviations by Category, Type, and Treatment Group

Category	Deviation Type	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
All Protocol Deviations															
Eligibility/enrollment	Any type														
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion														
	ICF not signed prior to study procedures														
	Other														
Treatment administration schedule	Any type														
	Out of window visit														
	Missed visit/visit not conducted														
	Missed treatment administration														
	Delayed treatment administration														
	Other														
Follow-up visit schedule	Any type														
	Out of window visit														
	Missed visit/visit not conducted														
	Other														

Table 3: Distribution of Protocol Deviations by Category, Type, and Treatment Group *(continued)*

Category	Deviation Type	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
All Protocol Deviations															
Protocol procedure/assessment	Any type														
	Incorrect version of ICF signed														
	Blood not collected														
	Urine not collected														
	Stool not collected														
	Other specimen not collected														
	Too few aliquots obtained														
	Specimen result not obtained														
	Required procedure not conducted														
	Required procedure done incorrectly														
	Study product temperature excursion														
	Specimen temperature excursion														
	Other														

Table 3: Distribution of Protocol Deviations by Category, Type, and Treatment Group *(continued)*

Category	Deviation Type	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
All Protocol Deviations															
Treatment administration	Any type														
	Required procedure done incorrectly														
	Study product temperature excursion														
	Other														
Blinding policy/procedure	Any type														
	Treatment unblinded														
	Other														
Major Protocol Deviations															
Eligibility/enrollment	Any type														
	...														
...	...														
Note: N = Number of enrolled participants.															

12.2.2 Displays of Adverse Events

Table 4: Clinical Adverse Events Toxicity Scale

Clinical Adverse Events			
CARDIOVASCULAR TOXICITY	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Arrhythmia[1]	N/A	Asymptomatic; transient signs; no medical intervention required	Recurrent/persistent; symptomatic medical intervention required
Hemorrhage, Blood Loss	Estimated blood loss ≤ 100 mL	Estimated blood loss > 100 mL, no transfusion required	Transfusion required
QTc (Fridericia's correction)[2]	**Females:** QTc interval > 470-479 msec	QTc interval 480 to 499 msec OR Increase in interval 30-50 msec above baseline	QTc interval ≥ 500 msec OR Increase in interval > 50 msec above baseline
	Males: Asymptomatic, QTc interval > 450-479 msec		
RESPIRATORY TOXICITY	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Cough	Transient; no treatment	Persistent cough	Interferes with daily activities
Bronchospasm, Acute	Transient; no treatment; 71% - 80% FEV1 of predicted peak flow	Requires medical intervention; normalizes with bronchodilator; FEV1 60% - 70% (of predicted peak flow)	No normalization with bronchodilator; FEV1 < 60% of predicted peak flow
Dyspnea	Does not interfere with usual and social activities	Interferes with usual and social activities; no treatment	Prevents daily and usual social activity OR requires treatment
GASTROINTESTINAL TOXICITY	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Nausea	No interference with activity	Some interference with activity	Prevents daily activities
Vomiting	No interference with activity OR 1 - 2 episodes/24 hours	Some interference with activity OR > 2 episodes/24 hours	Prevents daily activity OR requires IV hydration OR requires medical intervention
Diarrhea	2 - 3 loose or watery stools or < 400 gm/24 hours	4 - 5 loose or watery stools or 400 – 800 gm/24 hours	6 or more loose or watery stools or > 800 gm/24 hours OR requires IV hydration OR requires medical intervention
LOCAL REACTIONS	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Pain	Does not interfere with activity	Repeated use of non-narcotic pain reliever for more than 24 hours or interferes with activity	Any use of narcotic pain reliever or prevents daily activity
Tenderness	Discomfort only to touch	Discomfort with movement	Significant discomfort at rest
Erythema or Redness (measure local reaction at the greatest single diameter)	25 - 50 mm	51 - 100 mm	> 100 mm

Table 4: Clinical Adverse Events Toxicity Scale *(continued)*

Induration or Swelling	25 - 50 mm and does not interfere with activity	51 - 100 mm or interferes with activity	> 100 mm or prevents daily activity
SYSTEMIC REACTIONS	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Allergic Reaction	Pruritus without rash	Localized urticaria OR requires oral therapy	Generalized urticaria; angioedema OR anaphylaxis OR requires epinephrine
Infusion Related Reaction (Cytokine Release Syndrome)	Mild transient reaction, and Infusion interruption (i.e, antibody infusion) not indicated	Infusion interruption indicated but responds promptly to symptomatic treatment (e.g, antihistamines, NSAIDS); prophylactic medication indicated for ≤ 24 hours	Prolonged severe signs and symptoms or Recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae
Headache	No interference with activity	Repeated use of non-narcotic pain reliever > 24 hours OR some interference with activity	Significant; any use of narcotic pain reliever OR prevents daily activity OR requires triptans
Fatigue	No interference with activity	Some interference with activity	Significant; prevents daily activity
Myalgia	No interference with activity	Some interference with activity	Significant; prevents daily activity
All Other Conditions	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Illness or Clinical Adverse Event (as defined according to applicable regulations)	No interference with activity	Some interference with activity not requiring medical intervention	Prevents daily activity and requires medical intervention

Note: This toxicity table is to be used for subjects who screened and enrolled prior to Protocol Version 11.0. Subjects who screen and enroll with Protocol Version 11.0, toxicity will be assessed with the NCI CTCAE, Version 5.0 – November 2017.
[1] Sinus arrhythmia is a normal variant and will not be considered an adverse event.
[2] Inclusion dependent upon protocol requirements.

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 5: Laboratory and Vital Signs Eligibility Ranges and Toxicity Ranges – Duke Clinical Laboratory

	Reference Range [a]	LO/HI/N [b]	Mild (Grade 1) [c]	Moderate (Grade 2)	Severe (Grade 3)
Blood, Serum, or Plasma Chemistries [d]					
Sodium (mmol/L)	135 – 145	LO	< LLN - 132	131 - 130	< 130
		HI	> ULN - 148	149 - 150	> 150
Potassium (mmol/L)	3.5 - 5.0	LO	< LLN - 3.1	< 3.1 - 3.0	< 3.0
		HI	> ULN - 5.2	5.3 - 5.4	> 5.4
Bicarbonate/CO2 (mmol/L)	21 – 30	LO	20 - 17	16 - 12	< 12
		HI	31 - 35	36 - 40	> 40
Glucose (mg/dL)	70 - 99 [e]	LO	69 - 65	64 - 55	< 55
		HI	> ULN - 120	121 - 130	> 130
	70 – 140 [f]	HI	141 - 159	160 - 200	> 200
Blood Urea Nitrogen (mg/dL)	7 – 20	HI	21 - 26	27 - 31	> 31
Creatinine (mg/dL)	Female: 0.4 – 1.0	HI	> ULN - 1.7	1.8 - 2.0	> 2.0
	Male: 0.6 – 1.3				
eGFR (mL/min/1.73 m^2) by Modification of Diet in Renal Disease (MDRD) equation	≥ 60 mL/min/1.73 m^2	LO	59 - 45	44 - 30	< 30
Calcium (mg/dL)	8.7 - 10.2	LO	< LLN - 8.0	7.9 - 7.5	< 7.5
		HI	> ULN - 11.0	11.1 - 11.5	> 11.5
Albumin (g/dL)	3.5 - 4.8	LO	3.4 - 2.8	2.7 - 2.5	< 2.5
Total Protein (g/dL)	6.2 – 8.1	LO	< LLN - 5.5	5.4 - 5.0	< 5.0
Alkaline Phosphatase (U/L)	24 – 110	N	111 - 240	241 - 360	> 360
AST (U/L)	15 – 41	HI	42 - 105	106 - 175	> 175
ALT (U/L)	Female: 14 -54	HI	55 – 105	106 – 175	>175
	Male: 17 -63	HI	64 - 105	106 - 175	> 175
Bilirubin, Serum Total (mg/dL)	0.4 – 1.5	HI	1.6 - 2.0	2.1 - 2.5	> 2.5

Table 5: Laboratory and Vital Signs Eligibility Ranges and Toxicity Ranges – Duke Clinical Laboratory *(continued)*

	Reference Range [a]	LO/HI/N [b]	Mild (Grade 1) [c]	Moderate (Grade 2)	Severe (Grade 3)
Hematology [d]					
Hemoglobin (g/dL)					
Females	12.0 – 15.5	LO	11.9 - 11.0	10.9 - 9.5	< 9.5
Males	13.7 – 17.3	LO	13.6 - 12.0	11.9 - 10.0	< 10.0
WBC ($10^{9/L}$)	3.2 – 9.8	LO	3.19 - 2.50	2.49 - 1.50	< 1.50
		HI	9.90 – 14.99	15.00 - 20.00	> 20.00
Lymphocytes (10^9/L)	0.6 – 4.2	LO	0.59 – 0.50	0.49 - 0.40	< 0.40
Neutrophils (10^9/L)	2.0 – 8.6	LO	1.99 - 1.50	1.49 - 1.00	< 1.00
Eosinophils (10^9)/L	0.00-0.70	HI	0.71 - 0.75	0.76 - 1.50	> 1.50
Platelets (10^9/L)	150 – 450	LO	149 - 120	119 - 100	< 100
Coagulation					
Prothrombin Time (seconds)	9.5 – 13.1	HI	> ULN - 14.4	14.5 - 15.7	> 15.7
Prothrombin INR	0.9 – 1.1	HI	1.2-1.4	1.5-2.0	>2.0
Partial Thromboplastin Time (seconds)	26.8 – 37.1	HI	> ULN - 42.1	42.2 - 50.0	> 50.0
Urine					
Protein	Negative	HI	1+	2+	> 2+
Glucose	Negative	HI	1+	2+	> 2+
Bilirubin	Negative	HI	1+	2+	> 2+
Nitrite	Negative	HI	Positive	N/A	N/A
Blood (microscopic)—red blood cells per high power field (rbc/hpf)	0 – 3	HI	4 - 10	11 - 50	> 50 and/or gross blood
WBC (microscopic)—white blood cells per high power field (wbc/hpf)	0 – 5	HI	6 - 10	11 - 50	> 50 and/or gross blood
Urobilinogen (mg/dL)	0.2 – 1.0	HI	> ULN – 1.5	1.6 – 2.0	> 2.0
Vital Signs					
Fever (°C) [g]		HI	38.0 - 38.4	38.5 - 38.9	> 38.9
Fever (°F) [g]		HI	100.4 - 101.1	101.2 - 102.0	> 102.0
Tachycardia—beats per minute		HI	101 - 115	116 - 130	> 130 or ventricular dysrhythmias

Table 5: Laboratory and Vital Signs Eligibility Ranges and Toxicity Ranges – Duke Clinical Laboratory *(continued)*

	Reference Range [a]	LO/HI/N [b]	Mild (Grade 1) [c]	Moderate (Grade 2)	Severe (Grade 3)
Bradycardia—beats per minute					
Baseline ≥ 60		LO	54 - 50	49 - 45	< 45
Baseline < 60		LO	50 - 45	44 - 40	< 40
Hypertension (systolic)—mm Hg [h]		HI	141 - 150	151 - 160	> 160
Hypertension (diastolic)—mm Hg [h]		HI	91 - 95	96 - 100	> 100
Hypotension (systolic)—mm Hg [h]		LO	89 - 85	84 - 80	< 80
Tachypnea - breaths per minute		HI	23 - 25	26 - 30	> 30

Note: This table is to be used for subjects who screened and enrolled prior to Protocol Version 11.0. Subjects who screen and enroll with Protocol Version 11.0, toxicity will be assessed with the NCI CTCAE, Version 5.0 – November 2017.

[a] Reference range of Duke Clinical laboratory.

[b] High, Low, Not Graded.

[c] If initial bound of Grade 1 has gap from reference range, calculations based on *New England Journal of Medicine* reference ranges.

[d] Depending upon the lab used, references ranges and grading may be split out by sex and/or age.

[e] Fasting ≥ 8hours

[f] Non-fasting; includes subjects fasting ≥ 2 hours and < 8 hours.

[g] Oral temperature. A protocol should select either °C or °F for inclusion.

[h] Assuming subject is awake, resting, and supine; for adverse event, 3 measurements on the same arm with concordant results.

Table 6: Laboratory Eligibility and Toxicity Ranges – DEPRU Core Laboratory

	Reference Range	LO/HI/N [b]	Mild (Grade 1) [c]	Moderate (Grade 2)	Severe (Grade 3)
Blood, Serum, or Plasma Chemistries [d]					
Sodium (mmol/L)	135 – 146	LO	< LLN - 132	131 - 130	< 130
		HI	> ULN - 148	149 - 150	> 150
Potassium (mmol/L)	3.4 – 4.6	LO	< LLN - 3.1	< 3.1 - 3.0	< 3.0
		HI	> ULN - 5.2	5.3 - 5.4	> 5.4
Bicarbonate/CO2 (mmol/L)	23 – 34	LO	22 - 17	16 - 12	< 12
		HI	> ULN - 35	36 - 40	> 40
Glucose (mg/dL)	70 - 99 [e]	LO	69 - 65	64 - 55	< 55
		HI	> ULN - 120	121 - 130	> 130
	70 – 140 [f]	HI	141 - 159	160 - 200	> 200
Blood Urea Nitrogen (mg/dL)	5-37	HI	> ULN - 41	42-46	> 46
Creatinine (mg/dL)	0.5 – 1.2	HI	> ULN - 1.7	1.8 - 2.0	> 2.0
eGFR (mL/min/1.73 m^2) by Modification of Diet in Renal Disease (MDRD) equation	≥ 60 mL/min/1.73 m^2	LO	59 - 45	44 - 30	< 30
Calcium (mg/dL)	8.3 - 10.6	LO	< LLN - 8.0	7.9 - 7.5	< 7.5
		HI	> ULN - 11.0	11.1 - 11.5	> 11.5
Albumin (g/dL)	3.8 - 5.1	LO	3.7 - 2.8	2.7 - 2.5	< 2.5
Total Protein (g/dL)	5.9 – 8.3	LO	< LLN - 5.5	5.4 - 5.0	< 5.0
Alkaline Phosphatase (U/L)	34 – 138	N	139 - 240	241 - 360	> 360
AST (U/L)	6 – 40	HI	41 - 105	106 - 175	> 175
ALT (U/L)	Female: 6-35	HI	36 – 105	106 – 175	> 175
	Male: 6-40	HI	41 - 105	106 - 175	> 175
Bilirubin, Serum Total (mg/dL)	0.2-1.0	HI	1.1 - 2.0	2.1 - 2.5	> 2.5

Table 6: Laboratory Eligibility and Toxicity Ranges – DEPRU Core Laboratory *(continued)*

	Reference Range	LO/HI/N [b]	Mild (Grade 1) [c]	Moderate (Grade 2)	Severe (Grade 3)
Hematology [d]					
Hemoglobin (g/dL)					
Females	12.0 – 15.5	LO	11.9 - 11.0	10.9 - 9.5	< 9.5
Males	13.7 – 17.3	LO	13.6 - 12.0	11.9 - 10.0	< 10.0
WBC ($10^{9/L}$)	3.2 – 9.8	LO	3.19 - 2.50	2.49 - 1.50	< 1.50
		HI	9.90 – 14.99	15.00 - 20.00	> 20.00
Lymphocytes (10^9/L)	0.6 – 4.2	LO	0.59 – 0.50	0.49 - 0.40	< 0.40
Neutrophils (10^9/L)	2.0 – 8.6	LO	1.99 - 1.50	1.49 - 1.00	< 1.00
Eosinophils (10^9)/L	0.00-0.70	HI	0.71 - 0.75	0.76 - 1.50	> 1.50
Platelets (10^9/L)	150 – 450	LO	149 - 120	119 - 100	< 100
Urine					
Protein	Negative	HI	1+	2+	> 2+
Glucose	Negative	HI	1+	2+	> 2+
Bilirubin	Negative	HI	1+	2+	> 2+
Nitrite	Negative	HI	Positive	N/A	N/A
Blood (microscopic)—red blood cells per high power field (rbc/hpf)	0 – 3	HI	4 - 10	11 - 50	> 50 and/or gross blood
WBC (microscopic)—white blood cells per high power field (wbc/hpf)	0 – 5	HI	6 - 10	11 - 50	> 50 and/or gross blood
Urobilinogen (mg/dL)	0.2 – 1.0	HI	> ULN – 1.5	1.6 – 2.0	> 2.0

Note: This table is to be used for subjects who screened and enrolled prior to Protocol Version 11.0. Subjects who screen and enroll with Protocol Version 11.0, toxicity will be assessed with the NCI CTCAE, Version 5.0 – November 2017.
[a] Reference range of DEPRU Core laboratory.
[b] High, Low, Not Graded.
[c] If initial bound of Grade 1 has gap from reference range, calculations based on *New England Journal of Medicine* reference ranges.
[d] Depending upon the lab used, references ranges and grading may be split out by sex and/or age.
[e] Fasting ≥ 8 hours
[f] Nonfasting; includes subjects fasting ≥ 2 hours and < 8 hours.

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 7: Participant Disposition by Treatment Group

Participant Disposition	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Screened	--	--	--	--	--	--	--	--	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100	x	100	x	100	x	100	x	100
Received Treatment	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received Full Planned Amount of Treatment[a]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Had at Least One Quantifiable Post-Infusion Plasma Drug Concentration Measured														
Completed All PK Blood Draws														
Had at Least One Post-Infusion Immunogenicity Blood Draw with Valid Results														
Completed all Immunogenicity Blood Draws														
Completed Final Study Visit (Study Day 150)[a]														
Early Termination[a]														

Note: N = Number of enrolled participants.
[a] Refer to Listing 16.2.1 for reasons participants discontinued or terminated early.

Table 8: Analysis Population Exclusions by Treatment Group

Analysis Populations	Reason Participants Excluded	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	%	n
Safety Population	Did not receive study product	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
PK Population	Any Reason														
	Did not receive a complete dose of study product														
	Did not have at least one quantifiable post-dose concentration measurement														
Immunogenicity Population	Any Reason														
	Did not receive study product														
	Did not contribute at least one post-infusion immunogenicity plasma sample with valid results														
PK – Immunogenicity Subset Population	Any Reason														
	Did not receive a complete dose of study product														
	Did not have sufficient data to estimate at least one PK parameter														
	Did not contribute at least one post-infusion immunogenicity plasma sample with valid results														

Note: N = Number of enrolled participants.

Table 9: Dates of Treatment by Site and Treatment Group

[Implementation Note: The first period will start with the date of first participant enrollment. Each period displayed will be a year in length except the last period, which will end at the date of final participant enrollment.]

Dates of Dosing	**SAR440894 0.3 mg/kg (N=X)**	**SAR440894 1 mg/kg (N=X)**	**SAR440894 3 mg/kg (N=X)**	**SAR440894 10 mg/kg (N=X)**	**SAR440894 20 mg/kg (N=X)**	**Placebo (N=X)**	**All Participants (N=X)**
[Site 1]							
Total (Entire period of enrollment)							
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x	x
…							
[Site 2]							
Total (Entire period of enrollment)							
DDMMMYYYY-DDMMMYYYY							
…							
All Sites							
Total (Entire period of enrollment)							
DDMMMYYYY-DDMMMYYYY							
…							
Note: N = Number of enrolled participants.							

Table 10: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Any Category	Number of participants failing any eligibility criterion or eligible but not enrolled	x	100
Eligible but Not Enrolled	Any reason eligible but not enrolled	x	xx
	[reason eligible but not enrolled 1]	x	xx
	[reason eligible but not enrolled 2]	x	xx
	[reason eligible but not enrolled 3]	x	xx
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx

[a] More than one criterion may be marked per participant.
[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data by Study Group

Table 11: Summary of Categorical Demographic and Baseline Characteristics by Site – Safety Population

Variable	Characteristic	[Site 1] (N=X)		[Site 2] (N=X)		[Site 3] (N=X)		All Participants (N=X)	
		n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Sex	Male	x	xx	x	xx	x	xx	x	xx
	Female								
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino								
	Not Reported								
	Unknown								
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx
	Asian								
	Native Hawaiian or Other Pacific Islander								
	Black or African American								
	White								
	Multi-Racial								
	Unknown								

Note: N = Number of participants in the Safety Population.

Table 12: Summary of Continuous Demographic and Baseline Characteristics by Site – Safety Population

Variable	Statistic	[Site 1] (N=X)	[Site 2] (N=X)	[Site 3] (N=X)	All Participants (N=X)
Age (years)	Mean	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x
	Maximum	x	x	x	x
Height (cm)	Mean	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx
	Minimum	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x
Weight (kg)	Mean	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx
	Minimum	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x
BMI (kg/m^2)	Mean	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx
	Minimum	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x

Note: N = Number of participants in the Safety Population.

Table 13: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group – Safety Population

Variable	Characteristic	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Female														
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino														
	Not Reported														
	Unknown														
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian														
	Native Hawaiian or Other Pacific Islander														
	Black or African American														
	White														
	Multi-Racial														
	Unknown														

Note: N = Number of participants in the Safety Population.

Table 14: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group – Safety Population

Variable	Statistic	SAR440894 0.3 mg/kg (N=X)	SAR440894 1 mg/kg (N=X)	SAR440894 3 mg/kg (N=X)	SAR440894 10 mg/kg (N=X)	SAR440894 20 mg/kg (N=X)	Placebo (N=X)	All Participants (N=X)
Age (years)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x
Height (cm)	Mean	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Weight (kg)	Mean	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x	x.x	x.x	x.x
BMI (kg/m^2)	Mean	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x	x.x	x.x	x.x

Note: N = Number of participants in the Safety Population.

14.1.3 Prior and Concurrent Medical Conditions

Table 15: Summary of Participants with Pre-Existing and Concurrent Medical Conditions by MedDRA System Organ Class and Treatment Group – Safety Population

	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
MedDRA System Organ Class	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any SOC	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]														
[SOC 2]														

Note: N = Number of participants in the Safety Population; n = Number of participants reporting medical history within the specified SOC. A participant is only counted once per SOC.

14.2 Pharmacokinetic/Immunogenicity Data

Table 16: SAR440894 Concentrations in Plasma by Treatment Group – 0 to 72 h Post Dose – PK Population

	Nominal Time[a] (h)							
Treatment Group	**0**	**1**	**4**	**8**	**12**	**24**	**48**	**72**
SAR440894 0.3 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 1 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 3 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 10 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 20 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Notes: N = Number of participants in the PK Population. Concentrations are reported in units of µg/mL. Values of GM (CV %) are shown.
[a] Times are relative to time of dosing.

Table 17: SAR440894 Concentrations in Plasma by Treatment Group – 7 to 150 Days Post Dose – PK Population

	Nominal Time[a] (days)						
Treatment Group	**7**	**14**	**28**	**56**	**84**	**112**	**150**
SAR440894 0.3 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 1 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 3 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 10 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 20 mg/kg (N=X)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Notes: N = Number of participants in the PK Population. Concentrations are reported in units of µg/mL. Values of GM (CV %) are shown.
[a] Times are relative to time of dosing.

Table 18: SAR440894 Concentrations in Plasma, SAR440894 0.3 mg/kg – 0 to 72 h Post Dose – PK Population

[Implementation Note: Mark concentrations collected out of window with an asterisk (*) next to the concentration and include the footnote: "Samples collected out of window are noted by as asterisk (*)."

Mark concentrations collected substantially out of window with two asterisks (**) next to the concentration and include the footnote: "Samples collected substantially out of window are noted by two asterisks (**)."

Mark imputed concentration times with three asterisks (***) next to the concentration and include the footnote: "Samples with imputed collection times are noted by three asterisks (***)."]

	Nominal Time[a] (h)							
Participant ID	**0**	**1**	**4**	**8**	**12**	**24**	**48**	**72**
PH2.00123	x	x	x	x	x	x	x	x
PH2.00124	x	x	x	x	x	x	x	x
PH2.00125	x	x	x	x	x	x	x	x
…								
Statistics								
N[b]	x	x	x	x	x	x	x	x
Mean	x	x	x	x	x	x	x	x
SD	x	x	x	x	x	x	x	x
GM	x	x	x	x	x	x	x	x
CV%	x	x	x	x	x	x	x	x
Min	x	x	x	x	x	x	x	x
Max	x	x	x	x	x	x	x	x

Notes: Concentrations are reported in units of µg/mL.
[Out of window footnotes here, if applicable]
[a] Times are relative to time of dosing.
[b] Number of data points used to compute the summary statistics. For calculated of summary statistics, BQL values were imputed to 0 if the sample was taken before the first measurable PK sample with a concentration above the LLOQ. BQL values were treated as missing otherwise.

Table 19: SAR440894 Concentrations in Plasma, SAR440894 0.3 mg/kg – 7 to 150 Days Post Dose – PK Population

[Implementation Note: Mark concentrations collected out of window with an asterisk (*) next to the concentration and include the footnote: "Samples collected out of window are noted by as asterisk (*)."

Mark concentrations collected substantially out of window with two asterisks (**) next to the concentration and include the footnote: "Samples collected substantially out of window are noted by two asterisks (**)."

Mark imputed concentration times with three asterisks (***) next to the concentration and include the footnote: "Samples with imputed collection times are noted by three asterisks (***)."]

	Nominal Time[a] (days)						
Participant ID	**7**	**14**	**28**	**56**	**84**	**112**	**150**
PH2.00123	x	x	x	x	x	x	x
PH2.00124	x	x	x	x	x	x	x
PH2.00125	x	x	x	x	x	x	x
…							
Statistics							
N[b]	x	x	x	x	x	x	x
Mean	x	x	x	x	x	x	x
SD	x	x	x	x	x	x	x
GM	x	x	x	x	x	x	x
CV%	x	x	x	x	x	x	x
Min	x	x	x	x	x	x	x
Max	x	x	x	x	x	x	x

Notes: Concentrations are reported in units of µg/mL
[Out of window footnotes here, if applicable]
[a] Times are relative to time of dosing.
[b] Number of data points used to compute the summary statistics. For calculated of summary statistics, BQL values were imputed to 0 if the sample was taken before the first measurable PK sample with a concentration above the LLOQ. BQL values were treated as missing otherwise.

Tables with Similar Format:

Table 20: SAR440894 Concentrations in Plasma, SAR440894 1 mg/kg – 0 to 72 h Post Dose – PK Population

Table 21: SAR440894 Concentrations in Plasma, SAR440894 1 mg/kg – 7 to 150 Days Post Dose – PK Population

Table 22: SAR440894 Concentrations in Plasma, SAR440894 3 mg/kg – 0 to 72 h Post Dose – PK Population

Table 23: SAR440894 Concentrations in Plasma, SAR440894 3 mg/kg – 7 to 150 Days Post Dose – PK Population

Table 24: SAR440894 Concentrations in Plasma, SAR440894 10 mg/kg – 0 to 72 h Post Dose – PK Population

Table 25: SAR440894 Concentrations in Plasma, SAR440894 10 mg/kg – 7 to 150 Days Post Dose – PK Population

Table 26: SAR440894 Concentrations in Plasma, SAR440894 20 mg/kg – 0 to 72 h Post Dose – PK Population

Table 27: SAR440894 Concentrations in Plasma, SAR440894 20 mg/kg – 7 to 150 Days Post Dose – PK Population

Table 28: Summary Statistics for SAR440894 PK Parameters in Plasma by Treatment Group – PK Population

PK Parameter (Units)	SAR440894 0.3 mg/kg	SAR440894 1 mg/kg	SAR440894 3 mg/kg	SAR440894 10 mg/kg	SAR440894 20 mg/kg
C_{max}, (µg/mL)	x (x)	x (x)	x (x)	x (x)	x (x)
C_{max}/Dose, (µg/mL)/(mg/kg)	x (x)	x (x)	x (x)	x (x)	x (x)
T_{max}, (h)	x (x - x)	x (x - x)	x (x - x)	x (x - x)	x (x - x)
C_{min}, (µg/mL)	x (x)	x (x)	x (x)	x (x)	x (x)
$AUC_{(0\text{-}last)}$, (µg*h/mL)	x (x)	x (x)	x (x)	x (x)	x (x)
$AUC_{(0\text{-}last)}$/Dose, (µg*h/mL)/(mg/kg)	x (x)	x (x)	x (x)	x (x)	x (x)
$AUC_{(0\text{-}inf)}$, (µg*h/mL)	x (x)	x (x)	x (x)	x (x)	x (x)
λz, (1/h)	x (x)	x (x)	x (x)	x (x)	x (x)
$t_{1/2}$, (h)	x (x)	x (x)	x (x)	x (x)	x (x)
CL, (L/h/kg)	x (x)	x (x)	x (x)	x (x)	x (x)
V_d, (L/kg)	x (x)	x (x)	x (x)	x (x)	x (x)

Note: Values of GM (CV %) are shown, except for T_{max} for which values of median (min-max) are shown.

Table 29: Summary Statistics for SAR440894 PK Parameters in Plasma, SAR440894 0.3 mg/kg – PK Population

Statistics	C_{max} (µg/mL)	C_{max}/Dose (µg/mL)/(mg/kg)	T_{max} (h)	C_{min} (µg/mL)	$AUC_{(0\text{-}last)}$ (µg*h/mL)	$AUC_{(0\text{-}last)}$/Dose (µg*h/mL)/(mg/kg)	$AUC_{(0\text{-}inf)}$ (µg*h/mL)	λz (1/h)	$t_{1/2}$ (h)	CL (L/h/kg)	V_d (L/kg)
N	x	x	x	x	x	x	x	x	x	x	x
Mean	x	x	x	x	x	x	x	x	x	x	x
SD	x	x	x	x	x	x	x	x	x	x	x
GM	x	x	x	x	x	x	x	x	x	x	x
CV%	x	x	x	x	x	x	x	x	x	x	x
Min	x	x	x	x	x	x	x	x	x	x	x
Max	x	x	x	x	x	x	x	x	x	x	X

Note: N = Number of participants used to calculate the summary statistics.

Tables with Similar Format:

Table 30: Summary Statistics for SAR440894 PK Parameters in Plasma, SAR440894 1 mg/kg – PK Population

Table 31: Summary Statistics for SAR440894 PK Parameters in Plasma, SAR440894 3 mg/kg – PK Population

Table 32: Summary Statistics for SAR440894 PK Parameters in Plasma, SAR440894 10 mg/kg – PK Population

Table 33: Summary Statistics for SAR440894 PK Parameters in Plasma, SAR440894 20 mg/kg – PK Population

Table 34: Proportion of Participants with a Positive Screening Assay by Treatment Group and Time Point – Immunogenicity Population

Time Point	Positive Screening Assay													
	SAR440894 0.3 mg/kg (N = X)		SAR440894 1 mg/kg (N = X)		SAR440894 3 mg/kg (N = X)		SAR440894 10 mg/kg (N = X)		SAR440894 20 mg/kg (N = X)		Placebo (N = X)		All Participants (N = X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	x	xx												
Day 56														
Day 112														
Day 180														
Note: N = Number of participants in the Immunogenicity Population.														

Table 35: Post-Infusion ADA Assay Results by Planned Time Point and Treatment Group – Immunogenicity Population

Time Point	Treatment Group	N	ADA Result			
			Treatment-Induced ADA n (%)	Treatment-Boosted ADA n (%)	Pre-existing ADA n (%)	Negative n (%)
Day 56	All Participants	X	x (%)	x (%)	x (%)	x (%)
	SAR440894 0.3 mg/kg	X	x (%)	x (%)	x (%)	x (%)
	SAR440894 1 mg/kg	X	x (%)	x (%)	x (%)	x (%)
	SAR440894 3 mg/kg	X	x (%)	x (%)	x (%)	x (%)
	SAR440894 10 mg/kg	X	x (%)	x (%)	x (%)	x (%)
	SAR440894 20 mg/kg	X	x (%)	x (%)	x (%)	x (%)
	Placebo	X	x (%)	x (%)	x (%)	x (%)
Day 112	All Participants	X	x (%)	x (%)	x (%)	x (%)
	SAR440894 0.3 mg/kg	X	x (%)	x (%)	x (%)	x (%)
	…	X	x (%)	x (%)	x (%)	x (%)
	Placebo	X	x (%)	x (%)	x (%)	x (%)
Day 150	All Participants	X	x (%)	x (%)	x (%)	x (%)
	SAR440894 0.3 mg/kg	X	x (%)	x (%)	x (%)	x (%)
	…	X	x (%)	x (%)	x (%)	x (%)
	Placebo	X	x (%)	x (%)	x (%)	x (%)

Note: N=Number of participants in the Immunogenicity Population in each treatment group with results for the given time point, excluding those for whom treatment-induced, treatment-boosted, and pre-existing ADA cannot be assessed.

Table 36: Incidence of ADA by Treatment Group – Immunogenicity Population

Treatment Group	N	Incidence[a] of ADA	
		n	%
All Participants	x	x	xx
SAR440894 0.3 mg/kg			
SAR440894 1 mg/kg			
SAR440894 3 mg/kg			
SAR440894 10 mg/kg			
SAR440894 20 mg/kg			
Placebo			

Notes: N = Number of participants in the Immunogenicity Population, excluding those for whom treatment-induced and treatment-boosted ADA cannot be assessed.
[a] Incidence of ADA is defined as either treatment-induced or treatment-boosted ADA at any time point

Table 37: ADA Titer Results by Time Point and Treatment Group – Immunogenicity Population

Time Point	Statistic	Treatment Group						
		SAR440894 0.3 mg/kg (N=X)	SAR440894 1 mg/kg (N=X)	SAR440894 3 mg/kg (N=X)	SAR440894 10 mg/kg (N=X)	SAR440894 20 mg/kg (N=X)	Placebo (N=X)	All Participants (N=X)
Baseline	n	x	x	x	x	x	x	x
	Mean Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Titer Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Maximum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	GMT[a] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	GMFR[b] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	4-Fold Rise[c] (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 56	n	x	x	x	x	x	x	x
	Mean Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Titer Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Maximum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	GMT[a] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	GMFR[b] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	4-Fold Rise[c] (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 112	n	x	x	x	x	x	x	x
	Mean Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Titer Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Maximum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	GMT[a] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Table 37: ADA Titer Results by Time Point and Treatment Group – Immunogenicity Population *(continued)*

	GMFR[b] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	4-Fold Rise[c] (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 150	n	x	x	x	x	x	x	x
	Mean Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Titer Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median Titer	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Maximum Titer	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	GMT[a] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	GMFR[b] (95% CI)	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.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	4-Fold Rise[c] (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Notes: N = Number of participants in the Immunogenicity Population in each treatment group. n = Number of participants with available results.
[a] GMT represents geometric mean titer.
[b] GMFR represents the geometric mean fold rise in titer compared to baseline (pre-infusion).
[c] 4-Fold Rise represents the percentage of participants with at least a 4-fold rise in titer from baseline.

Table 38: ADA Incidence – Clearance Analysis Results – Pharmacokinetics – Immunogenicity Subset

[Implementation Note: If log(CL) is used in the ANOVA model, statistics will be provided after exponentiation to the original units for clearance and the third footnote will be updated to *"Statistics are provided on the original scale for CL, after being obtained using a mixed effects ANOVA model for log(CL) with fixed covariates for Dose Group and ADA Result, using Negative ADA as the reference group."*

If Dose Group is deemed unrelated to clearance and is excluded from the model, the third footnote will be updated to indicate the only fixed covariate in the model was ADA Result.]

Statistic	ADA Incidence Group	
	ADA Positive	ADA Negative
N	x	x
Mean Clearance	x.xx	x.xx
Mean Clearance 95% CI	(x.xx, x.xx)	(x.xx, x.xx)
Difference in Mean Clearance (Positive – Negative)	x.xx	-
Difference in Mean Clearance 95% CI	(x.xx, x.xx)	-

Notes: N = Number of participants in the Pharmacokinetics – Immunogenicity Subset with estimable clearance (CL), excluding those for whom treatment-induced and treatment-boosted ADA cannot be assessed.
For this analysis, Positive ADA is defined as experiencing either treatment-induced or treatment-boosted ADA at any time point, and Negative ADA will be defined as not experiencing treatment-induced or treatment-boosted ADA during the study period.
Statistics are obtained using a mixed effects ANOVA model for CL with fixed covariates for Dose Group and ADA Result, using Negative ADA as the reference group.

Table 39: ADA Titer – Clearance Analysis Parameter Estimates – Pharmacokinetics – Immunogenicity Subset

[Implementation Note: If log(CL) is used in the ANCOVA model, statistics will be provided after exponentiation to the original units for clearance and the second footnote will be updated to *"Statistics are provided on the original scale for CL, after being obtained using a mixed effects ANCOVA model for log(CL)…"*

If Dose Group is deemed unrelated to clearance and is excluded from the model, the second footnote will be updated to indicate the model only included centered ADA titer as a covariate.]

Statistic	Result
N	x
ADA Effect, $\hat{\gamma}$	x.xx
Standard Error ($\hat{\gamma}$)	x.xx
$\hat{\gamma}$ 95% CI	(x.xx, x.xx)

Notes: N = Number of participants in the Pharmacokinetics – Immunogenicity Subset with estimable clearance (CL).
Statistics are obtained using a mixed effects ANCOVA model for CL with a fixed covariate for Dose Group and centered ADA titer as a continuous covariate. $\hat{\gamma}$ represents the change in clearance for a 1-unit increase to titer from the overall mean titer, holding Dose Group constant.

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 40: Overall Summary of Adverse Events – Participants in the Safety Population Enrolled Prior to Protocol v11.0

	SAR440894 0.3 mg/kg (N = xx)		SAR440894 1 mg/kg (N = xx)		SAR440894 3 mg/kg (N = xx)		SAR440894 10 mg/kg (N = xx)		SAR440894 20 mg/kg (N = xx)		Placebo (N = xx)		All Participants (N = xx)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one adverse event														
At least one related adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)														
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one severe (Grade 3) unsolicited adverse event														
Related	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to discontinuation of study product[b]														
At least one adverse event leading to early termination[b]														
At least one laboratory abnormality														
At least one related laboratory abnormality														
At least one clinically significant laboratory abnormality[c]														
Related														
Unrelated														
At least one not clinically significant laboratory abnormality[c]														
Related														
Unrelated														

Notes: N = Number of participants in the Safety Population
[a] Participants are counted once for each category regardless of the number of events.
[b] As reported on the Adverse Event eCRF.
[c] As reported on the Local Laboratory Results eCRFs.

Table 41: Overall Summary of Adverse Events – Participants in the Safety Population Enrolled Under Protocol v11.0

	SAR440894 0.3 mg/kg (N = xx)		SAR440894 1 mg/kg (N = xx)		SAR440894 3 mg/kg (N = xx)		SAR440894 10 mg/kg (N = xx)		SAR440894 20 mg/kg (N = xx)		Placebo (N = xx)		All Participants (N = xx)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one adverse event														
At least one related adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Grade 1 (Mild)	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Grade 2 (Moderate)														
Grade 3 (Severe)	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Grade 4 (Life threatening)														
Grade 5 (Death)														
At least one Grade 3 (Severe) or Higher unsolicited adverse event														
Related	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to discontinuation of study product[b]														
At least one adverse event leading to early termination[b]														
At least one laboratory abnormality														
At least one related laboratory abnormality														
At least one clinically significant laboratory abnormality[c]														
Related														
Unrelated														
At least one not clinically significant laboratory abnormality[c]														
Related														
Unrelated														

Notes: N = Number of participants in the Safety Population
[a] Participants are counted once for each category regardless of the number of events.
[b] As reported on the Adverse Event eCRF.
[c] As reported on the Local Laboratory Results eCRFs.

14.3.1.2 Unsolicited Adverse Events

Table 42: Summary of Adverse Events by MedDRA System Organ Class, High Level Group Term, Preferred Term, and Treatment Group – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: If there is only 1 PT for an SOC and HLGT, there will be no "Any PT" row.

Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term	n (%)	95% CI[a]	Number of Events
All Participants (N=X)	Any SOC	Any HLGT	Any PT	x (x)	xx, xx	x
	[SOC 1]	Any HLGT	Any PT	x (x)	xx, xx	x
		HLGT1	Any PT	x (x)	xx, xx	x
			[PT 1]	x (x)	xx, xx	x
	[SOC 2]	Any HLGT	Any PT	x (x)	xx, xx	x
		HLGT1	Any PT	x (x)	xx, xx	x
			[PT 1]	x (x)	xx, xx	x
SAR440894 0.3 mg/kg (N=X)	…		…	x (x)	xx, xx	x
…	…		…	x (x)	xx, xx	x
Placebo (N=X)	…		…	x (x)	xx, xx	x

Notes: N = Number of participants in the Safety Population enrolled before Protocol v11.0 in the specified treatment group.
n=Number of participants reporting adverse events within each SOC/HLGT/PT.
A participant is only counted once per PT per treatment group.
[a] Exact Clopper-Pearson Confidence Interval.

Table with Similar Format:

Table 43: Summary of Adverse Events by MedDRA System Organ Class, High Level Group Term and Preferred Term, and Treatment Group – Participants in the Safety Population Enrolled Under Protocol v11.0

Table 44: Adverse Events by MedDRA System Organ Class, High Level Group Term and Preferred Term, Maximum Severity, Relationship, and Treatment Group – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: If there is only 1 PT for an SOC and HLGT, there will be no "Any PT" row. Likewise, if there is only 1 HLGT for an SOC, there will be no "Any HLGT" row.

Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term	Severity	Related n (%)	Not Related n (%)	Total n (%)
All Participants (N=X)	Any SOC	Any HLGT	Any PT	Any Severity	x (%)	x (%)	x (%)
				Mild	x (%)	x (%)	x (%)
				Moderate	x (%)	x (%)	x (%)
				Severe	x (%)	x (%)	x (%)
	[SOC 1]	Any HLGT	Any PT	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
		HLGT1	Any PT	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
		HLGT1	[PT1]	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
	…		…	…	x (%)	x (%)	x (%)
SAR440894 0.3 mg/kg (N=X)	…		…	…	x (%)	x (%)	x (%)
…	…		…	…	x (%)	x (%)	x (%)
Placebo (N=X)	…		…	…	x (%)	x (%)	x (%)

Notes: N = Number of participants in the Safety Population enrolled before Protocol v11.0 in each treatment group.

Participants are only counted once per PT and treatment group, in the highest reported severity. Participants may be counted for either or both Related and Not Related to study treatment.

Table 45: Adverse Events by MedDRA System Organ Class, High Level Group Term and Preferred Term, Maximum Severity, Relationship, and Treatment Group – Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: If there is only 1 PT for an SOC and HLGT, there will be no "Any PT" row. Likewise, if there is only 1 HLGT for an SOC, there will be no "Any HLGT" row.

Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term	Severity	Related n (%)	Not Related n (%)	Total n (%)
All Participants (N=X)	Any SOC	Any HLGT	Any PT	Any Severity	x (%)	x (%)	x (%)
				Mild	x (%)	x (%)	x (%)
				Moderate	x (%)	x (%)	x (%)
				Severe	x (%)	x (%)	x (%)
				Life-threatening	x (%)	x (%)	x (%)
				Death	x (%)	x (%)	x (%)
	[SOC 1]	Any HLGT	Any PT	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
		HLGT1	Any PT	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
		HLGT1	[PT1]	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
…	…		…	…	x (%)	x (%)	x (%)
SAR440894 0.3 mg/kg (N=X)	…		…	…			
…	…		…	…			
Placebo (N=X)	…		…	…			

Notes: N = Number of participants in the Safety Population enrolled under Protocol v11.0 in each treatment group.
Participants are only counted once per PT and treatment group, in the highest reported severity. Participants may be counted for either or both Related and Not Related to study treatment.

Table 46: Adverse Events by MedDRA System Organ Class, High Level Group Term and Preferred Term, Action Taken, and Treatment Group – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: If there is only 1 PT for an SOC and HLGT, there will be no "Any PT" row. Likewise, if there is only 1 HLGT for an SOC, there will be no "Any HLGT" row.

Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term	Dose Unchanged n (%)	Study Product Interrupted n (%)	Study Product Discontinued n (%)	Total n (%)
All Participants (N=X)	Any SOC	Any HLGT	Any PT	x (%)	x (%)	x (%)	x (%)
	[SOC 1]	Any HLGT	Any PT	x (%)	x (%)	x (%)	x (%)
		HLGT1	Any PT	x (%)	x (%)	x (%)	x (%)
			[PT1]	x (%)	x (%)	x (%)	x (%)
	…	…	…	x (%)	x (%)	x (%)	x (%)
SAR440894 0.3mg/kg (N=X)	Any SOC	Any HLGT	Any PT	x (%)	x (%)	x (%)	x (%)
	…	…	…	x (%)	x (%)	x (%)	x (%)
…	…	…	…	x (%)	x (%)	x (%)	x (%)
Placebo (N=X)	…		…	x (%)	x (%)	x (%)	x (%)
Notes: N = Number of participants in the Safety Population enrolled before Protocol v11.0 in each treatment group							

Table 47: Adverse Events by MedDRA System Organ Class, High Level Group Term and Preferred Term, Action Taken, and Treatment Group – Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: If there is only 1 PT for an SOC and HLGT, there will be no "Any PT" row. Likewise, if there is only 1 HLGT for an SOC, there will be no "Any HLGT" row.

Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term	Dose Unchanged n (%)	Study Product Interrupted n (%)	Study Product Discontinued n (%)	Total n (%)
All Participants (N=X)	Any SOC	Any HLGT	Any PT	x (%)	x (%)	x (%)	x (%)
	[SOC 1]	Any HLGT	Any PT	x (%)	x (%)	x (%)	x (%)
		HLGT1	Any PT	x (%)	x (%)	x (%)	x (%)
			[PT1]	x (%)	x (%)	x (%)	x (%)
	…	…	…	x (%)	x (%)	x (%)	x (%)
SAR440894 0.3 mg/kg (N=X)	Any SOC	Any HLGT	Any PT	x (%)	x (%)	x (%)	x (%)
	…	…	…	x (%)	x (%)	x (%)	x (%)
…	...	…	…	x (%)	x (%)	x (%)	x (%)
Placebo (N=X)	…		…	x (%)	x (%)	x (%)	x (%)
Notes: N = Number of participants in the Safety Population enrolled under Protocol v11.0 in each treatment group.							

Table 48: Serious Adverse Events by MedDRA System Organ Class, High Level Group Term and Preferred Term, Relationship, and Treatment Group – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: If there is only 1 PT for an SOC and HLGT, there will be no "Any PT" row. Likewise, if there is only 1 HLGT for an SOC, there will be no "Any HLGT" row.

Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term	Related n (%)	Not Related n (%)	Total n (%)
All Participants (N=X)	Any SOC	Any HLGT	Any PT	x (%)	x (%)	x (%)
	[SOC 1]	Any HLGT	Any PT	x (%)	x (%)	x (%)
		HLGT1	Any PT	x (%)	x (%)	x (%)
			[PT1]	x (%)	x (%)	x (%)
		…	,,,	x (%)	x (%)	x (%)
…	…		…	x (%)	x (%)	x (%)
SAR440894 0.3 mg/kg (N=X)	…		…	x (%)	x (%)	x (%)
…	…		…	x (%)	x (%)	x (%)
Placebo (N=X)	…		…	x (%)	x (%)	x (%)

Notes: N = Number of participants in the Safety Population enrolled before Protocol v11.0 in each treatment group.
Participants are only counted once per PT and treatment group, in the highest reported severity. Participants may be counted for either or both Related and Not Related to study treatment.

Tables with Similar Format:

Table 49: Serious Adverse Events by MedDRA System Organ Class, High Level Group Term and Preferred Term, Relationship, and Treatment Group – Participants in the Safety Population Enrolled Under Protocol v11.0

Table 50: Adverse Events Leading to Study Product Discontinuation by MedDRA System Organ Class, High Level Group Term and Preferred Term, Relationship, and Treatment Group – Participants in the Safety Population Enrolled Before Protocol v11.0

Table 51: Adverse Events Leading to Study Product Discontinuation by MedDRA System Organ Class, High Level Group Term and Preferred Term, Relationship, and Treatment Group – Participants in the Safety Population Enrolled Under Protocol v11.0

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 52: Listing of Serious Adverse Events – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. If the event is ongoing (no stop date), indicate "ongoing" for the "Duration". If more than one reason is selected for the reason reported as an SAE, list all reasons in the column, separated by a comma. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. If there are no comments for an event, populate 'Comments' row with 'None'. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Treatment Group, Participant ID, AE Number.]

Adverse Event	No. of Days Post Dose (Duration)	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term
Treatment Group: , Participant ID: , AE Number:												
Comments:												
Treatment Group: , Participant ID: , AE Number:												
Comments:												

Tables with Similar Format:

Table 53: Listing of Serious Adverse Events – Participants in the Safety Population Enrolled Under Protocol v11.0

Table 54: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: This listing is included in the tables document, as it is included in the body of the CSR. If the event is ongoing (no stop date), indicate "ongoing" in the "Duration" column. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. If there are no comments for an event, populate 'Comments' row with 'None'. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Treatment Group, Participant ID, AE Number.]

Adverse Event	No. of Days Post Dose (Duration)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term
Treatment Group: , Participant ID: , AE Number:										
Comments:										
Treatment Group: , Participant ID: , AE Number:										
Comments:										

Tables with Similar Format:

Table 55: Listing of Non-Serious, Unsolicited, Moderate or Greater Severity Adverse Events – Participants in the Safety Population Enrolled Under Protocol v11.0

Table 56: Listing of Adverse Events Leading to Discontinuation – Participants in the Safety Population Enrolled Before Protocol v11.0

Table 57: Listing of Adverse Events Leading to Discontinuation – Participants in the Safety Population Enrolled Under Protocol v11.0

Table 58: Listing of SUSARs – Participants in the Safety Population Enrolled Before Protocol v11.0

Table 59: Listing of SUSARs – Participants in the Safety Population Enrolled Under Protocol v11.0

Tables with Similar Format *(continued)*

Table 60: Listing of Unanticipated Problems – Participants in the Safety Population Enrolled Before Protocol v11.0

Table 61: Listing of Unanticipated Problems – Participants in the Safety Population Enrolled Under Protocol v11.0

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

(not included in SAP, but this is a placeholder for the CSR)

14.3.4 Abnormal Laboratory Value Listings (by Participant)

Table 62: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Prior to Protocol v11.0 - Chemistry

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. This listing should include all results for any subject that had at least one abnormal chemistry laboratory result. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL).This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Participant ID	Treatment Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Clinically Significant?	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Participant Discontinued Due to Result?

Tables with Similar Format:

Table 63: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Under Protocol v11.0 - Chemistry

Table 64: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Prior to Protocol v11.0 - Hematology

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. This listing should include all results for any subject that had at least one abnormal hematology laboratory result. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL).This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Participant ID	Treatment Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Clinically Significant?	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Participant Discontinued Due to Result?

Tables with Similar Format:

Table 65: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Under Protocol v11.0 - Hematology

Table 66: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Prior to Protocol v11.0 - Coagulation

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. This listing should include all results for any subject that had at least one abnormal urinalysis laboratory result. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL).This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Participant ID	Treatment Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Clinically Significant?	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Participant Discontinued Due to Result?

Tables with Similar Format:

Table 67: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Under Protocol v11.0 - Coagulation

Table 68: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Prior to Protocol v11.0 - Urinalysis

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. This listing should include all results for any subject that had at least one abnormal urinalysis laboratory result. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL).This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Participant ID	Treatment Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Clinically Significant?	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Participant Discontinued Due to Result?

Tables with Similar Format:

Table 69: Listing of Abnormal Laboratory Results for Participants in the Safety Population Enrolled Under Protocol v11.0 – Urinalysis

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 70: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Chemistry Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
		…								
	Placebo (N=X)	None								
		Mild								
…	…	…								
Max Severity Post Baseline	All Participants (N=X)	None								
		Mild								
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
		…								

Table 70: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Chemistry Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
	Placebo (N=X)	None								
		Mild								

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.

Table 71: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Chemistry Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												
	Placebo (N=X)	None												
		Mild												
	…	…												
Max Severity Post Baseline	All Participants (N=X)	None												
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												
	Placebo (N=X)	None												
		Mild												

Table 71: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Chemistry Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.														

Table 72: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Sodium

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 102** as an example).]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity													
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild														
	SAR440894 0.3 mg/kg (N=X)	None														
		Mild														
	…	…														
		…														
	Placebo (N=X)	None														
		Mild														
…	…	…														
Max Severity Post Baseline	All Participants (N=X)	None														
		Mild														
	SAR440894 0.3 mg/kg (N=X)	None														
		Mild														

Table 72: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Sodium *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity													
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
	…	…														
		…														
	Placebo (N=X)	None														
		Mild														

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.

Table 73: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Sodium

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 103** as an example).]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity																					
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Life-threatening/ Grade 4 (Low)		Life-threatening/ Grade 4 (High)		Death/ Grade 5 (Low)		Death/ Grade 5 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None																						
		Mild																						
	SAR440894 0.3 mg/kg (N=X)	None																						
		Mild																						
	…	…																						
		…																						
	Placebo (N=X)	None																						
		Mild																						
…	…	…																						
Max Severity Post Baseline	All Participants (N=X)	None																						
		Mild																						

Table 73: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Sodium *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity																			
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Life-threatening/ Grade 4 (Low)		Life-threatening/ Grade 4 (High)		Death/ Grade 5 (Low)		Death/ Grade 5 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	SAR440894 0.3 mg/kg (N=X)	None																						
		Mild																						
	…	…																						
		…																						
	Placebo (N=X)	None																						
		Mild																						

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.

Tables with Similar Format:

Table 74: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Potassium

[Implementation Note: This table will have similar format to Table 72.]

Table 75: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Potassium

[Implementation Note: This table will have similar format to Table 73.]

Tables with Similar Format *(continued)*:

Table 76: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Bicarbonate

[Implementation Note: This table will have similar format to Table 72.]

Table 77: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Bicarbonate

[Implementation Note: This table will have similar format to Table 73]

Table 78: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Glucose

[Implementation Note: This table will have similar format to Table 72.]

Table 79: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Glucose

[Implementation Note: This table will have similar format to Table 73.]

Table 80: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Blood Urea Nitrogen

[Implementation Note: This table will have similar format to Table 70.]

Table 81: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Blood Urea Nitrogen

[Implementation Note: This table will have similar format to Table 72.]

Table 82: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Creatinine

[Implementation Note: This table will have similar format to Table 70.]

Table 83: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Creatinine

[Implementation Note: This table will have similar format to Table 71.]

Tables with Similar Format *(continued)*:

Table 84: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – eGFR

[Implementation Note: This table will have similar format to Table 70.]

Table 85: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – eGFR

[Implementation Note: This table will have similar format to Table 71.]

Table 86: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Calcium

[Implementation Note: This table will have similar format to Table 72.]

Table 87: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Calcium

[Implementation Note: This table will have similar format to Table 73.]

Table 88: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Albumin

[Implementation Note: This table will have similar format to Table 70.]

Table 89: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Albumin

[Implementation Note: This table will have similar format to Table 71.]

Table 90: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Total Protein

[Implementation Note: This table will have similar format to Table 70.]

Table 91: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Total Protein

[Implementation Note: This table will have similar format to Table 71.]

Tables with Similar Format *(continued)*:

Table 92: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Alkaline Phosphatase

[Implementation Note: This table will have similar format to Table 70.]

Table 93: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Alkaline Phosphatase

[Implementation Note: This table will have similar format to Table 71.]

Table 94: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – AST

[Implementation Note: This table will have similar format to Table 70.]

Table 95: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – AST

[Implementation Note: This table will have similar format to Table 71.]

Table 96: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – ALT

[Implementation Note: This table will have similar format to Table 70.]

Table 97: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – ALT

[Implementation Note: This table will have similar format to Table 71.]

Table 98: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Direct Bilirubin

[Implementation Note: This table will have similar format to Table 70.]

Table 99: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Direct Bilirubin

[Implementation Note: This table will have similar format to Table 71.]

Tables with Similar Format *(continued)*:

Table 100: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Total Bilirubin

[Implementation Note: This table will have similar format to Table 70.]

Table 101: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Total Bilirubin

[Implementation Note: This table will have similar format to Table 71.]

Table 102: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Cystatin-C

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				
…	…	…				
Max Severity Post Baseline	All Participants (N=X)	None				
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				

Table 102: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Cystatin-C *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point. ONR = Outside of Normal Range.						

Table 103: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Cystatin-C

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				
…	…	…				
Max Severity Post Baseline	All Participants (N=X)	None				
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				

Table 103: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Cystatin-C *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point. ONR = Outside of Normal Range.						

Table 104: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Sodium (mmol/L)

[Implementation Note: Repeat for the following treatment groups: SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150).]

Time Point	Treatment Group	Value at Visit					Change from Baseline				
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max
Baseline	SAR440894 0.3 mg/kg (N = X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-
	…						-	-	-	-	-
	Placebo (N = X)						-	-	-	-	-
Day 2	SAR440894 0.3 mg/kg (N = X)						x	xx.x	xx.x	xx.x	xx.x, xx.x
	…										
	Placebo (N = X)										
…	…										

Notes: N = Number of participants in the Safety population. n = Number of participants with a non-missing lab value at the respective visit. For the change from baseline, n represents the number of participants with non-missing values at baseline and the respective visit. SD = Standard Deviation. Min = Minimum. Max = Maximum..

Tables with Similar Format:

Table 105: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Potassium (mmol/L)

Table 106: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Bicarbonate (mg/dL)

Table 107: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Glucose (mg/dL)

Table 108: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Blood Urea Nitrogen (mg/dL)

Table 109: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Creatinine (mg/dL)

Table 110: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – eGFR (mL/min/1.73m^2)

Tables with Similar Format *(continued)*:

Table 111: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Calcium (mg/dL)

Table 112: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Albumin (g/dL)

Table 113: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Total Protein (g/dL)

Table 114: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Alkaline Phosphatase (U/L)

Table 115: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – AST (U/L)

Table 116: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – ALT (U/L)

Table 117: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Direct Bilirubin (mg/dL)

Table 118: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Total Bilirubin (mg/dL)

Table 119: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Cystatin-C (mg/L)

Table 120: Clinically Significant Graded Chemistry Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Sodium (High), Sodium (Low), Potassium (High), Potassium (Low), Bicarbonate (High), Bicarbonate (Low), Glucose High), Glucose (Low), Blood Urea Nitrogen, Creatinine, eGFR, Calcium (High), Calcium (Low), Albumin, Total Protein, Alkaline Phosphatase, AST, ALT, Direct Bilirubin, and Total Bilirubin.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Sodium (High)	All Participants	x	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
Sodium (Low)	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
Potassium (High)	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
…	…							

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 121: Clinically Significant Graded Chemistry Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Sodium (High), Sodium (Low), Potassium (High), Potassium (Low), Bicarbonate (High), Bicarbonate (Low), Glucose High), Glucose (Low), Blood Urea Nitrogen, Creatinine, eGFR, Calcium (High), Calcium (Low), Albumin, Total Protein, Alkaline Phosphatase, AST, ALT, Direct Bilirubin, and Total Bilirubin.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%
Sodium (High)	All Participants	x	x	xx	x	xx	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
Sodium (Low)	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
Potassium (High)	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
…	…											

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

Table 122: Other Clinically Significant Abnormal Chemistry Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Cystatin-C.]

Parameter	Treatment Group	N	Within Normal Range		Outside Normal Range	
			n	%	n	%
Cystatin-C	All Participants	x	x	xx	x	xx
	SAR440894 0.3 mg/kg					
	…					
	Placebo					

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 123: Other Clinically Significant Abnormal Chemistry Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Cystatin-C.]

Parameter	Treatment Group	N	Within Normal Range		Outside Normal Range	
			n	%	n	%
Cystatin-C	All Participants	x	x	xx	x	xx
	SAR440894 0.3 mg/kg					
	…					
	Placebo					

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

14.3.5.2 Hematology Results

Table 124: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Hematology Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline].

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None								
		Mild								
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
		…								
	Placebo (N=X)	None								
		Mild								
…	…	…								
Max Severity Post Baseline	All Participants (N=X)	None								
		Mild								
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
	Placebo (N=X)	None								
		Mild								

Table 124: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Hematology Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.										

Table 125: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Hematology Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline].

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None												
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												
	Placebo (N=X)	None												
		Mild												
…	…	…												
Max Severity Post Baseline	All Participants (N=X)	None												
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												

Table 125: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Hematology Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
	Placebo (N=X)	None												
		Mild												

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.

Tables with Similar Format:

Table 126: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Hemoglobin

[Implementation Note: This table will have similar format to Table 124.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 138** as an example).]

Table 127: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Hemoglobin

[Implementation Note: This table will have similar format to Table 125.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 139** as an example).]

Table 128: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – WBC

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 138** as an example).]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity													
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None														
		Mild														
	SAR440894 0.3 mg/kg (N=X)	None														
		Mild														
	…	…														
		…														
	Placebo (N=X)	None														
		Mild														
…	…	…														
Max Severity Post Baseline	All Participants (N=X)	None														
		Mild														
	SAR440894 0.3 mg/kg (N=X)	None														
		Mild														

Table 128: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – WBC *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity													
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
	…	…														
		…														
	Placebo (N=X)	None														
		Mild														

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.

Table 129: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – WBC

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 139** as an example).]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity																					
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Life-threatening/ Grade 4 (Low)		Life-threatening/ Grade 4 (High)		Death/ Grade 5 (Low)		Death/ Grade 5 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None																						
		Mild																						
	SAR440894 0.3 mg/kg (N=X)	None																						
		Mild																						
	…	…																						
		…																						
	Placebo (N=X)	None																						
		Mild																						
…	…	…																						
Max Severity	All Participants (N=X)	None																						

Table 129: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – WBC *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity																			
			None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Life-threatening/ Grade 4 (Low)		Life-threatening/ Grade 4 (High)		Death/ Grade 5 (Low)		Death/ Grade 5 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Post Baseline		Mild																						
	SAR440894 0.3 mg/kg (N=X)	None																						
		Mild																						
	…	…																						
		…																						
	Placebo (N=X)	None																						
		Mild																						

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.

Tables with Similar Format:

Table 130: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Lymphocytes

[Implementation Note: This table will have similar format to Table 124.]

Table 131: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Lymphocytes

[Implementation Note: This table will have similar format to Table 125.]

Tables with Similar Format *(continued)*:

Table 132: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Neutrophils

[Implementation Note: This table will have similar format to Table 124.]

Table 133: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Neutrophils

[Implementation Note: This table will have similar format to Table 125.]

Table 134: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Eosinophils

[Implementation Note: This table will have similar format to Table 124.]

Table 135: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Eosinophils

[Implementation Note: This table will have similar format to Table 125.]

Table 136: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Platelets

[Implementation Note: This table will have similar format to Table 124.]

Table 137: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Platelets

[Implementation Note: This table will have similar format to Table 125.]

Table 138: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Hematocrit

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline].

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				
…	…	…				
Max Severity Post Baseline	All Participants (N=X)	None				
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				

Table 138: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Hematocrit *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point. ONR = Outside of Normal Range.						

Table 139: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Hematocrit

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline].

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				
…	…	…				
Max Severity Post Baseline	All Participants (N=X)	None				
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				

Table 139: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Hematocrit *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point. ONR = Outside of Normal Range.						

Tables with Similar Format:

Table 140: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – RBC

[Implementation Note: This table will have similar format to Table 138.]

Table 141: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – RBC

[Implementation Note: This table will have similar format to Table 139.]

Table 142: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Basophils

[Implementation Note: This table will have similar format to Table 138.]

Table 143: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Basophils

[Implementation Note: This table will have similar format to Table 139.]

Table 144: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Monocytes

[Implementation Note: This table will have similar format to Table 138.]

Table 145: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Monocytes

[Implementation Note: This table will have similar format to Table 139.]

Table 146: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Hemoglobin (g/dL)

[Implementation Note: Repeat for the following treatment groups: SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150)].

Time Point	Treatment Group	Value at Visit					Change from Baseline				
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max
Baseline	SAR440894 0.3 mg/kg (N = X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-
	…						-	-	-	-	-
	Placebo (N = X)						-	-	-	-	-
Day 2	SAR440894 0.3 mg/kg (N = X)						x	xx.x	xx.x	xx.x	xx.x, xx.x
	…										
	Placebo (N = X)										
…	…										

Notes: N = Number of participants in the Safety population. n = Number of participants with a non-missing lab value at the respective visit. For the change from baseline, n represents the number of participants with non-missing values at baseline and the respective visit. SD = Standard Deviation. Min = Minimum. Max = Maximum.

Tables with Similar Format:

Table 147: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – WBC (10^9/L)

Table 148: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Lymphocytes (10^9/L)

Table 149: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Neutrophils (10^9/L)

Table 150: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Eosinophils (10^9/L)

Table 151: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Platelets (10^9/L)

Table 152: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Hematocrit (%)

Tables with Similar Format *(continued)*:

Table 153: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – RBC (10^{12}/L)

Table 154: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Basophils (10^{9}/L)

Table 155: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Monocytes (10^{9}/L)

Table 156: Clinically Significant Graded Hematology Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Hemoglobin, WBC (High), WBC (Low), Lymphocytes, Neutrophils, Eosinophils, and Platelets.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Hemoglobin	All Participants	x	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
WBC (High)	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
WBC (Low)	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
…	…							

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 157: Clinically Significant Graded Hematology Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Hemoglobin, WBC (High), WBC (Low), Lymphocytes, Neutrophils, Eosinophils, and Platelets.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%
Hemoglobin	All Participants	x	x	xx	x	xx	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
WBC (High)	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
WBC (Low)	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
…	…											

Notes: Participants are counted once per maximum severity among all clinically significant experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

Table 158: Other Clinically Significant Abnormal Hematology Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Hematocrit, RBC, Basophils, and Monocytes.]

Parameter	Treatment Group	N	Within Normal Range		Outside Normal Range	
			n	%	n	%
Hematocrit	All Participants	x	x	xx	x	xx
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
RBC	All Participants					
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
Basophils	All Participants					
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
…	…					

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 159: Other Clinically Significant Abnormal Hematology Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Hematocrit, RBC, Basophils, and Monocytes.]

Parameter	Treatment Group	N	Within Normal Range		Outside Normal Range	
			n	%	n	%
Hematocrit	All Participants	x	x	xx	x	xx
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
RBC	All Participants					
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
Basophils	All Participants					
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
…	…					

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

14.3.5.3 Coagulation Results

Table 160: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Coagulation Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline].

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None								
		Mild								
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
		…								
	Placebo (N=X)	None								
		Mild								
…	…	…								
Max Severity Post Baseline	All Participants (N=X)	None								
		Mild								
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
		…								

Table 160: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Coagulation Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
	Placebo (N=X)	None								
		Mild								

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.

Table 161: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Coagulation Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None												
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												
	Placebo (N=X)	None												
		Mild												
…	…	…												
Max Severity Post Baseline	All Participants (N=X)	None												
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												
	Placebo (N=X)	None												
		Mild												

Table 161: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Coagulation Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.														

Tables with Similar Format:

Table 162: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – APTT

[Implementation Note: This table will have similar format to Table 160.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 138** as an example).]

Table 163: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – APTT

[Implementation Note: This table will have similar format to Table 161.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 139** as an example).]

Table 164: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Prothrombin Time

[Implementation Note: This table will have similar format to Table 160.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 138** as an example).]

Tables with Similar Format *(continued)*:

Table 165: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Prothrombin Time

[Implementation Note: This table will have similar format to Table 161.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 139** as an example).]

Table 166: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – INR

[Implementation Note: This table will have similar format to Table 160.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 138** as an example).]

Table 167: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – INR

[Implementation Note: This table will have similar format to Table 161.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see **Table 139** as an example).]

Table 168: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – APTT (sec)

[Implementation Note: Repeat for the following treatment groups: SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150).]

Time Point	Treatment Group	Value at Visit					Change from Baseline				
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max
Baseline	SAR440894 0.3 mg/kg (N = X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-
	…						-	-	-	-	-
	Placebo (N = X)						-	-	-	-	-
Day 2	SAR440894 0.3 mg/kg (N = X)						x	xx.x	xx.x	xx.x	xx.x, xx.x
	…										
	Placebo (N = X)										
…	…										

Notes: N = Number of participants in the Safety population. n = Number of participants with a non-missing lab value at the respective visit. For the change from baseline, n represents the number of participants with non-missing values at baseline and the respective visit. SD = Standard Deviation. Min = Minimum. Max = Maximum.

Tables with Similar Format:

Table 169: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Prothrombin Time (sec)

[Implementation Note: Generate one table for each chemistry parameter. For calculated fields (Mean, SD, Median), decimal place should be the format in which the data were collected + 1 extra place. For Min, Max, decimal place should be in the same format in which the data were collected.]

[Repeat for each Chemistry Laboratory Parameter, number each table separately]

Table 170: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – INR (Ratio)

Table 171: Clinically Significant Graded Coagulation Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: APTT, Prothrombin Time, and INR.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
APTT	All Participants	x	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
Prothrombin Time	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
INR	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 172: Clinically Significant Graded Coagulation Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: APTT, Prothrombin Time, and INR.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%
APTT	All Participants	x	x	xx	x	xx	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
Prothrombin Time	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
INR	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
…	…											

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

14.3.5.4 Urinalysis Results

Table 173: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Urinalysis Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None								
		Mild								
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
		…								
	Placebo (N=X)	None								
		Mild								
…	…	…								
Max Severity Post Baseline	All Participants (N=X)	None								
		Mild								
	SAR440894 0.3 mg/kg (N=X)	None								
		Mild								
	…	…								
		…								

Table 173: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Urinalysis Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity							
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
	Placebo (N=X)	None								
		Mild								

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.

Table 174: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Urinalysis Parameter

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Day 2	All Participants (N=X)	None												
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												
	Placebo (N=X)	None												
		Mild												
…	…	…												
Max Severity Post Baseline	All Participants (N=X)	None												
		Mild												
	SAR440894 0.3 mg/kg (N=X)	None												
		Mild												
	…	…												
		…												
	Placebo (N=X)	None												
		Mild												

Table 174: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Urinalysis Parameter *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity											
			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.														

Tables with Similar Format:

Table 175: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Urine Protein

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Table 176: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Urine Protein

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Table 177: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Urine Glucose

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Tables with Similar Format *(continued)*:

Table 178: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Urine Glucose

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Table 179: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Bilirubin

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Table 180: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Bilirubin

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Table 181: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Nitrite

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Table 182: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Nitrite

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Tables with Similar Format *(continued)*:

Table 183: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Occult Blood

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Table 184: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Occult Blood

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Table 185: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Urine WBC

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Table 186: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Urine WBC

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Table 187: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Urine RBC

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Tables with Similar Format *(continued)*:

Table 188: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Urine RBC

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Table 189: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Urobilinogen

[Implementation Note: This table will have similar format to Table 173.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 191 as an example).]

Table 190: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Urobilinogen

[Implementation Note: This table will have similar format to Table 174.

If parameter is not graded, then only "Within Normal Range" and "Outside Normal Range" columns will be included, baseline severity will be either "None" or "ONR" and "ONR = Outside Normal Range." Will be added to the footnote (see Table 192 as an example).]

Table 191: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Ketones

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				
…	…	…				
Max Severity Post Baseline	All Participants (N=X)	None				
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				

Table 191: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Ketones *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point. ONR = Outside of Normal Range.						

Table 192: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Ketones

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Day 2	All Participants (N=X)	None	x	xx	x	xx
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				
…	…	…				
Max Severity Post Baseline	All Participants (N=X)	None				
		ONR				
	SAR440894 0.3 mg/kg (N=X)	None				
		ONR				
	…	…				
		…				
	Placebo (N=X)	None				
		ONR				

Table 192: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Ketones *(continued)*

Time Point	Treatment Group	Baseline Severity	Post-Baseline Severity			
			Within Normal Range		Outside Normal Range	
			n	%	n	%
Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point. ONR = Outside of Normal Range.						

Tables with Similar Format:

Table 193: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Leukocyte Esterase

[Implementation Note: This table will have similar format to Table 191.]

Table 194: Laboratory Results by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Leukocyte Esterase

[Implementation Note: This table will have similar format to Table 192.]

Table 195: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Urine WBC (wbc/hpf)

[Implementation Note: Repeat for the following treatment groups: SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150).]

Time Point	Treatment Group	Value at Visit					Change from Baseline				
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max
Baseline	SAR440894 0.3 mg/kg (N = X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-
	…						-	-	-	-	-
	Placebo (N = X)						-	-	-	-	-
Day 2	SAR440894 0.3 mg/kg (N = X)						x	xx.x	xx.x	xx.x	xx.x, xx.x
	…										
	Placebo (N = X)										
...	…										

Notes: N = Number of participants in the Safety population. n = Number of participants with a non-missing lab value at the respective visit. For the change from baseline, n represents the number of participants with non-missing values at baseline and the respective visit. SD = Standard Deviation. Min = Minimum. Max = Maximum.

Tables with Similar Format:

Table 196: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Urine RBC (rbc/hpf)

Table 197: Laboratory Summary Statistics by Time Point and Treatment Group for the Safety Population – Urobilinogen (mg/dL)

[Implementation Note: Generate one table for each chemistry parameter. For calculated fields (Mean, SD, Median), decimal place should be the format in which the data were collected + 1 extra place. For Min, Max, decimal place should be in the same format in which the data were collected.]

[Repeat for each Chemistry Laboratory Parameter, number each table separately]

Table 198: Clinically Significant Graded Urinalysis Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Urine Protein, Urine Glucose, Bilirubin, Nitrite, Occult Blood, Urine WBC, Urine RBC, and Urobilinogen.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Urine Protein	All Participants	x	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
Urine Glucose	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
Bilirubin	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
…	…							

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 199: Clinically Significant Graded Urinalysis Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Urine Protein, Urine Glucose, Bilirubin, Nitrite, Occult Blood, Urine WBC, Urine RBC, and Urobilinogen.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%
Urine Protein	All Participants	x	x	xx	x	xx	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
Urine Glucose	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
Bilirubin	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
…	…											

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

Table 200: Other Clinically Significant Abnormal Urinalysis Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Ketones and Leukocyte Esterase.]

Parameter	Treatment Group	N	Within Normal Range		Outside Normal Range	
			n	%	n	%
Ketones	All Participants	x	x	xx	x	xx
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
Leukocyte Esterase	All Participants					
	SAR440894 0.3 mg/kg					
	…					
	Placebo					

Notes: Participants are counted once per maximum severity experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 201: Other Clinically Significant Abnormal Urinalysis Results by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Ketones.]

Parameter	Treatment Group	N	Within Normal Range		Outside Normal Range	
			n	%	n	%
Ketones	All Participants	x	x	xx	x	xx
	SAR440894 0.3 mg/kg					
	…					
	Placebo					
Leukocyte Esterase	All Participants					
	SAR440894 0.3 mg/kg					
	…					
	Placebo					

Notes: Participants are counted once per maximum severity among all clinically significant labs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

14.3.6 Displays of Vital Signs

Table 202: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Any Assessment

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 1 – 0.25h Post-Infusion Start, Day 1 – 0.5h Post-Infusion Start, Day 1 – 0.75h Post-Infusion Start, Day 1 – 1h Post-Infusion Start, Day 1 – 1h Post-Infusion, Day 1 – 2h Post-Infusion, Day 1 – 4h Post-Infusion, Day 1 – 6h Post-Infusion, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Baseline	All Participants									
	SAR440894 0.3 mg/kg									
	…									
	Placebo									
Day 1 – 0.25h Post-Infusion Start	All Participants									
	SAR440894 0.3 mg/kg									
	…									
	Placebo									
…	…									
Max Severity Post Baseline	All Participants									
	SAR440894 0.3 mg/kg									
	…									
	Placebo									

Notes: The “Max Post Baseline” rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.

Table 203: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Any Assessment

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 1 – 0.25h Post-Infusion Start, Day 1 – 0.5h Post-Infusion Start, Day 1 – 0.75h Post-Infusion Start, Day 1 – 1h Post-Infusion Start, Day 1 – 1h Post-Infusion, Day 1 – 2h Post-Infusion, Day 1 – 4h Post-Infusion, Day 1 – 6h Post-Infusion, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	All Participants													
	SAR440894 0.3 mg/kg													
	…													
	Placebo													
Day 1 – 0.25h Post-Infusion Start	All Participants													
	SAR440894 0.3 mg/kg													
	…													
	Placebo													
…	…													
Max Severity Post Baseline	All Participants													
	SAR440894 0.3 mg/kg													
	…													
	Placebo													

Notes: The “Max Post Baseline” rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.

Table 204: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Systolic Blood Pressure

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 1 – 0.25h Post-Infusion Start, Day 1 – 0.5h Post-Infusion Start, Day 1 – 0.75h Post-Infusion Start, Day 1 – 1h Post-Infusion Start, Day 1 – 1h Post-Infusion, Day 1 – 2h Post-Infusion, Day 1 – 4h Post-Infusion, Day 1 – 6h Post-Infusion, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	All Participants															
	SAR440894 0.3 mg/kg															
	…															
	Placebo															
Day 1 – 0.25h Post-Infusion Start	All Participants															
	SAR440894 0.3 mg/kg															
	…															
	Placebo															
…	…															
Max Severity Post Baseline	All Participants															
	SAR440894 0.3 mg/kg															
	…															
	Placebo															

Notes: The “Max Post Baseline” rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with non-missing results at the given time point.

Table 205: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Systolic Blood Pressure

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Baseline, Day 1 – 0.25h Post-Infusion Start, Day 1 – 0.5h Post-Infusion Start, Day 1 – 0.75h Post-Infusion Start, Day 1 – 1h Post-Infusion Start, Day 1 – 1h Post-Infusion, Day 1 – 2h Post-Infusion, Day 1 – 4h Post-Infusion, Day 1 – 6h Post-Infusion, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150), Max Severity Post Baseline.]

Time Point	Treatment Group	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Life-threatening/ Grade 4 (Low)		Life-threatening/ Grade 4 (High)		Death/ Grade 5 (Low)		Death/ Grade 5 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	All Participants																							
	SAR440894 0.3 mg/kg																							
	…																							
	Placebo																							
Day 1 0.25h Post-Infusion Start	All Participants																							
	SAR440894 0.3 mg/kg																							
	…																							
	Placebo																							
…	…																							
Max Severity Post Baseline	All Participants																							
	SAR440894 0.3 mg/kg																							
	…																							

Table 205: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Systolic Blood Pressure *(continued)*

Time Point	Treatment Group	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Life-threatening/ Grade 4 (Low)		Life-threatening/ Grade 4 (High)		Death/ Grade 5 (Low)		Death/ Grade 5 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Placebo																							

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with non-missing results at the given time point.

Tables with Similar Format:

Table 206: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Diastolic Blood Pressure

[Implementation Note: This table will have similar format to Table 202.]

Table 207: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Diastolic Blood Pressure

[Implementation Note: This table will have similar format to Table 203.]

Table 208: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Heart Rate

[Implementation Note: This table will have similar format to Table 204.]

Table 209: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Heart Rate

[Implementation Note: This table will have similar format to Table 205.]

Table 210: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Respiratory Rate

[Implementation Note: This table will have similar format to Table 202.]

Tables with Similar Format *(continued)*:

Table 211: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Respiratory Rate

[Implementation Note: This table will have similar format to Table 203.]

Table 212: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0 – Temperature

[Implementation Note: This table will have similar format to Table 202.]

Table 213: Vital Signs by Severity, Time Point, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0 – Temperature

[Implementation Note: This table will have similar format to Table 203.]

Table 214: Vital Signs Summary Statistics by Time Point and Treatment Group for the Safety Population – Systolic Blood Pressure (mmHg)

[Implementation Note: Repeat for the following treatment groups: SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following time points: Screening, Baseline, Day 1 – 0.25h Post-Infusion Start, Day 1 – 0.5h Post-Infusion Start, Day 1 – 0.75h Post-Infusion Start, Day 1 – 1h Post-Infusion Start, Day 1 – 1h Post-Infusion, Day 1 – 2h Post-Infusion, Day 1 – 4h Post-Infusion, Day 1 – 6h Post-Infusion, Day 2, Day 3, Day 4, Day 7, Day 14, Day 28, Day 56, Day 84, Day 112, Final Visit (Day 150).]

Time Point	Treatment Group	Value at Visit					Change from Baseline				
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max
Screening	SAR440894 0.3 mg/kg (N = X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-
	…										
	Placebo (N = X)						-	-	-	-	-
Baseline	SAR440894 0.3 mg/kg (N = X)						-	-	-	-	-
	…										
	Placebo (N = X)						-	-	-	-	-
Day 1 – 0.25h Post-Infusion Start	SAR440894 0.3 mg/kg (N = X)						x	xx.x	xx.x	xx.x	xx.x, xx.x
	…										
	Placebo (N = X)										
...	…										

Notes: N = Number of participants in the Safety population. n = Number of participants with a non-missing vital sign value at the respective visit. For the change from baseline, n represents the number of participants with non-missing values at baseline and the respective visit. SD = Standard Deviation. Min = Minimum. Max = Maximum.

Tables with Similar Format:

Table 215: Vital Signs Summary Statistics by Time Point and Treatment Group for the Safety Population – Diastolic Blood Pressure (mmHg)

Table 216: Vital Signs Summary Statistics by Time Point and Treatment Group for the Safety Population – Heart Rate (beats/min)

Tables with Similar Format *(continued)*:

Table 217: Vital Signs Summary Statistics by Time Point and Treatment Group for the Safety Population – Respiratory Rate (breaths/min)

Table 218: Vital Signs Summary Statistics by Time Point and Treatment Group for the Safety Population – Temperature (ºC)

Table 219: Clinically Significant Vital Signs by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Systolic Blood Pressure (High), Systolic Blood Pressure (Low), Diastolic Blood Pressure, Heart Rate (High), Heart Rate (Low), Respiratory Rate, and Temperature.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Systolic Blood Pressure (High)	All Participants	x	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
Systolic Blood Pressure (Low)	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
Diastolic Blood Pressure	All Participants							
	SAR440894 0.3 mg/kg							
	…							
	Placebo							
…	…							

Notes: Participants are counted once per maximum severity among all clinically significant vital signs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled prior to Protocol v11.0 with available results post-baseline.

Table 220: Clinically Significant Vital Signs by Maximum Severity Post-Baseline, Parameter, and Treatment Group for Participants in the Safety Population Enrolled Under Protocol v11.0

[Implementation Note: Repeat for the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.

The table will include the following parameters: Systolic Blood Pressure (High), Systolic Blood Pressure (Low), Diastolic Blood Pressure, Heart Rate (High), Heart Rate (Low), Respiratory Rate, and Temperature.]

Parameter	Treatment Group	N	Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-threatening/ Grade 4		Death/ Grade 5	
			n	%	n	%	n	%	n	%	n	%
Systolic Blood Pressure (High)	All Participants	x	x	xx	x	xx	x	xx	x	xx	x	xx
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
Systolic Blood Pressure (Low)	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
Diastolic Blood Pressure	All Participants											
	SAR440894 0.3 mg/kg											
	…											
	Placebo											
…	…											

Notes: Participants are counted once per maximum severity among all clinically significant vital signs experienced at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Population enrolled under Protocol v11.0 with available results post-baseline.

Table 221: Summary of Post Dose ECG Change in Overall Interpretations from Baseline by Treatment Group and Time Point - Safety Population

[Implementation Note: This table will include the following treatment groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.]

Treatment Group	N	Change from Baseline in ECG Interpretation					
		Normal at Both Times n (%)	Normal to Abnormal, NCS n (%)	Normal to Abnormal, CS n (%)	Abnormal, NCS at Both Times n (%)	Abnormal, NCS to Abnormal, CS n (%)	Abnormal, NCS to Normal n (%)
Day 1							
All Participants	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 0.3 mg/kg	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
…							
Placebo	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Day 4							
All Participants	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 0.3 mg/kg	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
…							
Placebo	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Final Visit (Day 150)							
All Participants	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
SAR440894 0.3 mg/kg	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
…							
Placebo	x	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Notes: N = Number of participants in the Safety Population with ECG measurements at the time points indicated.
NCS = Not clinically significant, CS = Clinically significant.

Table 222: ECG Summary Statistics by Parameter, Time Point, and Treatment Group – Safety Population

[Implementation Note: This table will include the following treatment groups: SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, Placebo.

The table will include the following parameters: PR Interval (msec), QRS Duration (msec), QT Interval (msec), QTcF Correction (msec), RR Interval (msec), Ventricular Rate (bpm).]

Time Point	Treatment Group	Value at Visit					Change from Baseline				
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max
PR Interval (msec)											
Screening	SAR440894 0.3mg/kg (N = X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-
	…										
	Placebo (N = X)						-	-	-	-	-
Baseline	SAR440894 0.3mg/kg (N = X)						-	-	-	-	-
	…										
	Placebo (N = X)						-	-	-	-	-
Day 1	SAR440894 0.3mg/kg (N = X)						x	xx.x	xx.x	xx.x	xx.x, xx.x
	…										
	Placebo (N = X)										
Day 4	SAR440894 0.3mg/kg (N = X)										
	…										
	Placebo (N = X)										
Final Visit (Day 150)	SAR440894 0.3mg/kg (N = X)										
	…										
	Placebo (N = X)										

Table 222: ECG Summary Statistics by Parameter, Time Point, and Treatment Group – Safety Population *(continued)*

Time Point	Treatment Group	Value at Visit					Change from Baseline				
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max
QRS Duration (msec)											
Screening	SAR440894 0.3mg/kg (N = X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-
	…										
	Placebo (N = X)						-	-	-	-	-
...	…										

Notes: N = Number of participants in the Safety population. n = Number of participants with a non-missing ECG result at the respective visit. For the change from baseline, n represents the number of participants with non-missing values at baseline and the respective visit. SD = Standard Deviation. Min = Minimum. Max = Maximum.

14.4 Summary of Concomitant Medications

Table 223: Number and Percentage of Participants with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group – Safety Population

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	SAR440894 0.3 mg/kg (N=X)		SAR440894 1 mg/kg (N=X)		SAR440894 3 mg/kg (N=X)		SAR440894 10 mg/kg (N=X)		SAR440894 20 mg/kg (N=X)		Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 2]														
	[ATC 2 - 1]														
	[ATC 2 - 2]														
	[ATC 2 - 3]														
[ATC Level 1 – 2]	Any [ATC 2]														
	[ATC 2 - 1]														
	[ATC 2 - 2]														
	[ATC 2 - 3]														

Notes: N = Number of participants in the Safety Population. n = Number of participants reporting taking at least one medication in the specific WHO Drug Class.

APPENDIX 2. FIGURE MOCK-UPS

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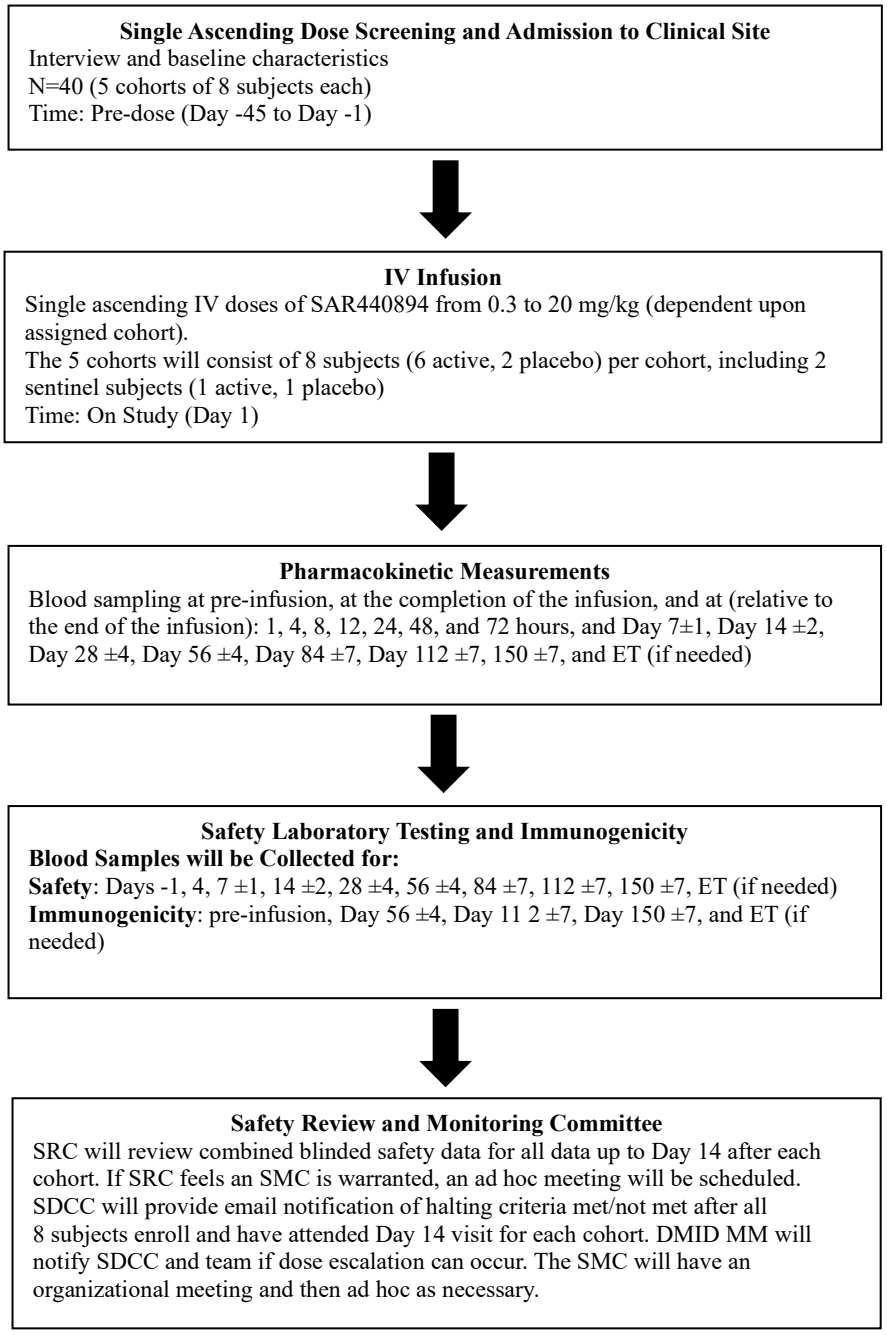
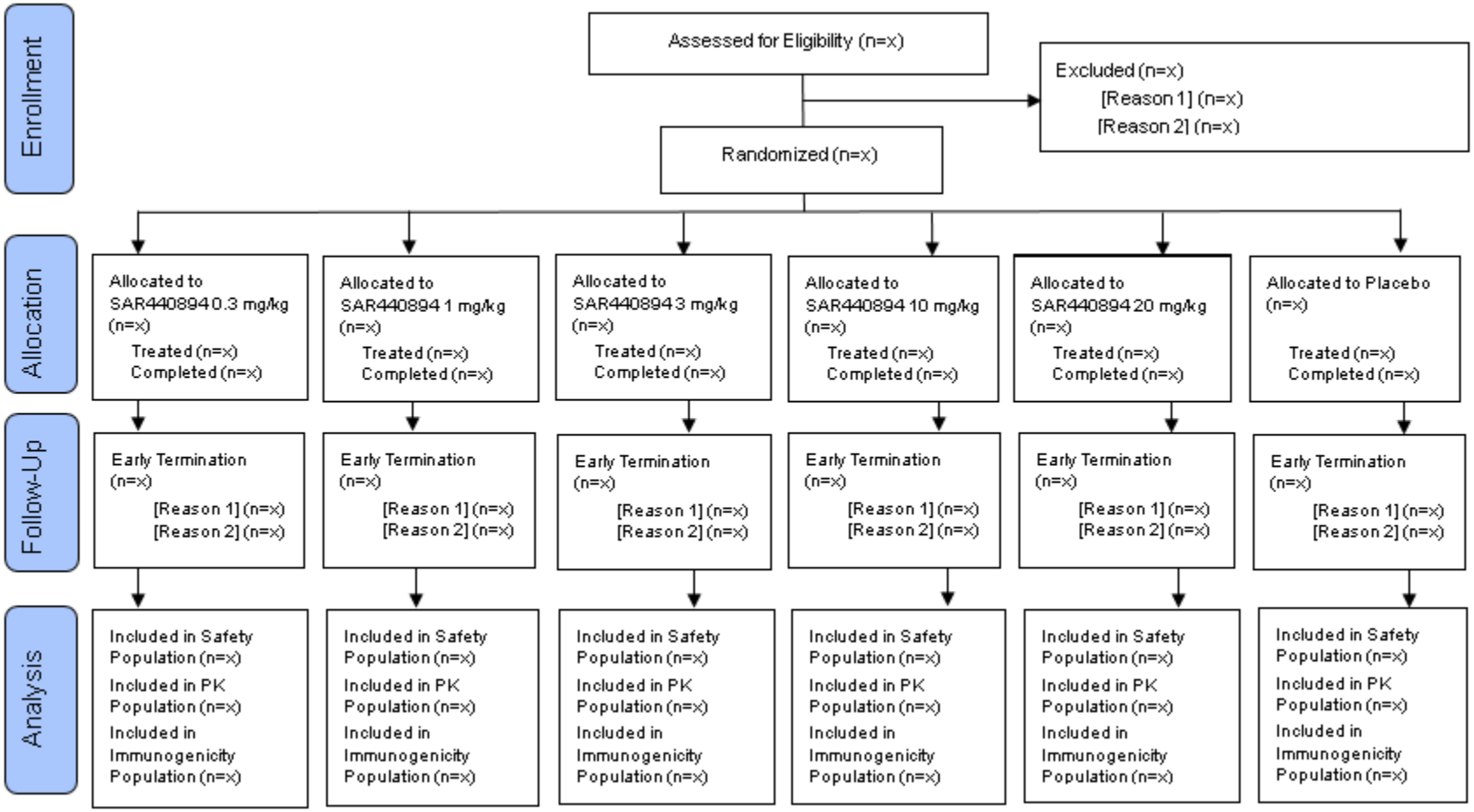
Figure 1: Schematic of Study Design



10.1 Disposition of Subjects

Figure 2: CONSORT Flow Diagram



14.2.2 Pharmacokinetic Figures by Treatment Group, and Time Point

Figure 3: Individual SAR440894 Concentration in Plasma Profiles by Treatment Group, 0 h to 72 h Post Dose

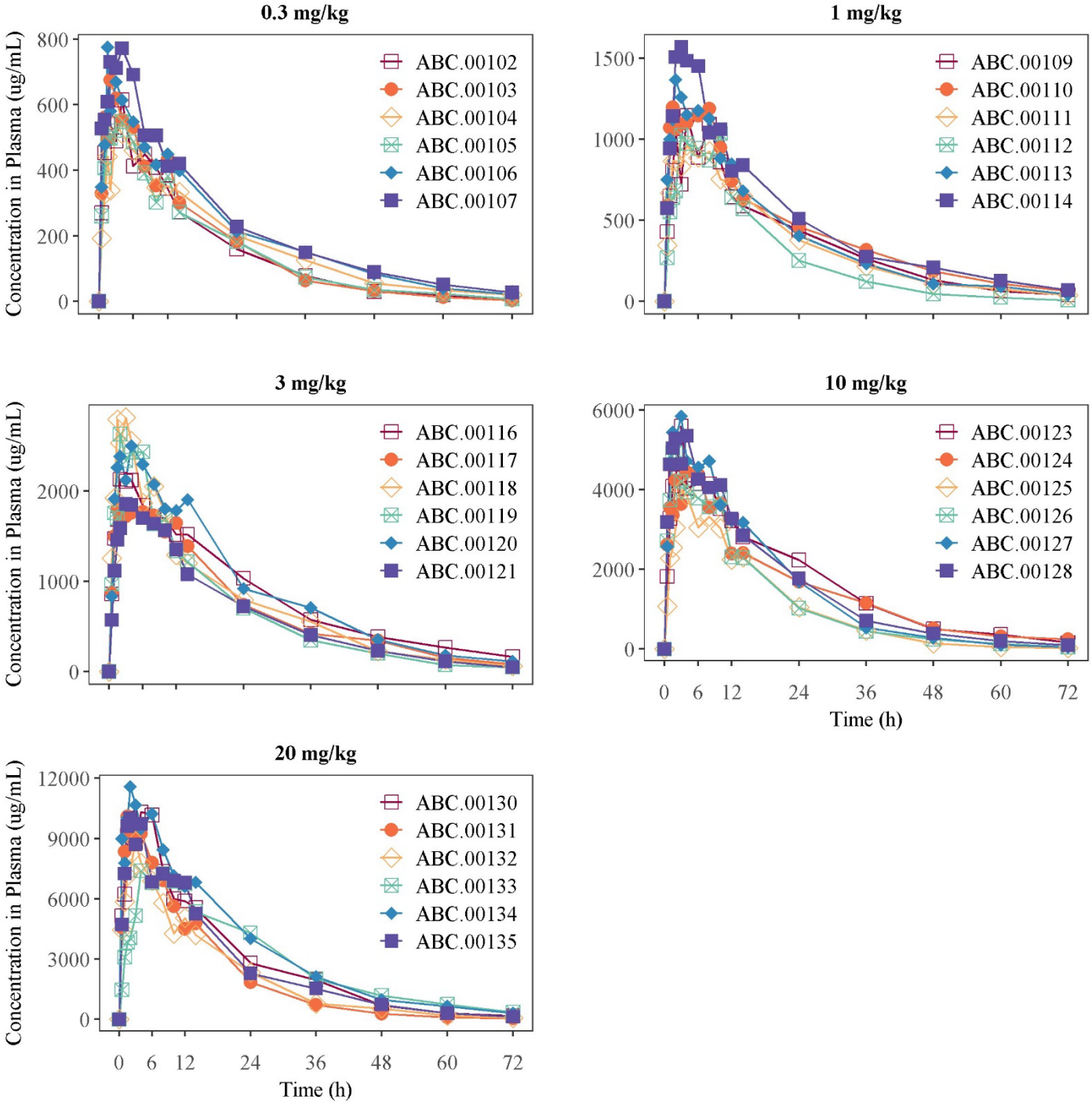


Figure 4: Individual SAR440894 Concentration in Plasma Profiles by Treatment Group, All Time Points Post Dose

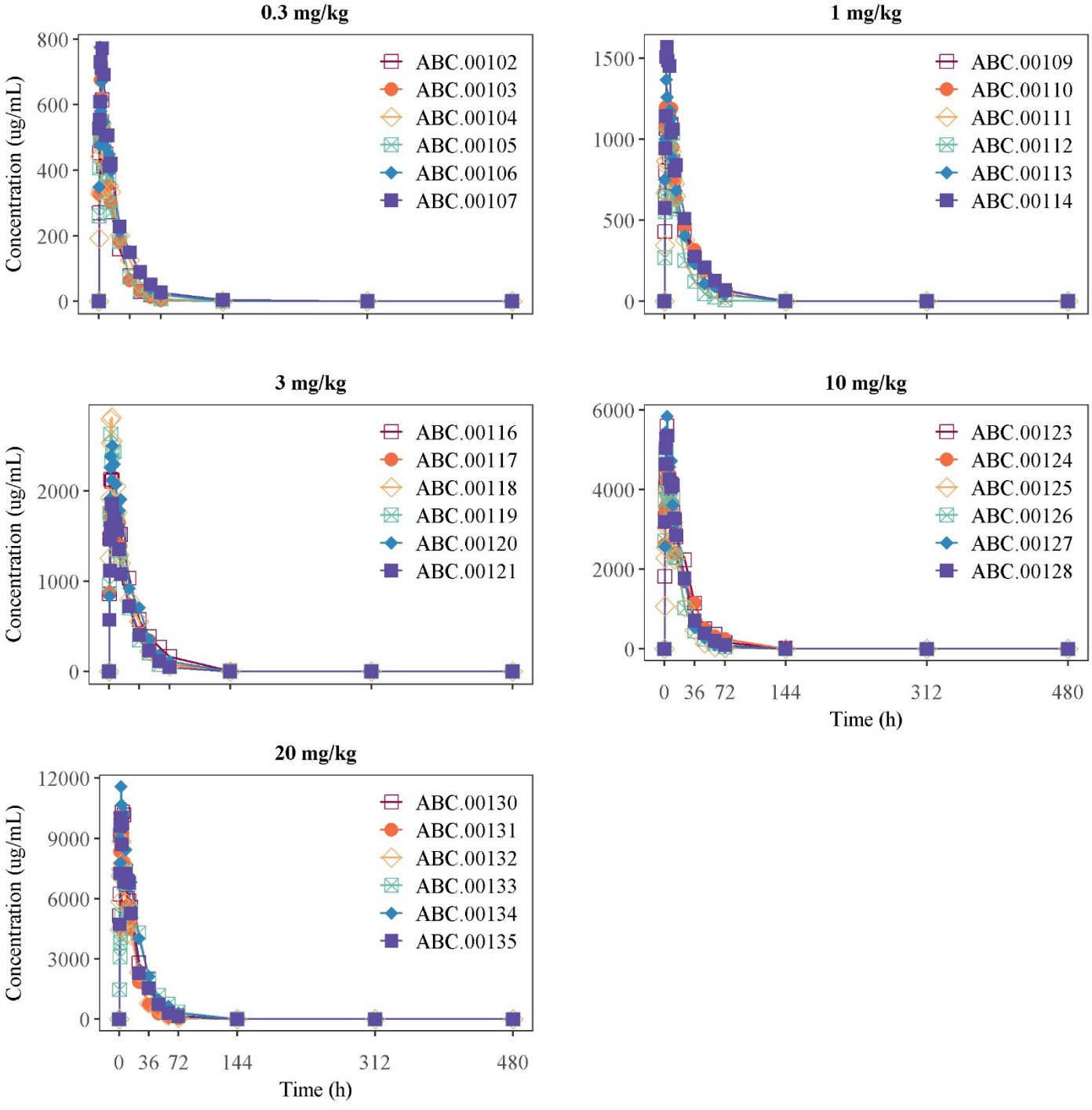


Figure 5: Semi-Log Individual SAR440894 Concentration in Plasma Profiles by Treatment Group, 0 h to 72 h Post Dose

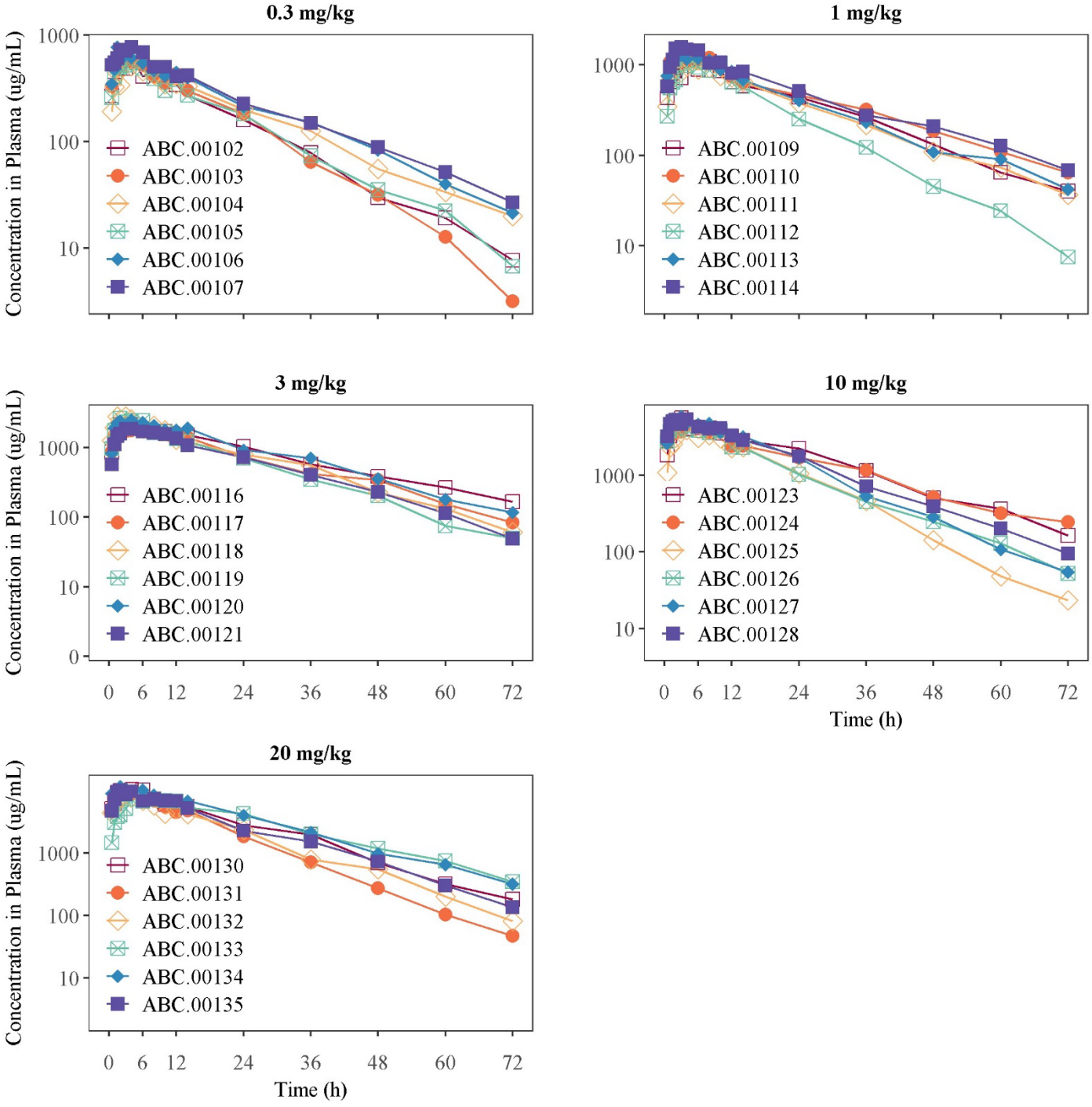


Figure 6: Semi-Log Individual SAR440894 Concentration in Plasma Profiles by Treatment Group, All Time Points Post Dose

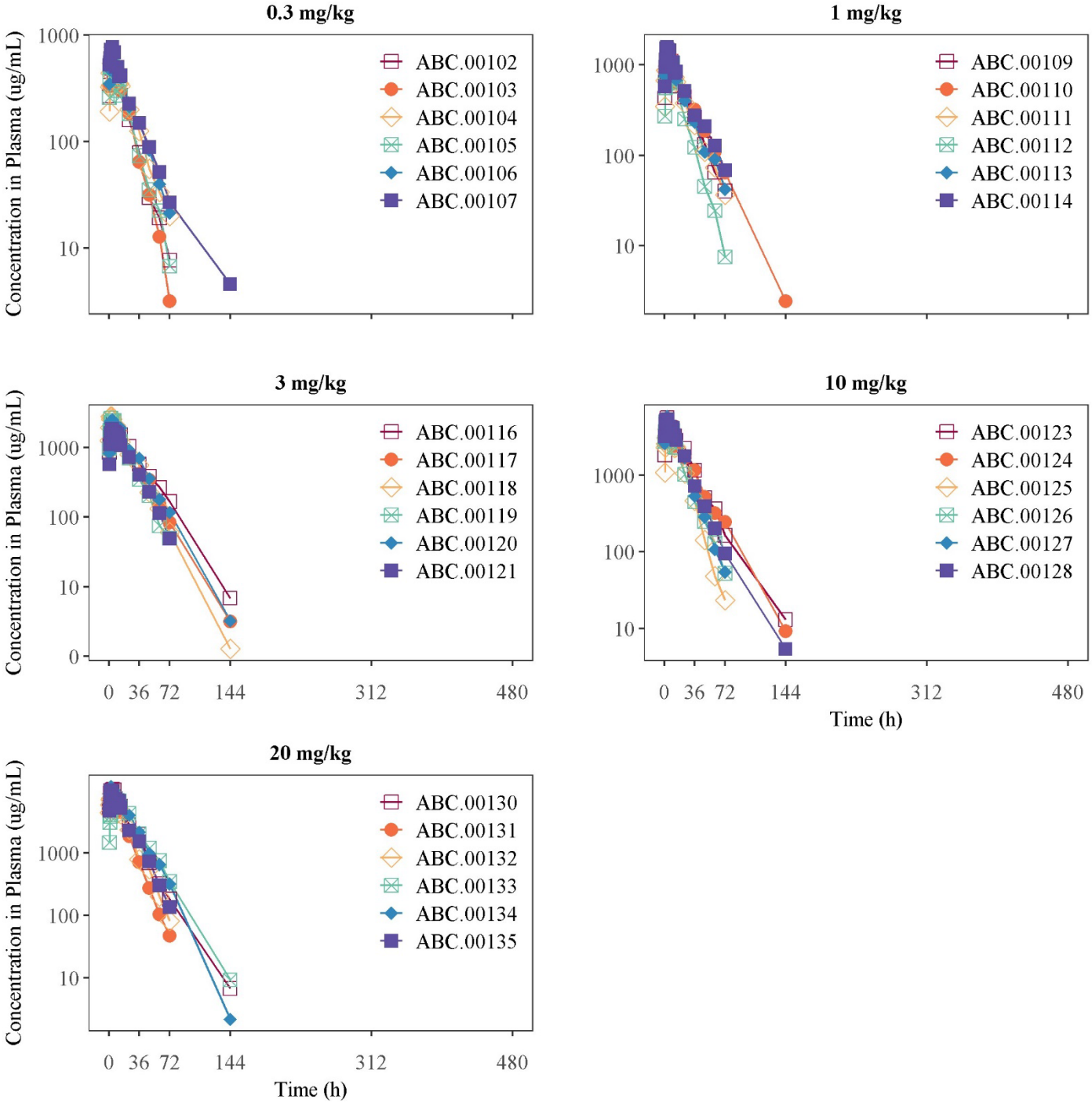


Figure 7: Mean SAR440894 Concentration in Plasma Profiles by Treatment Group, 0 h to 72 h Post Dose

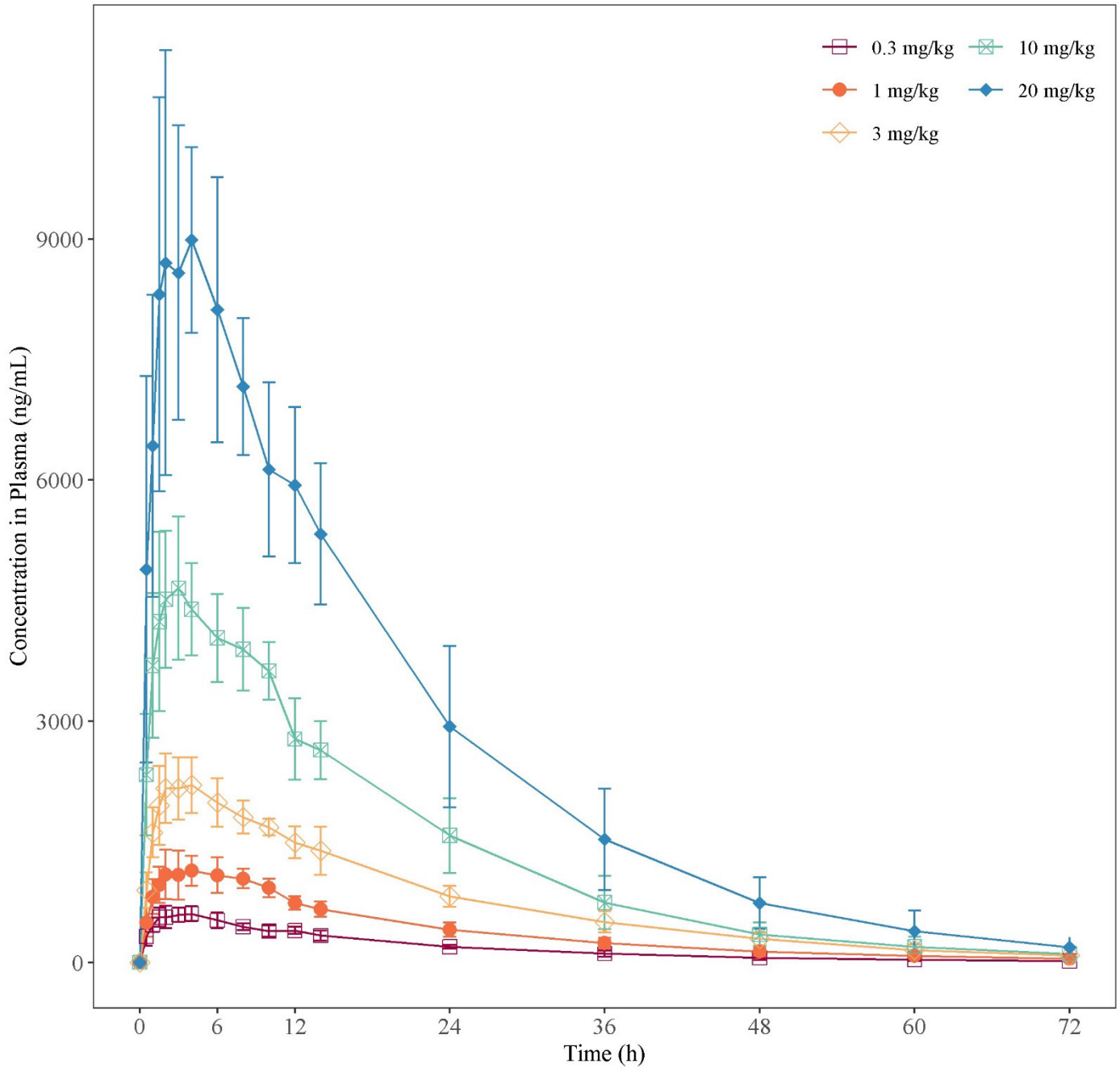


Figure 8: Mean SAR440894 Concentration in Plasma Profiles by Treatment Group, All Time Points Post Dose

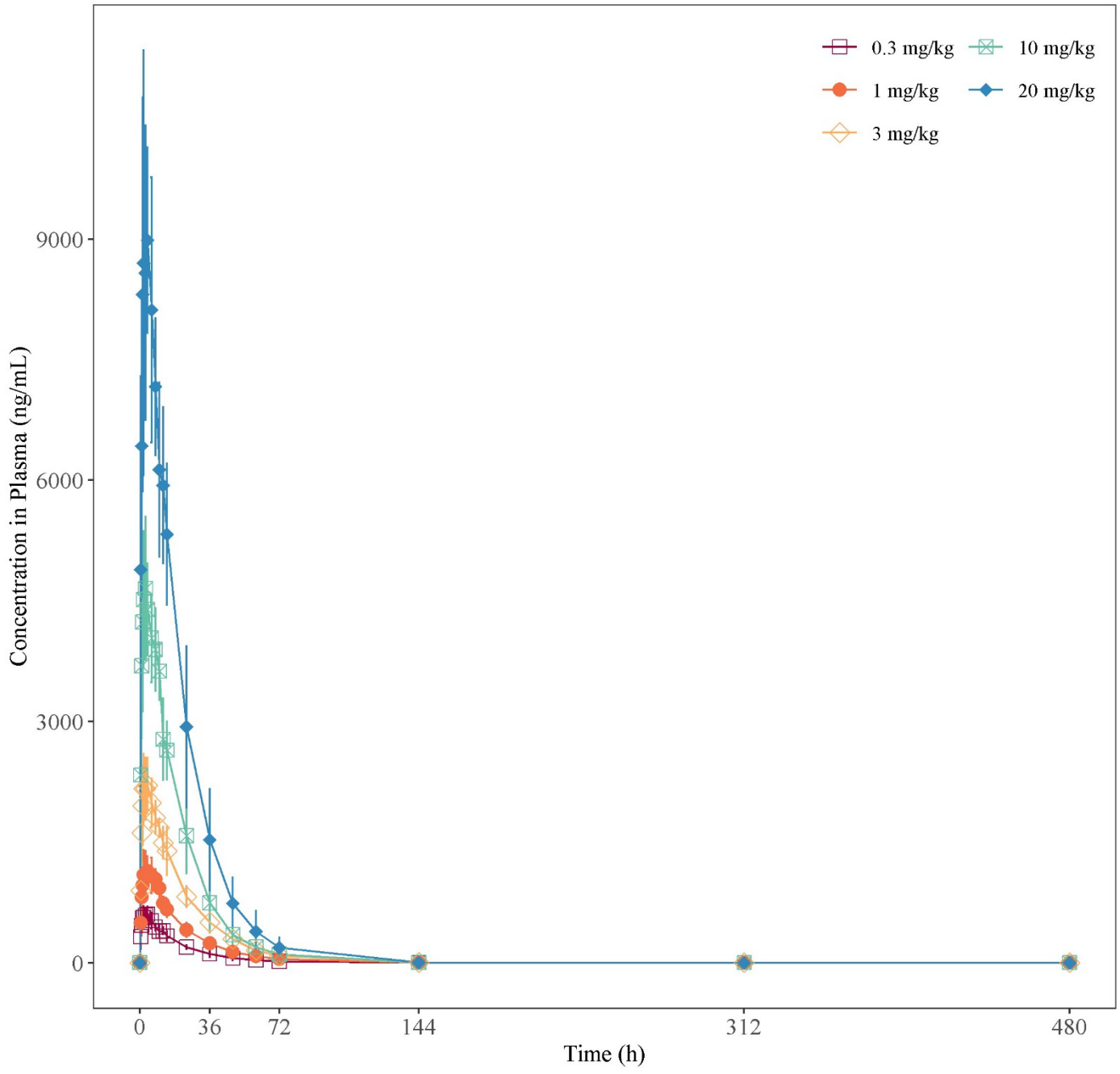


Figure 9: Mean Semi-Log SAR440894 Concentration in Plasma Profiles by Treatment Group, 0 h to 72 h Post Dose

[Implementation Note: Plot the mean and SD from Figure 7 on the log scale.]

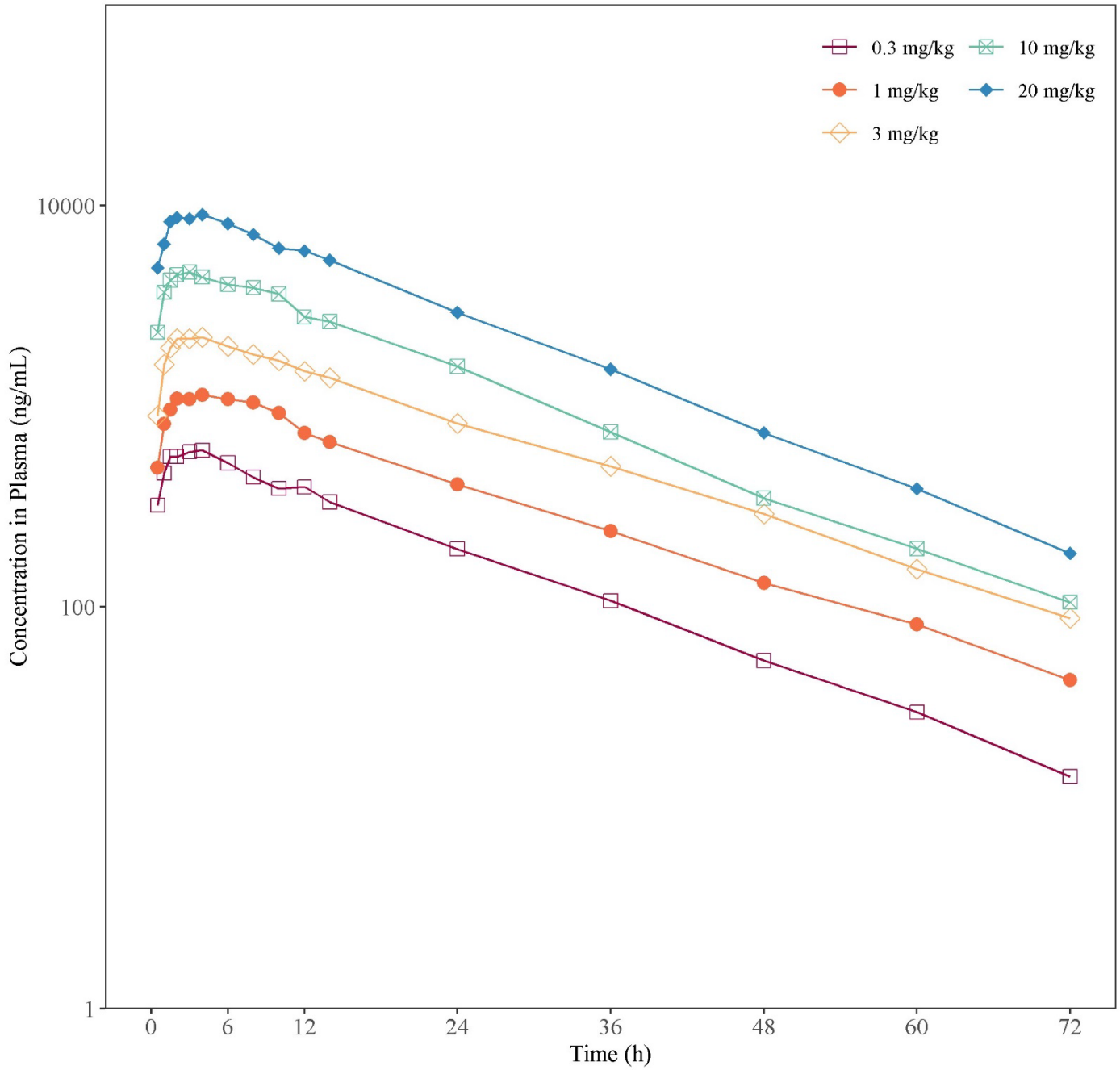
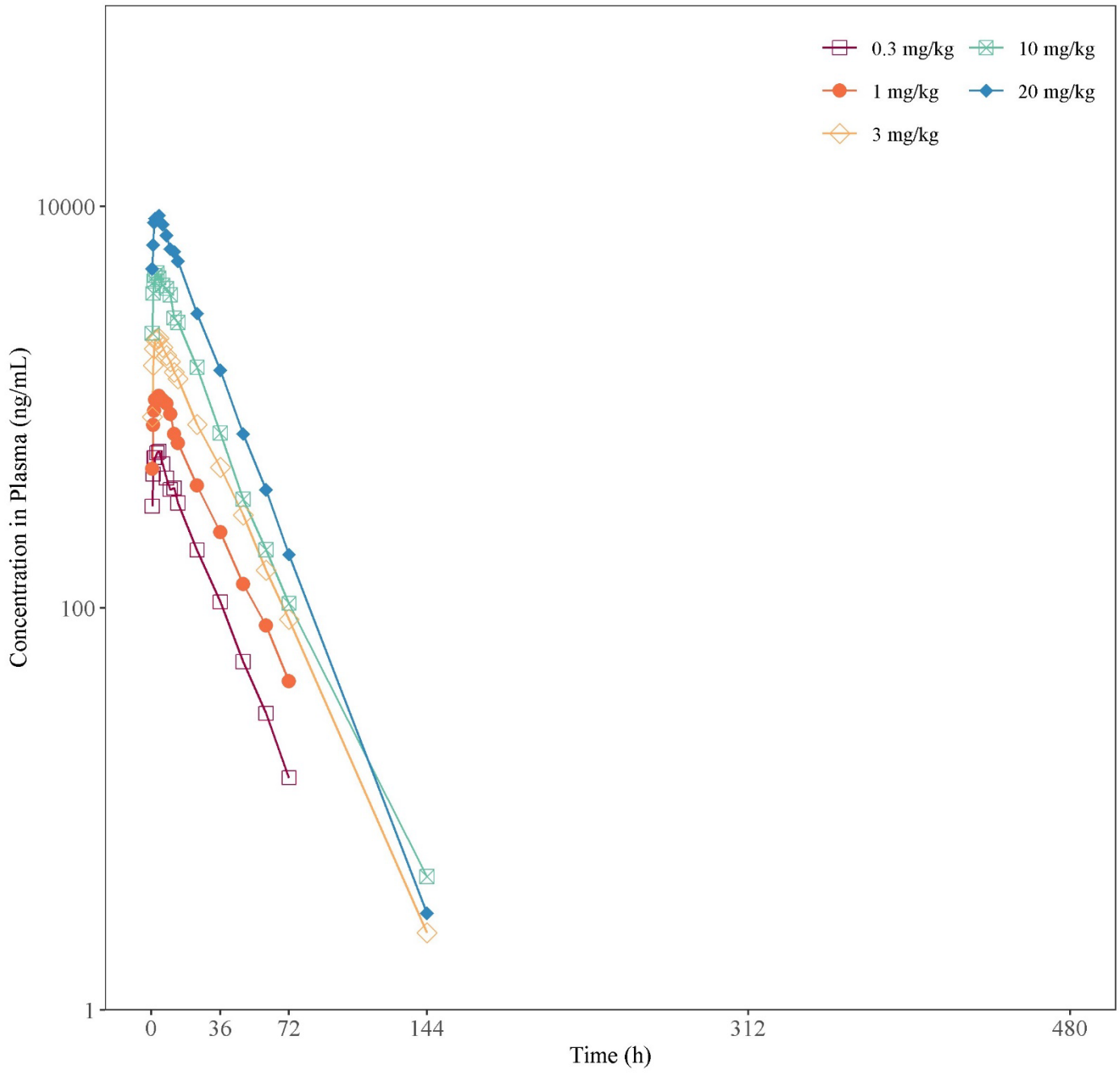


Figure 10: Mean Semi-Log SAR440894 Concentration in Plasma Profiles by Treatment Group, All Time Point Post Dose

[Implementation Note: Plot the mean and SD from Figure 8 on the log scale.]



14.2.3 Immunogenicity Response Figures by Measure, Treatment Group, and Time Point

Figure 11: Reverse Cumulative Distribution of ADA Titer by Time Point and Treatment Group – Immunogenicity Population

[Implementation Note: The following is just an example figure.]

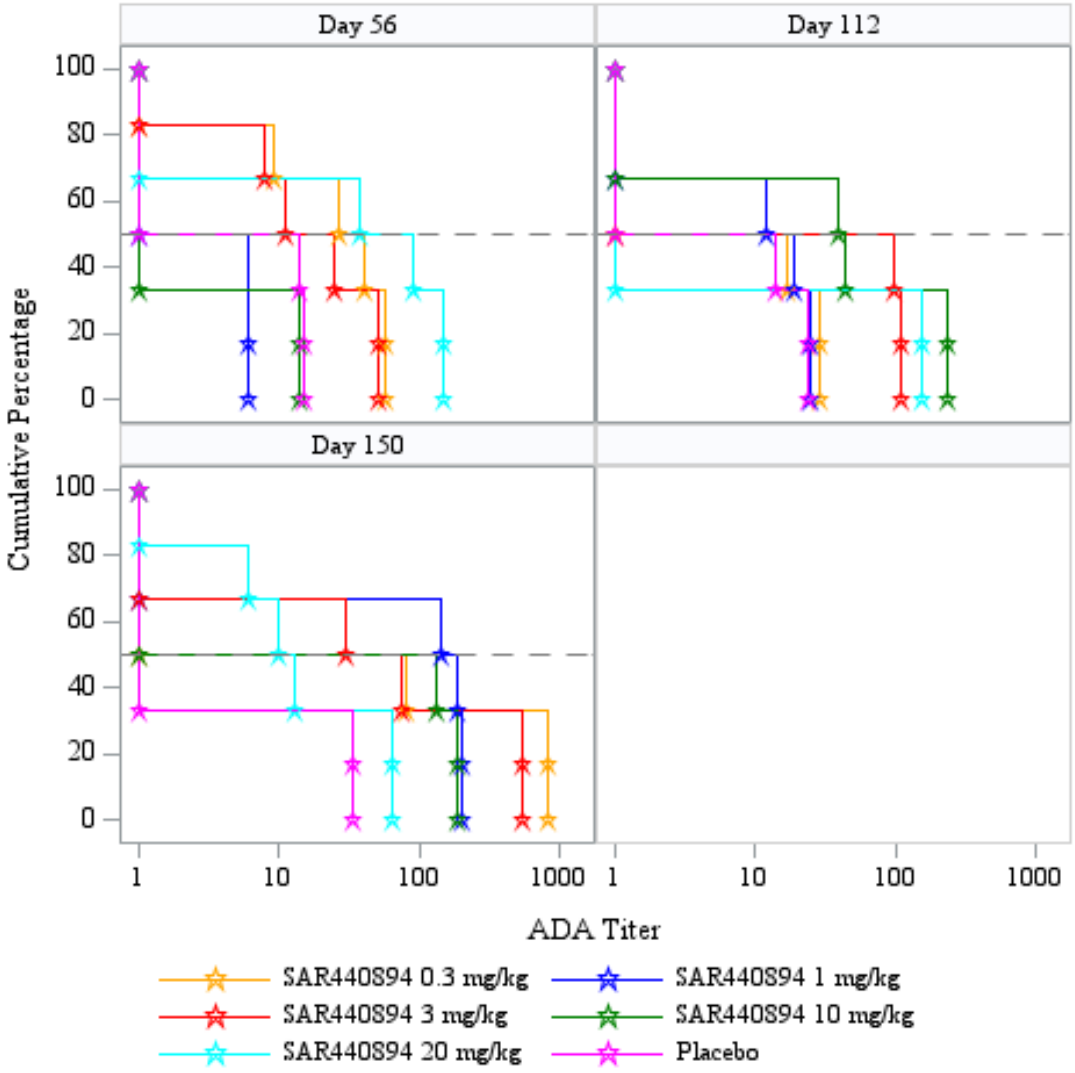
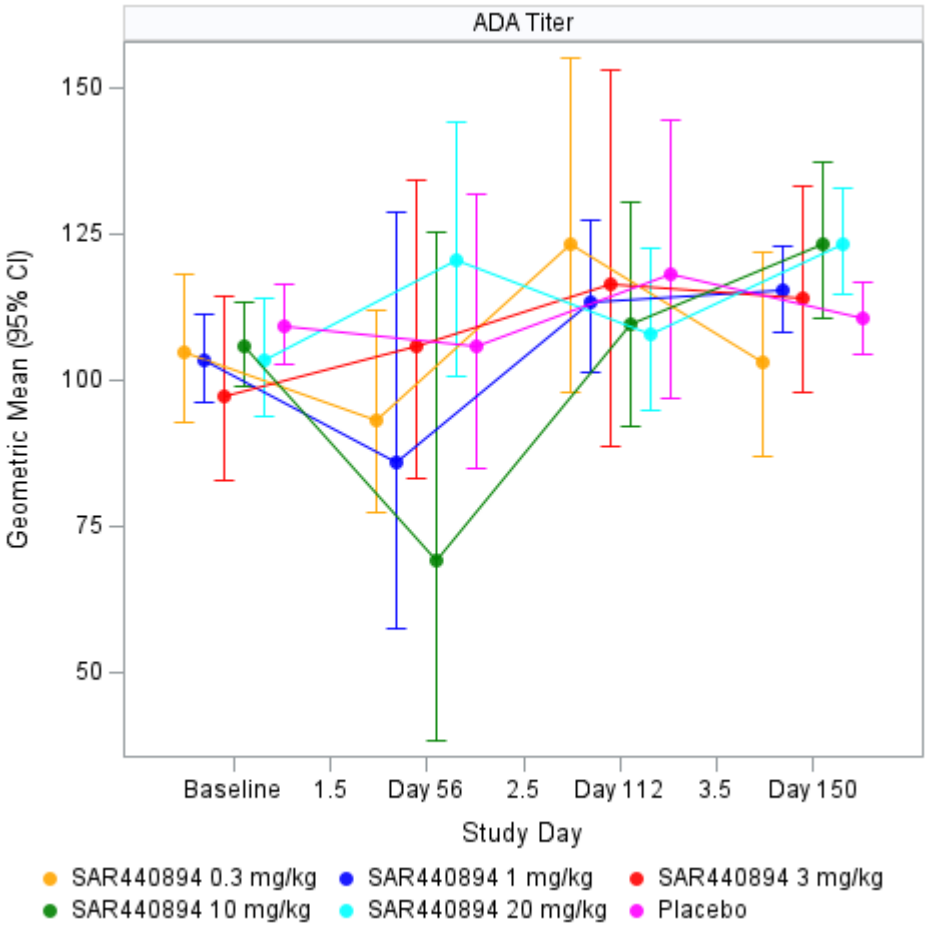


Figure 12: Geometric Mean ADA Titer by Time Point and Treatment Group – Immunogenicity Population

[Implementation Note: The following is just an example figure. The bars represent the lower and upper limits of the 95% confidence interval for the GMT.]



14.3.1.2 Unsolicited Adverse Events

Figure 13: Frequency of Related Adverse Events by MedDRA System Organ Class and Severity – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: This figure includes serious and non-serious unsolicited adverse events related to the study product. Note that this figure will present the number of events for each type of SOC.
There will be one panel for each of the following groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo.
Order SOCs alphabetically.]

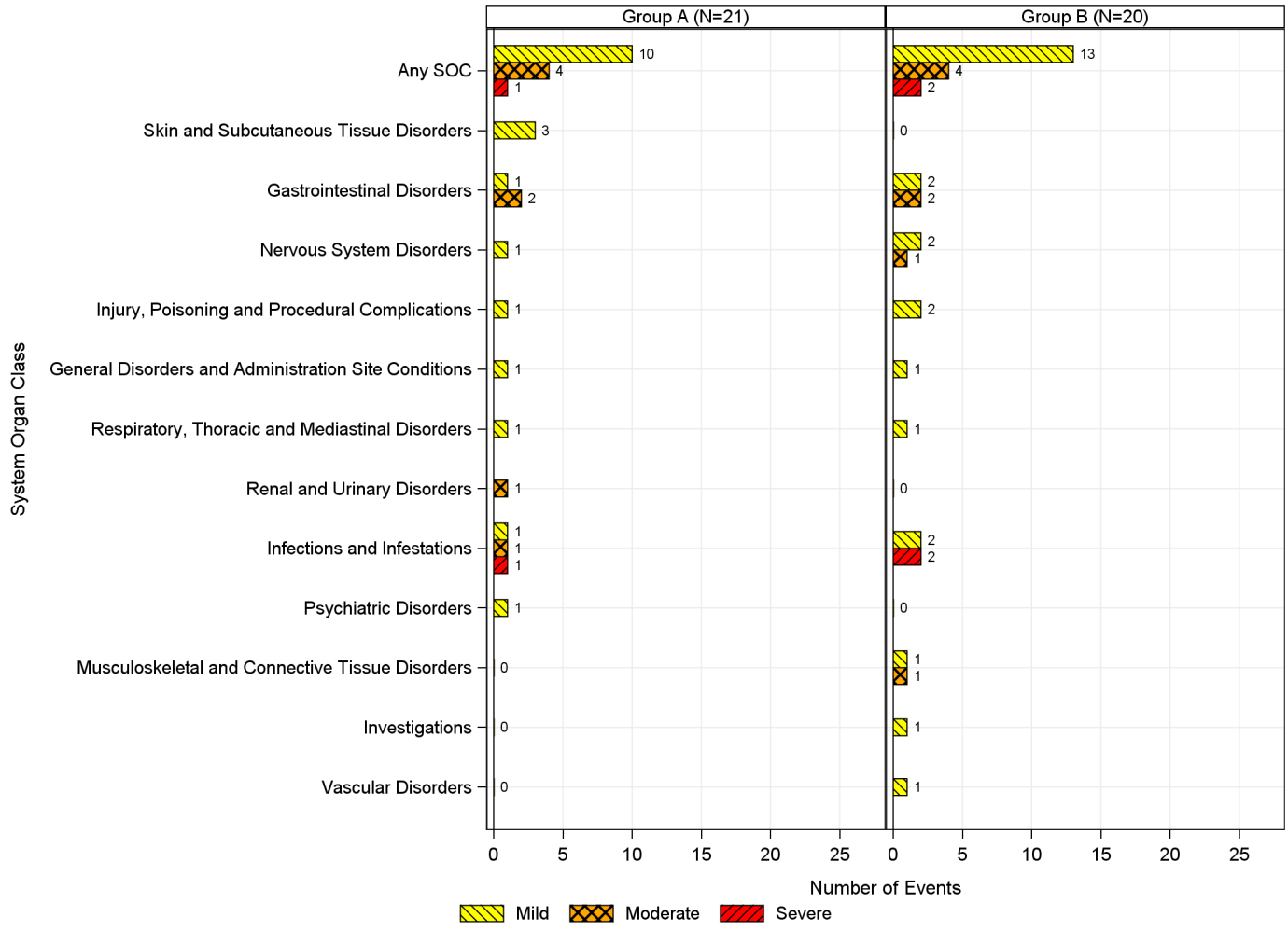


Figure with Similar Format:

Figure 14: Frequency of Related Adverse Events by MedDRA System Organ Class and Severity – Participants in the Safety Population Enrolled Under Protocol v11.0

Figure 15: Incidence of Related Adverse Events by MedDRA® System Organ Class and Maximum Severity – Participants in the Safety Population Enrolled Before Protocol v11.0

[Implementation Note: This figure includes serious and non-serious unsolicited adverse events related to the study product. Note that this figure will present the number of participants with each type of SOC. A participant will only be counted once for the same SOC for the maximum severity reported.
There will be one panel for each of the following groups: All Participants, SAR440894 0.3 mg/kg, SAR440894 1 mg/kg, SAR440894 3 mg/kg, SAR440894 10 mg/kg, SAR440894 20 mg/kg, and Placebo. Order SOCs alphabetically.]

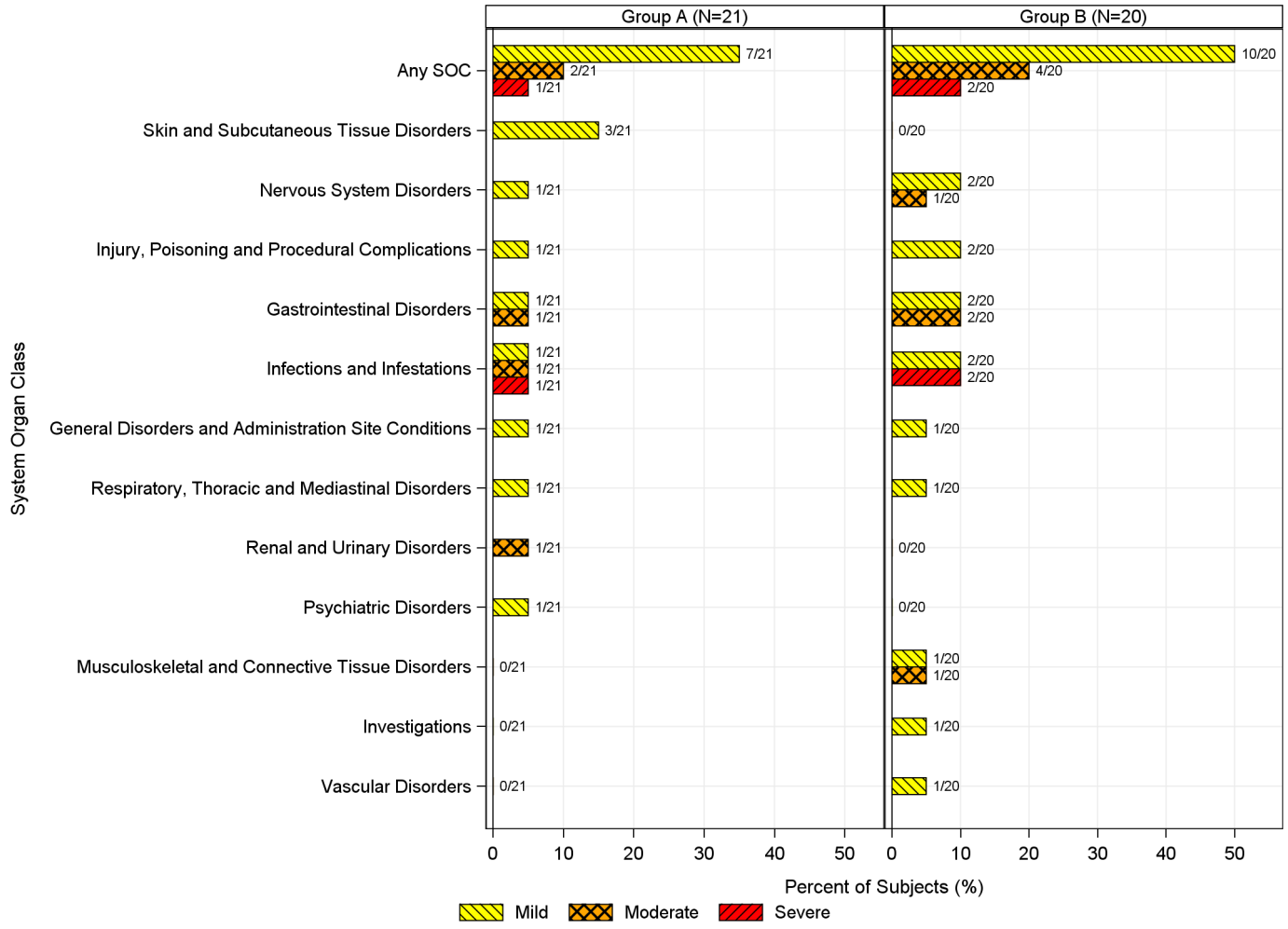


Figure with Similar Format:

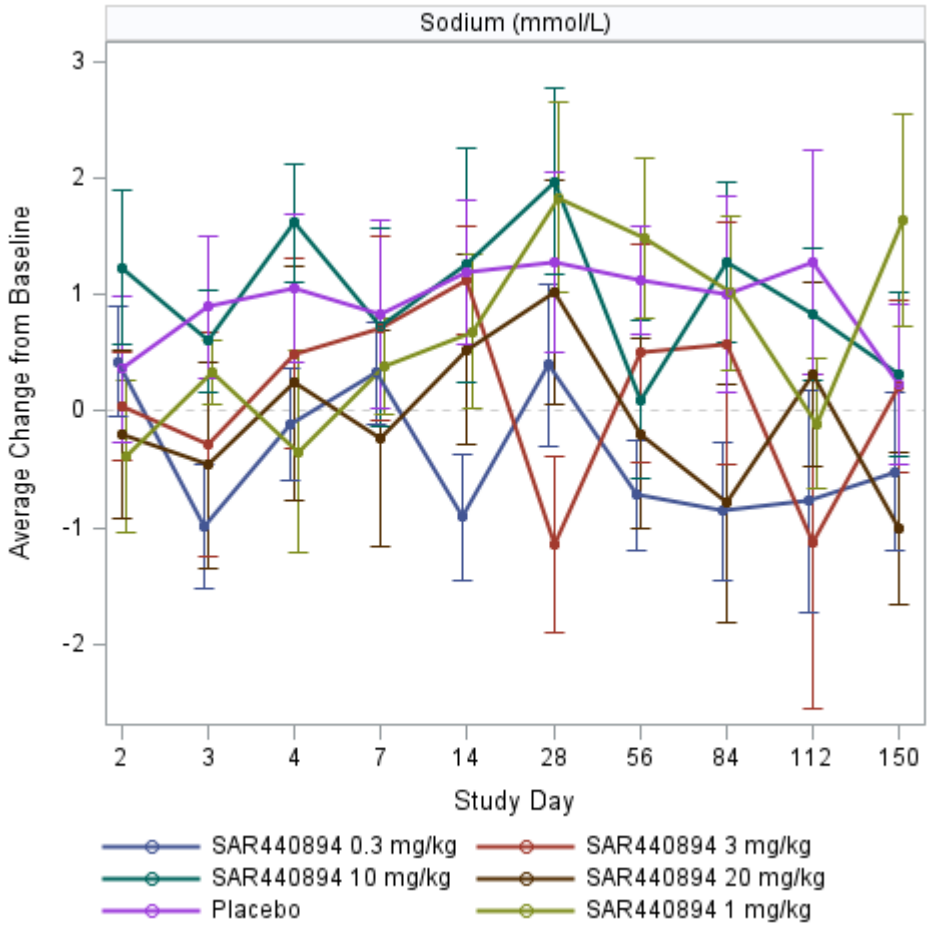
Figure 16: Incidence of Related Adverse Events by MedDRA® System Organ Class and Maximum Severity – Participants in the Safety Population Enrolled Under Protocol v11.0

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Figure 17: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Sodium

[Implementation Note: The figure below is an example. The bars represent the mean change from baseline ±1 SD at each visit.]



Figures with Similar Format:

Figure 18: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Potassium

Figure 19: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Bicarbonate

Figure 20: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Glucose

Figures with Similar Format *(continued)*:

Figure 21: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Blood Urea Nitrogen

Figure 22: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Creatinine

Figure 23: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – eGFR

Figure 24: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Calcium

Figure 25: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Albumin

Figure 26: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Total Protein

Figure 27: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Alkaline Phosphatase

Figure 28: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – AST

Figure 29: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – ALT

Figure 30: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Direct Bilirubin

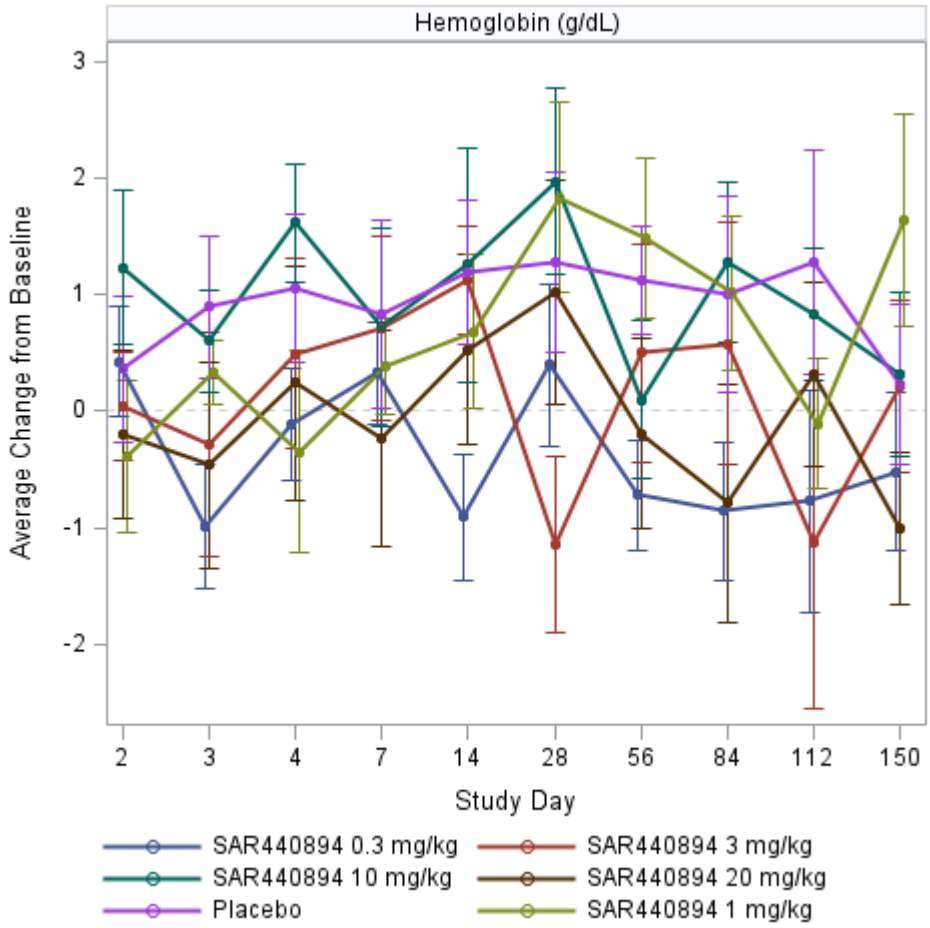
Figure 31: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Total Bilirubin

Figure 32: Chemistry Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Cystatin-C

14.3.5.2 Hematology Results

Figure 33: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Hemoglobin

[Implementation Note: The figure below is an example.]



The bars represent the mean change from baseline ±1 SD at each visit.

Figures with Similar Format:

Figure 34: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – WBC

Figure 35: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Neutrophils

Figure 36: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Eosinophils

Figure 37: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Platelets

Figures with Similar Format *(continued)*:

Figure 38: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Hematocrit

Figure 39: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – RBC

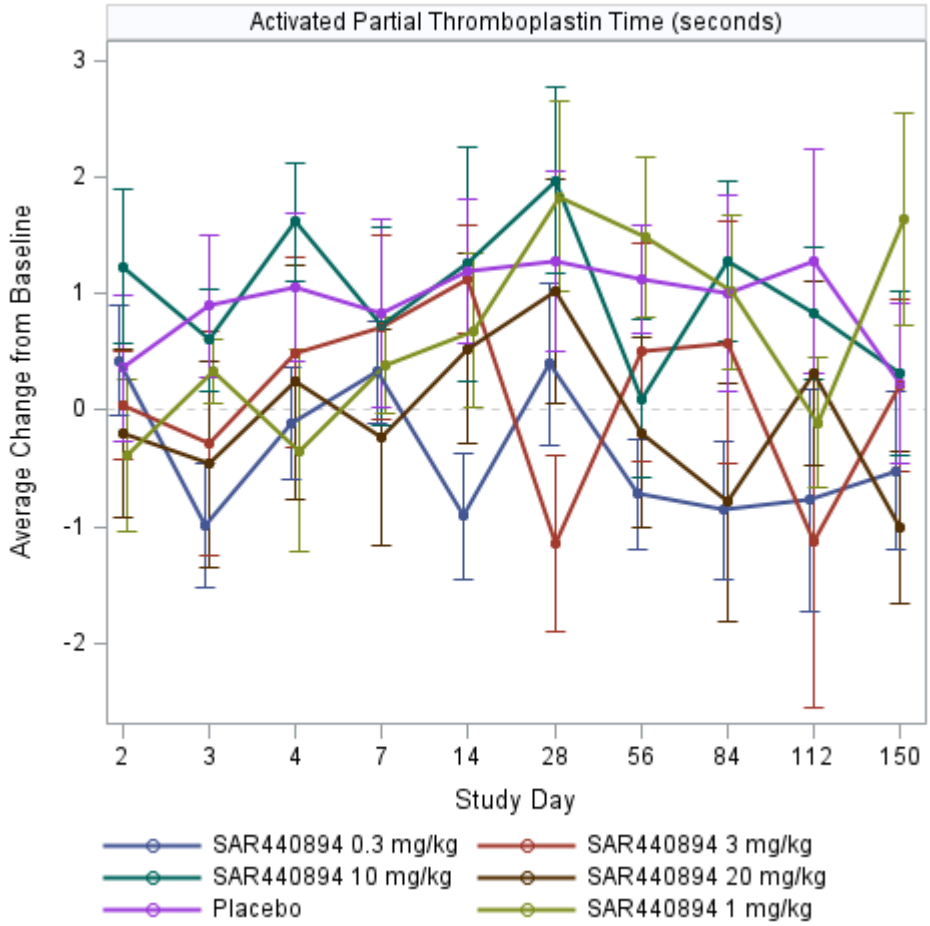
Figure 40: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Basophils

Figure 41: Hematology Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Monocytes

14.3.5.3 Coagulation Results

Figure 42: Coagulation Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – APTT

[Implementation Note: The figure below is an example. The bars represent the mean change from baseline ±1 SD at each visit.]



Figures with Similar Format:

Figure 43: Coagulation Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Prothrombin Time

Figure 44: Coagulation Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – INR

14.3.5.4 Urinalysis Results

Figure 45: Urinalysis Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Urine WBC

[Implementation Note: The figure below is an example. The bars represent the mean change from baseline ±1 SD at each visit.]

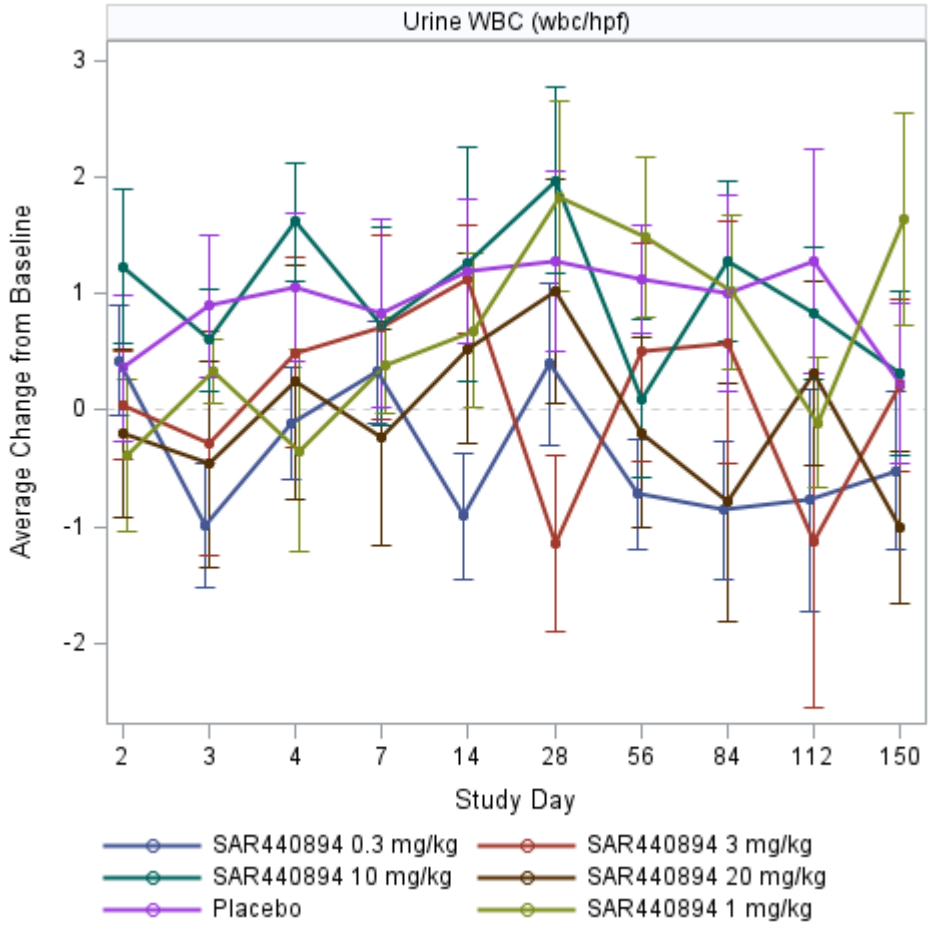


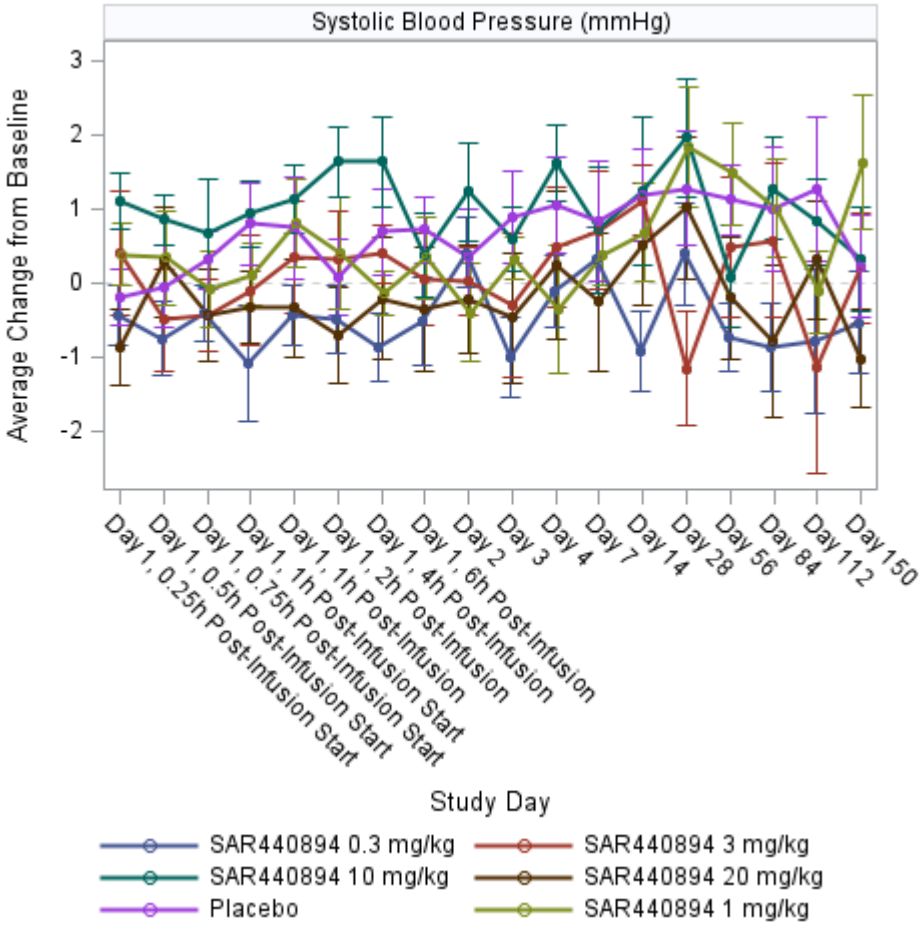
Figure with Similar Format:

Figure 46: Urinalysis Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Urobilinogen

14.3.6 Displays of Vital Signs Results

Figure 47: Vital Signs Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Systolic Blood Pressure

[Implementation Note: The figure below is an example. The bars represent the mean change from baseline ±1 SD at each visit. If points overlap in the plot, the jitter option will be applied.]



Figures with Similar Format:

Figure 48: Vital Signs Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Diastolic Blood Pressure

Figure 49: Vital Signs Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Heart Rate

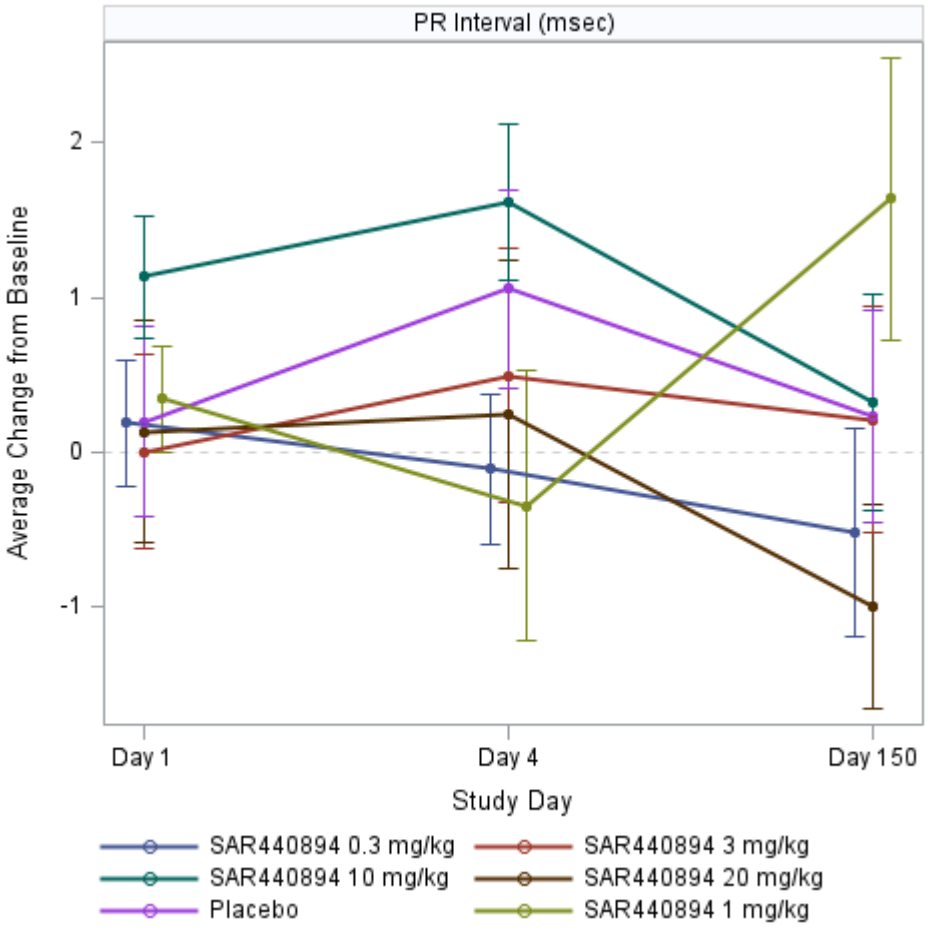
Figure 50: Vital Signs Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Respiratory Rate

Figure 51: Vital Signs Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Temperature

14.3.7 Displays of ECG Measurements

Figure 52: ECG Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – PR Interval (msec)

[Implementation Note: The figure below is an example. The bars represent the mean change from baseline ±1 SD at each visit. If points overlap in the plot, the jitter option will be applied.]



Figures with Similar Format:

Figure 53: ECG Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – QRS Duration (msec)

Figure 54: ECG Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – QT Interval (msec)

Figure 55: ECG Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – QTcF Correction (msec)

Figures with Similar Format *(continued)*:

Figure 56: ECG Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – RR Interval (msec)

Figure 57: ECG Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Ventricular Rate Interval (bpm)

APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

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Listing 1: **16.1.6: Listing of Subjects Receiving Investigational Product**

(not included in SAP, but this is a placeholder for the CSR)

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 2: 16.2.1: Early Terminations or Discontinued Participants

[Implementation Note: Sort order: Treatment Group, Participant ID, Category]

Treatment Group	Participant ID	Category	Reason for Early Termination or Treatment Discontinuation	Study Day

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1: Participant-Specific Protocol Deviations

[Implementation Note: Sort order: Treatment Group, Participant ID, DV Number]

Treatment Group	Participant ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	Deviation Resolution	Deviation Classification (Major/Minor)	Comments

Listing 4: 16.2.2.2: Non-Participant-Specific Protocol Deviations

[Implementation Note: Sort order: Site, Start Date, End Date, Deviation]

Site	Start Date	Deviation	End Date	Reason for Deviation	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	Deviation Category	Deviation Resolution	Deviation Classification (Major/Minor)	Comments

16.2.3 Subjects Excluded from the Efficacy Analysis

Listing 5: 16.2.3: Participants Excluded from Analysis Populations

[Implementation Note: Sort order: Treatment Group, Participant ID, Analyses from which Participant is Excluded (order: Safety, PK, Immunogenicity, PK-Immunogenicity Subset).]

Treatment Group	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
		[e.g., Safety, PK, Immunogenicity, PK-Immunogenicity Subset]	[e.g., Safety, PK, Immunogenicity, PK-Immunogenicity Subset]		
Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.					

16.2.4 Demographic Data

Listing 6: 16.2.4.1: Demographic Data

[Implementation Note: Sort order: Treatment Group, Participant ID]

Treatment Group	Participant ID	Sex	Ethnicity	Race	Age at Enrollment (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)

Listing 7: 16.2.4.2: Pre-Existing and Concurrent Medical Conditions

[Implementation Note: "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). Rather than use exact study days, categorize as follows:

- 5 years prior to enrollment
- 1-5 years prior to enrollment
- 1-12 months prior to enrollment
- Within 1 month of enrollment
- During study
- If ongoing, display "Ongoing" in the "Condition End Day" column
- Sort order: Treatment Group, Participant ID, MH Number.]

Treatment Group	Participant ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

16.2.5 Compliance and/or Drug Concentration Data (if available)

Listing 8: 16.2.5: Compliance Data

[Implementation Note: Sort order: Treatment Group, Participant ID, Infusion Start Date, Infusion Start Time]

Treatment Group	Participant ID	Planned Volume	Planned Volume Administered?	Actual Volume Administered	Infusion Start Date	Infusion Start Time	Infusion End Time	Infusion Interrupted?

Listing 9: 16.2.5: Infusion Interruptions

[Implementation Note: Sort order: Treatment Group, Participant ID, Interruption Number]

Treatment Group	Participant ID	Interruption Number	Reason Infusion Interrupted	Infusion Restarted?	Duration of Interruption	Comments

16.2.6 Individual PK Concentrations and Immunogenicity Response Data

Listing 10: Participant Level SAR440894 Plasma Concentrations

[Implementation Note: Units of nominal time and actual time point vary by time point and will be provided for each time rather than in the column heading. Laboratory Reported Concentration will give verbatim value reported by lab (with minimal formatting, as needed) and will use a character value such as PC.PCORRES. Analysis Concentration will report the value actually used for analysis and will use a numeric variable such as ADNCA.AVAL. If one or more samples are excluded from NCA, two additional columns will be provided in the PK report listing: Excluded from NCA (Yes/No) and Reason for Exclusion from NCA.

In the actual time column, mark out of window times with one asterisk (*), mark substantially out of window times with two asterisks (**), and mark imputed times with three asterisks (***).

Sort order: Treatment Group, Participant ID, Actual Time.]

Treatment Group	Participant ID	Nominal Time[a]	Actual Time[a]	Laboratory Reported Concentrations (µg/mL)	Analysis Concentrations (µg/mL)	Used in λz Calculations

[a] Times are relative to time of dosing. For actual time, out of window times are indicated by an asterisk (*), substantially out of window times are indicated by two asterisks (**) and imputed times are indicated by three asterisks (***).

Listing 11: 16.2.6: Participant Level SAR440894 PK Parameters Concentrations

[Implementation Note: Sort order: Treatment Group, Participant ID.]

Treatment Group	Participant ID	C_{max} (µg/mL)	T_{max} (h)	C_{mein} (µg/mL)	$AUC_{(0\text{-}last)}$ (µg*h/mL)	$AUC_{(0\text{-}inf)}$ (µg*h/mL)	λz (1/h)	$t_{1/2}$ (h)	CL (L/h/kg)	V_d (L/kg)

Listing 12: 16.2.6: Individual Immunogenicity Response Data

[Implementation Note: Sort order: Treatment Group, Participant ID, and Planned Time Point]

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	ADA Result	ADA Titer
SAR440894 0.3 mg/kg	PH2.00100	Baseline	1	Negative	0
SAR440894 0.3 mg/kg	PH2.00100	Day 56	57	Positive	40

16.2.7 Adverse Events

Listing 13: 16.2.7.3: Unsolicited Adverse Events – Participants in the Safety Population Enrolled Prior to Protocol v11.0

[Implementation Note: Sort order: Treatment Group, Participant ID, and AE Number]

Adverse Event	No. of Days Post Dose (Duration)	Severity	SAE?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA High Level Group Term	MedDRA Preferred Term
Treatment Group: , Participant ID: , AE Number:											
Comments:											
Treatment Group: , Participant ID: , AE Number:											
Comments:											
Note: For additional details about SAEs, see Section 14.3.2.											

Listings with Similar Format:

Listing 14: 16.2.7.3: Unsolicited Adverse Events – Participants in the Safety Population Enrolled Under Protocol v11.0

16.2.8 Individual Laboratory Measurements

Listing 15: 16.2.8.1: Clinical Laboratory Results – Chemistry

[Implementation Note: Sort order: Treatment Group, Participant ID, Planned Time Point, Laboratory Parameter]

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Clinically Significant?	Reference Range Low	Reference Range High	Change from Baseline

Listing 16: 16.2.8.2: Clinical Laboratory Results – Hematology

[Implementation Note: Sort order: Treatment Group, Participant ID, Planned Time Point, Laboratory Parameter]

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Clinically Significant?	Reference Range Low	Reference Range High	Change from Baseline

Listing 17: 16.2.8.3: Clinical Laboratory Results – Coagulation

[Implementation Note: Sort order: Treatment Group, Participant ID, Planned Time Point, Laboratory Parameter]

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Clinically Significant?	Reference Range Low	Reference Range High	Change from Baseline

Listing 18: 16.2.8.3: Clinical Laboratory Results – Urinalysis

[Implementation Note: Sort order: Treatment Group, Participant ID, Planned Time Point, Laboratory Parameter]

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Clinically Significant?	Reference Range Low	Reference Range High	Change from Baseline

Listing 19: 16.2.8.4: Screening Laboratory Results – Serology

[Implementation Note: If there are serology results on an Unscheduled visit, then the Study Day will be included in parentheses for the Visit.

Sort Order: Treatment Group, Participant ID, Visit (visit order: Screening, Admission, Unscheduled).]

Treatment Group	Participant ID	Visit	Hepatitis B Surface Antigens	Hepatitis C Antibodies	HIV Antibodies	CHIKV Antibodies
SAR440894 0.3 mg/kg	PH2.00101	Screening	Negative	Negative	Negative	Negative
SAR440894 0.3 mg/kg	PH2.00101	Unscheduled (Day 3)	Negative	Negative	Negative	Negative
Note: ND = Test Not Done.						

Listing 20: 16.2.8.4: Screening Laboratory Results – Serum ß-hCG and Serum FSH Tests

[Implementation Note: If there are results for serum hCG on an Unscheduled visit, then the Study Day will be included in parentheses for the Visit. Type of hCG test will be given in parentheses after the hCG result, e.g..., Negative (serum) or Negative (urine). If obtained, FSH testing results will be shown in this listing.

Sort Order: Treatment Group, Participant ID, Visit (visit order: Screening, Admission, Unscheduled).]

Treatment Group	Participant ID	Visit	hCG Result	FSH Result
SAR440894 0.3 mg/kg	PH2.00101	Screening	Negative (serum)	ND
SAR440894 0.3 mg/kg	PH2.00101	Admission	Negative (urine)	ND
Note: ND = Test Not Done				

Listing 21: 16.2.8.4: Screening Laboratory Results – Urine Toxicology

[Implementation Note: If there are results for urine toxicology on an Unscheduled visit, then the Study Day will be included in parentheses for the Visit.

Sort Order: Treatment Group, Participant ID, Visit (visit order: Screening, Admission, Unscheduled).]

Treatment Group	Participant ID	Visit	Cannabinoids	Amphetamines	Barbiturates	Cocaine	Opiates	Benzodiazepines	Phencyclidine	Cotinine	Methadone	Alcohol
SAR440894 0.3 mg/kg	PH2.00101	Screening	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
SAR440894 0.3 mg/kg	PH2.00101	Admission	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Note: ND = Test Not Done.												

16.2.9 Vital Signs and Physical Exam Findings

Listing 22: 16.2.9.1: Vital Signs

[Implementation Note: This listing includes all vital sign assessments, scheduled and unscheduled. All height, weight, and BMI measurements will also be included in this listing. These listings are not color-coded, but the severity should be included in parentheses after the result for abnormal assessments, e.g., 100.7 (Mild).

Sort order: Treatment group, participant ID, parameter (Order: height, weight, BMI, systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, temperature), planned time point, actual study day, time of assessment]

Treatment Group	Participant ID	Parameter	Planned Time Point	Actual Study Day	Time of Assessment	Result (Severity)	Change from Baseline
					hh:mm		

Listing 23: 16.2.9.2: Physical Exam Findings

[Implementation Note: This listing includes all physical exam findings, scheduled and unscheduled. If a participant does not have any findings upon examination, they will not be included in this listing. If reported as an AE, display "Yes" with the AE description and number in parentheses, e.g., "Yes (AE Description; 007)".

Sort order: Treatment Group, Participant ID, Planned Time Point, Date of Assessment, Time of Assessment, Body System, and Finding.]

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	Time of Assessment	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)

Listing 24: 16.2.9.3: Listing of ECG Interval Measurements

[Implementation Note: This listing includes all ECG assessments, scheduled and unscheduled. For the mean of triplicate readings, no assessment time should be presented and the replicate number should specify "Mean".

Sort order: Treatment Group, Participant ID, Parameter (Order: PR interval, QRS duration, QT interval, QTcF correction, RR interval, ventricular rate), Date of Assessment, Time of Assessment.]

Treatment Group	Participant ID	Sex	Parameter	Time Point	Assessment Date	Assessment Time	Result	Change from Baseline	Replicate Number
SAR440894 0.3 mg/kg	PH2.00100	Male	PR Interval	Screening	ddMMMyyy	hh:mm	210	-	1
SAR440894 0.3 mg/kg	PH2.00100	Male	PR Interval	Baseline	ddMMMyyy	hh:mm	220	-	1
SAR440894 0.3 mg/kg	PH2.00100	Male	PR Interval	Day 1	ddMMMyyy	hh:mm	250	30	1

Listing 25: 16.2.9.3: Listing of ECG Overall Interpretation and Comments

[Implementation Note: This listing includes all ECG assessments, scheduled and unscheduled.

Sort order: Treatment Group, Participant ID, Time Point, Date of Assessment.]

Treatment Group	Participant ID	Sex	Time Point	Assessment Date	Interpretation	Change from Baseline	Comments
SAR440894 0.3 mg/kg	PH2.00100	Male	Screening	ddMMMyyy	Abnormal NCS	-	Sinus Bradycardia
SAR440894 0.3 mg/kg	PH2.00100	Male	Baseline	ddMMMyyy	Abnormal NCS	-	Sinus Bradycardia
SAR440894 0.3 mg/kg	PH2.00100	Male	Day 1	ddMMMyyy	Abnormal NCS	NCB	Sinus Bradycardia

Notes: NCB= No change from baseline. NNSB= Normal to not clinically significant, change from baseline. NCSB= Normal to clinically significant, change from baseline. NSNB= Not clinically significant to normal, change from baseline. NSCSB= Not clinically significant to clinically significant, change from baseline.

Listing 26: 16.2.9.3: Listing of ECG Abnormal Findings

[Implementation Note: This listing includes all abnormal ECG assessments, scheduled and unscheduled. List all abnormal findings as reported on the ECG form separated by a ";".

Sort order: Treatment Group, Participant ID, Time Point.]

Treatment Group	Participant ID	Sex	Time Point	Abnormal Finding(s)
SAR440894 0.3 mg/kg	PH2.00100	Male	Screening	Sinus bradycardia
SAR440894 0.3 mg/kg	PH2.00100	Male	Baseline	Sinus bradycardia; Right axis deviation
SAR440894 0.3 mg/kg	PH2.00100	Male	Day 1	Sinus bradycardia

16.2.10 Concomitant Medications

Listing 27: 16.2.10: Concomitant Medications

[Implementation Note: "Medication Start Day" and "Medication End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). For medication start dates that are >30 days prior to enrollment, rather than use exact study days, categorize as follows:

- 5 years prior to enrollment
- 1-5 years prior to enrollment
- 1-12 months prior to enrollment

If ongoing, display "Ongoing" in the "Medication End Day" column. If taken for an AE or MH, display "Yes" with the AE or MH Number in parentheses, e.g., "Yes (&)". In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification.

Sort order: Treatment Group, Participant ID, MH Number.]

Sort order: Treatment Group, Participant ID, CM Number]

Treatment Group	Participant ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

16.2.11 Pregnancy Reports

Listing 28: 16.2.11.1: Pregnancy Reports – Maternal Information

[Implementation Note: Sort order: Treatment Group, Participant ID, Pregnancy Number]

Treatment Group	Participant ID	Pregnancy Number	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?
Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.											

Listing 29: 16.2.11.2: Pregnancy Reports – Gravida and Para

[Implementation Note: Sort order: Participant ID, Pregnancy Number]

			Live Births												
Participant ID	Pregnancy Number	Gravida	Extremely PB[a]	Very Early PB[a]	Early PB[a]	Late PB[a]	Early TB[b]	Full TB[b]	Late TB[b]	Post TB[b]	Still Births	Spontaneous Abortion/ Miscarriage	Elective Abortions	Therapeutic Abortions	Major Congenital Anomaly with Previous Pregnancy?
Note: Gravida includes the current pregnancy, para events do not.															

[a] Preterm Birth
[b] Term Birth

Listing 30: 16.2.11.3: Pregnancy Reports – Live Birth Outcomes

[Implementation Note: Sort order: Participant ID, Pregnancy Number, Fetus Number]

Participant ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?
Note: Congenital Anomalies are included in the Adverse Event listing.												

Listing 31: 16.2.11.4: Pregnancy Reports – Still Birth Outcomes

[Implementation Note:

Sort order: Participant ID, Fetus Number]

Participant ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 32: 16.2.11.5: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

[Implementation Note:

Sort order: Participant ID, Fetus Number]

Participant ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion

APPENDIX 4. MAJOR PROTOCOL DEVIATION EXAMPLES

Protocol Deviation	Deviation Category	Example Deviations
Enrollment		
Did not meet inclusion criterion	Eligibility/enrollment	- Subject enrolled and did not meet inclusion criteria.
Met exclusion criterion	Eligibility/enrollment	- One or more of the exclusion criteria were met before subject randomization or enrollment for treatment. - Subject met one or more exclusion criteria and received study agent.
Participant inappropriately randomized/registered	Eligibility/enrollment	- Study agent was administered prior to confirming all eligibility criteria was met (e.g. laboratory results not received prior to randomization). - Failure to complete all assessments for randomization/registration (i.e. vital signs check, clinical lab assessment, or negative results needed prior to randomization).
Informed Consent		
Incorrect version of ICF	Informed consent	- Incorrect or incomplete version of informed consent used.
ICF not signed prior to study procedures	Informed consent	- Informed consent not obtained. - Informed consent not obtained prior to the start of study activities. - Informed consent not dated on the signature page.
Unapproved consent/reconsent method used	Informed consent	- Conducting the consent process via methods not approved by the IRB (e.g. telephone or electronic consent). - Reconsent did not occur according to the IRB approval letter (i.e., at the next visit or by X date).
Protocol Procedures		
Conduct of non-protocol procedure	Protocol procedure/ assessment	- Performing a study procedure not approved by IRB, the protocol/not included in the protocol/informed consent (e.g. performing an HIV test not listed in the protocol, collection of additional blood, providing participants with unapproved questionnaire or diary card).
Conduct of non-protocol procedure with increased risk	Safety	- Performing a procedure that put the participant at increased risk of harm (e.g. blood collection over the institutional safety limits, blood collection on a day not required by protocol resulting in an additional stick).
Regulatory		
Other	Administrative/regulatory	- Lapse in IRB/EC approval. - Lapse of approval by regulatory agency.
Safety		
AE/SAE/UP or other safety event not reported per protocol	Safety	- SAE/UP not reported per protocol to Sponsor, IRB and/or entered into the eCRF according to the protocol/MOP. - Unreported safety event related to halting not entered in eCRFs in the timelines per the MOP or protocol.
Required procedure not conducted	Safety	- Failure to perform a required clinical lab test, procedure, or assessment that may affect subject safety because a safety parameter was not collected therefore cannot be assessed. - Failure to complete and/or review the results of any discharge assessments per protocol prior to discharge (i.e., vital signs check,
Safety lab not collected	Safety	
Other specimen not collected	Safety	

Protocol Deviation	Deviation Category	Example Deviations
		clinical lab assessment, or negative results needed prior to release of quarantine).
Study Product		
Study product temperature excursion	Product storage	- Storage conditions depart from requirements per protocol/IB, and may have compromised product stability. (Excursion not identified/reported to the Sponsor by site prior to site monitor identification).
Improper study agent accountability	Product storage	- Missing or unaccounted study product.
Incorrect dosing/study product administration	Product administration	- Incorrect treatment assignment. - Incorrect study product dispensed/ administered. - Incorrect dose dispensed/administered. - Study product administered to incorrect participant.
Delayed study product administration	Product administration	- Study product was administered out of protocol defined window for administration.
Study product inappropriately unblinded	Blinding policy/procedure	- Participant/study unblinded without adhering to the protocol or MOP unblinding procedures.
Missed study product administration	Product administration	- Participant attends visit but does not get treatment for reasons other than the subject declined or it was held for safety reasons.
Research Laboratory		
Specimen temperature excursion	Laboratory/specimen	- Storage conditions depart from requirements per protocol/MOP and specimen stability may be compromised. (Excursion not identified by site prior to site monitor identification).
Research lab not collected	Laboratory/specimen	- Samples required by protocol for the primary endpoint (or main lab-based endpoint) are not obtained.
Other specimen not collected	Laboratory/specimen	
Too few aliquots obtained	Laboratory/specimen	
Specimen result not obtained	Laboratory/specimen	
Specimen processing not conducted correctly	Laboratory/specimen	