Statistical Analysis Plan Cover Page

Study Official Title: A Phase 1a Randomized, Double-blind, Placebo-controlled, Single Site, Single Ascending Dose Study of the Safety, Tolerability, and Pharmacokinetics of Kindolor Tosylate in Healthy Adults

NCT #: NCT06243835

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STATISTICAL ANALYSIS PLAN

for

PROTOCOL NO: KIND-2022-01

A Phase 1a Randomized, Double-blind, Placebo-controlled, Single Site, Single Ascending Dose Study of the Safety, Tolerability, and Pharmacokinetics of Kindolor Tosylate in Healthy Adults

Protocol Version No.: 8.0 Version Date: 30 August 2024

Study Sponsor:
Lohocla Research Corporation

Plan Authors:

[redacted]

Version Number 1.0

Date: 05 Nov 2024

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A Phase 1a Randomized, Double-blind, Placebo-controlled, Single Site, Single Ascending Dose Study of the Safety, Tolerability, and Pharmacokinetics of Kindolor Tosylate in Healthy Adults

Date: 30 August 2024

Prepared by: _____ Date: _____

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Reviewed By: _____ Date: _____

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Reviewed By: _____ Date: _____
Sponsor

TABLE OF CONTENTS

1 LIST OF ABBREVIATIONS

Abbreviation	*Definition*
λz	Elimination rate constant
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration-time curve
CI	Confidence interval
CL	Cutaneous leishmaniasis
C_{max}	Maximum observed plasma concentration
CrCl	Creatinine Clearance
CRF	Case report form
CV	Coefficient of variation
DSU	Drug Studies Unit
EDTA	Ethylendiaminetetraacetic acid
FDA	Food and Drug Administration
g	Grams
h	Hour
ICH	International Conference on Harmonization
ID	Identification
IND	Investigational New Drug
IPT	Integrated Product Team
IV	Intravenous
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligrams
mL	Milliliter
mm	Millimeter
ng	Nonograms
PK	Pharmacokinetic(s)
QA	Quality Assurance
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System, Organ, Class
$t_{1/2}$	Apparent terminal exponential half-life
T_{max}	Observed time of maximum plasma concentration
USCD	University of California San Diego
WBC	White Blood Cells

2 INTRODUCTION

This statistical analysis plan (SAP) for Protocol No. KIND-2022-01, "A Phase 1a Randomized, Double-blind, Placebo-controlled, Single Site, Single Ascending Dose Study of the Safety, Tolerability, and Pharmacokinetics of Kindolor Tosylate in Healthy Adults" describes and expands upon the analytical plan presented in the protocol.

This document contains all planned analyses, reasons and justifications for these analyses for all study data. This plan also includes sample tables, figures, and listings that will be populated. The SAP will follow the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines as indicated in Topic E3 (Structure and Content of Clinical Study Reports), Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH.

The following sources were used in preparation of this SAP:

- Protocol # KIND-2022-01, Protocol Version No.: 8.0; Version Date: 30 August 2024
- ICH Guidance Topics E9, E3 and E8

3 PROTOCOL SUMMARY

3.1 Study Objectives

Primary: The primary objective of the study is to determine the safety and maximum tolerated dose (MTD) of kindolor tosylate in healthy volunteers.

Secondary: The secondary objective of the study is to determine the PK of kindolor tosylate by quantitating kindolor levels in plasma across a range of doses in healthy volunteers.

3.2 Study Design

This is a Phase 1a, randomized, double-blind, single ascending dose study designed to assess the safety, tolerability, and PK of kindolor tosylate. Healthy male and female adults were screened for eligibility by medical history, physical examination including height and body weight, vital signs, 12-lead electrocardiogram (ECG), clinical laboratory tests (amylase, lipase, chemistry, hematology, and coagulation tests, medical urinalysis, and infectious disease screen), urine drug screen for drugs of abuse, fecal occult blood tests (FOBT), and medication use. Females will have a pregnancy test.

Using a dose escalating design, eligible subjects received randomly assigned enteric coated oral tablets of kindolor tosylate (100 mg and 300 mg strengths) or identically matched Placebo tablets in 4 cohorts of 8 subjects (6 kindolor tosylate subjects and 2 placebo subjects in each cohort). A sentinel cohort of 2 subjects (1 active and 1 placebo) were dosed and closely monitored for at least 24 hours prior to dosing the remaining 6 subjects in each successive cohort. Ascending doses of kindolor tosylate include 100 mg (1 x 100 mg tablet), 300 mg (1 x 300 mg tablet), 900 mg (3 x 300 mg tablet), and 1800 mg (6 x 300 mg tablet). The safety data for each completed cohort was reviewed by the UCSD Clinical and Translational Research Data and Safety Monitoring Board (DSMB) that recommend continuation to the next cohort or stopping the study due to safety concerns.

Eligible subjects received intake procedures at the UCSD Clinical and Translational Research Institute Phase I unit on Study Day -1 (the day before the start of dosing) and completed final

screening and baseline evaluations including baseline assessments. On Study Day 1, subjects received the study drug after an overnight fast (about 8 hours) with no food allowed until 4 hours after dosing. Study drug tablets were administered with 240 mL of water. Subjects remained in the unit for at least an additional 48-hours for safety assessments and blood collections to determine plasma levels of kindolor. Pre-dose assessments were conducted prior to administration of study drug on Study Day 1. Blood for PK will be collected ~ 15 minutes prior to dosing, then at 0.25, 0.5, 1, 1.5, 2, 4, 8, 12, 24, and 48 hours after dosing. Safety will be assessed by collecting adverse events (AEs), vital signs, physical examination, ECG, FOBT, Stool Consistency Questionnaire, GI Symptoms Checklist, and clinical laboratory tests (amylase, lipase, chemistry, hematology, coagulation tests, pregnancy tests, and urinalysis). AEs were assessed daily after the start of dosing, with closer evaluations in the 4-hour period after the start of dosing. Sitting (3 minutes) vital signs were taken during screening, at clinic check in, pre-dose, then at 15, 30, 60 minutes and 2, 4, 6, 12, 24, and 48 hours post dose. A 12-lead ECG will be obtained prior to dosing, then at 2, 6, 12, 24, and 48 hours post dose. When vital signs or ECG were scheduled at the same time as a PK blood draw, these assessments were performed before drawing any blood. The FOBT will be performed at screening, clinic intake on Day -1, pre-discharge on Day 3, and at follow-up on Day 7. Subjects returned for a final follow-up visit 7±2 days after discharge for a final safety assessment including vital signs, ECG, AEs, FOBT, Stool Consistency Questionnaire, GI Symptoms Checklist, and clinical laboratory tests.

3.3 Study Endpoints

Safety Endpoints:

- AEs
- Stool Consistency Questionnaire indicative of a GI AE
- GI Signs and Symptoms Checklist indicative of a GI AE
- Clinical laboratory data
- ECG results
- FOBT results
- Vital signs
- Rate of urine output (24 hrs)

PK Endpoints:

AUC_t: Area under the plasma concentration-time curve from time 0 to the time (t) of last quantifiable concentration (C_t) calculated by the log-linear trapezoidal rule.

AUC_∞: Area under the plasma concentration-time curve from time 0 extrapolated to infinity. The terminal area from C_t to infinity was calculated by using the approximation as C_t/λ_z thus $AUC_\infty = AUC_t + C_t/\lambda_z$.

C_{max}: The maximum observed plasma concentration.

t_{max}: The observed time to reach maximum plasma concentration.

λ_z: The terminal-phase exponential rate constant as calculated from the negative slope of the regression line for the terminal linear portion of the LN transformed plasma concentration versus time curve.

$t_{½}$: The apparent terminal exponential half-**life, calculated as ln(2)/λ_z.**

4 DEFINITION OF ANALYSIS SETS

For PK Assessments:

PK Analysis Set: The PK population will include subjects who received kindolor tosylate and had sufficient plasma concentrations to reliably calculate PK parameters.

For Safety Outcome Measures:

Safety Analysis Set: The safety population will include all subjects who received a dose of investigational product.

5 ASSSESSMENT AND JUSTIFICATION OF STUDY ENDPOINTS

The Schedule of Assessments for the study is shown in **Table 1**.

5.1 Measurement of Plasma Concentrations of Kindolor and its metabolites and Determination of PK Parameters

Sample collection and analysis: Blood will be collected in 4 mL K_2EDTA Vacutainer tubes to obtain plasma for PK determination at the 29 times specified in the protocol timetable. The time of blood collection will be recorded. Blood samples will be placed on ice immediately after collection and then centrifuged to separate plasma within 30 minutes of collection. Approximately 1 mL of plasma will be aliquoted into the primary vial and the remaining volume of plasma will be aliquoted into a back-up tube. The primary and back-up tubes are to be stored at -60°C to -80°C until analysis.

Plasma samples for DCUKA / 8-OH DCUKA determination will be analyzed using a validated LC/MS/MS method. A method validation report will be issued for the validated method and a bioanalytical report for the sample analysis.

PK analysis: The concentration-time profiles will be evaluated by non-compartmental analysis. Actual sample times will be utilized for calculations. Calculations of parameters will be performed with Phoenix WinNonLin 6.2 (Pharsight Corporation, St. Louis, MO). The **elimination rate constants (λ_z)** will be estimated from the terminal log-linear decline in plasma concentrations and $t_{½}$**calculated as ln(2)/λ_z** . Area under the plasma concentration curves will be determined till the last time of a quantifiable plasma concentration (AUC_t) by the log/linear trapezoidal rule and to infinity (AUC_∞) **based on the last plasma concentration (Ct) and λ_z** . The value of t_{max} will be the observed time of the highest plasma concentration and C_{max} would be the plasma concentration at that time.

Table 1 Schedule of Visits and Assessments for Each Cohort

	Outpatient	Inpatient				Outpatient		Early Termination
Activity	**Screening**	**Clinic Intake**	**Treatment**	**Follow-up**	**Clinic Discharge**	**Follow-up**	**Telephone Contact[q]**	
Study Day	**-30 to -2**	**-1**	**1**	**2**	**3**	**7±2**		
Informed Consent	X							
Demographics	X							
Medical/Surgical History	X	update						
Physical Examination	X	update			X			X
Height/Weight	X	Weight only				Weight only		Weight only
12-Lead ECG[a]	X		X	X	X	X		X
Vital Signs[b]	X	X	X[c]	X	X	X		X
Serum amylase	X	X			X	X		X
Serum lipase	X	X			X	X		X
Clinical Chemistry[d]	X	X			X	X		X
Hematology[e]	X	X			X	X		X
Coagulation[f]	X	X			X	X		X
Urinalysis[g]	X	X			X	X		X
Monitor urine output[h]			X	X	X			
Infectious Diseases[i]	X							
SARS-CoV-2 Antigen Test[j]	X							

	Outpatient	Inpatient				Outpatient		Early Termination
Activity	**Screening**	**Clinic Intake**	**Treatment**	**Follow-up**	**Clinic Discharge**	**Follow-up**	**Telephone Contact[q]**	
Study Day	**-30 to -2**	**-1**	**1**	**2**	**3**	**7±2**		
Pregnancy Test[k]	X	X				X		X
Birth control methods	X	update			update		update	
Sperm, ova, donation and breast feeding check		X				X	X	
FOBT	X	X			X	X		
Urine Alcohol & Drug Screen[l]	X	X						
Prior and Concomitant medications[m]	X	X	X	X	X	X		X
Eligibility Checklist	X	Final check						
Genetics Tests[n]		X						
Study Drug Administration			X					
Blood Samples for PK[o]			X	X	X			
Adverse Events[p]			X	X	X	X		X
Stool Consistency		X	X	X	X	X		X
Final Subject Disposition						X		X

[a] A 12-lead resting ECG will be obtained at Screening, Day 1 prior to dosing, at 2, 6, 12, 24, and 48 hours post dose, and early termination.

[b] Vital signs include sitting (3 minutes) blood pressure, and heart rate, and oral temperature, respiration rate, and pulse oximetry.

[c] Blood pressure. and heart rate, respiration rate, and pulse oximetry will be taken pre-dose, then at 15, 30, 60 minutes and 2, 4, 6, 12, 24, and 48 hours post dose. Temperature will be taken pre-dose, 24, and 48 hours post dose. All vital signs will be taken at Day 3 before clinic discharge and Day 7.

[d] Chemistry tests include albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine, direct bilirubin, total bilirubin, alkaline phosphatase, creatinine phosphokinase (CPK), lactate dehydrogenase (LDH), sodium, potassium, chloride, calcium, inorganic phosphorus, bicarbonate, uric acid, total cholesterol, total protein, glucose, and triglycerides. Details are provided in Section 11.1.5.

[c] Hematology tests include hematocrit, hemoglobin, red blood cell (RBC) count, white blood cell (WBC) count, absolute counts for neutrophils, lymphocytes, monocytes, basophils, eosinophils, and platelets.

[f] Coagulation tests include prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, and international normalized ratio (INR).

[g] Urinalysis tests include specific gravity, pH, bilirubin, urobilinogen, ketones, protein, blood, glucose, nitrites, and leukocyte esterase. A microscopic evaluation will be performed if blood or leukocyte esterase are detected.

[h] Urine output will be monitored by collection of urine for two 24 hr periods, starting with the morning void on Day 1 then again starting over with the morning void on Day 2 to 24 hours later.

[i] Hepatitis A virus immunoglobulin M (HAV-IgM), hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab), HIV antibodies (HIV Ab).

[j] Results must be available within 72 hours of clinic intake.

[k] A serum test for beta-human chorionic gonadotropin (β-hCG) will be performed on all women unless they are menopausal. For any post-menopausal females, a follicle stimulating hormone (FSH) test will be performed to confirm sterilization in lieu of a β-hCG test. If clinic intake is within 72 hours of a negative test, it does not need to be repeated at intake. At intake, a rapid test for β-hCG may be performed.

[l] The urine drug test panel includes amphetamines, barbiturates, benzodiazepines, buprenorphine, cocaine, fentanyl, MDMA, methadone, methamphetamine, morphine, opioids, oxycodone, phencyclidine, and THC. Recent alcohol use will be assessed via ethyl glucuronide urine test strip.

[m] Medication use in the two months prior to the start of screening and at any time during the study after signing informed consent will be recorded.

[n] CYP2C9 polymorphisms

[o] Blood for PK will be collected ~ 15 minutes prior to dosing, then at 0.25, 0.5, 1, 1.5, 2, 4, 8, 12, 24, and 48 hours after dosing.

[p] GI AEs will be assessed specifically using a GI Signs and Symptoms Checklist, Stool Consistency Questionnaire, and endoscopy if indicated along with other laboratory tests as scheduled.

[q] Telephone contact for males at 90 days and for females at 28 days after dosing.

5.2 Safety Endpoints

Adverse Events (AEs): An AE is defined as any reaction, side effect, or untoward event that occurs during the course of the clinical trial, whether or not the event is considered related to the investigational agent or clinically significant. For this study, AEs will include events reported by the subject, observed by clinical staff, clinically significant abnormal clinical laboratory results, or a positive pregnancy test. Reports of AEs will be elicited by a verbal probe (e.g., "How are you feeling?") administered starting on Day 1 and daily during residency and at all other clinic visits.

Any events spontaneously reported by the subject or observed by the investigative staff will also be recorded. Each AE will be graded for severity, and the date and time of onset, cessation and resolution will be recorded.

Severity: All AEs (except application site reactions described below) will be graded according to the following definitions. Assignment of grade based on the intensity of symptoms and the degree of limitation of usual daily activities will be done according to severity using the following criteria:

Grade 1: Mild symptoms invoking a minimum degree of discomfort that are easily tolerated.

Grade 2: Moderate symptoms that result in a reduction in normal daily activity, but is not totally incapacitating. This may or may not require medical intervention.

Grade 3: Severe symptoms that may be totally incapacitating or result in marked reduction in normal daily activity. Medical intervention is usually required.

Grade 4: Potentially life-threatening event that requires emergency intervention or hospitalization.

Relationship: The degree of certainty for which the AE/SAE is attributed to the investigational product or alternative causes (e.g. natural history of the underlying disease, concomitant therapies, etc.) should be determined by how well the experience can be understood in terms of one or more of the following. The relatedness of an AE to the study drug is the best estimate of the causal relationship between the study drug and an AE at the time of reporting. Causality will be assessed by the Principal Investigator or designee.

The following drug relationships will be used for this clinical study:

Unrelated: There is no temporal relationship between the event and the administration of the study drug or the event is clearly due to the subject's medical condition, other therapies, or accident.

Unlikely: There is evidence of exposure to the study drug but there is another more likely cause of the event.

Possibly Related: There is some temporal relationship between the event and the administration of the study drug and the event is unlikely to be explained by the subject's medical condition or other therapies.

Probably Related: The temporal relationship between the event and the administration of the study drug is compelling, and the subject's medical condition and other therapies cannot explain the event.

Definitely Related: The event follows a reasonable temporal sequence from administration of the medication or follows a known or suspected response pattern to the medication.

The categories of Definitely, Probably, and Possibly will be considered investigational product related with regards to summary statistics.

Serious Adverse Events. Each AE or reaction will be classified by the study investigator as serious or non-serious. The International Conference on Harmonization (ICH) Guideline for Industry: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, ICH-E2A March 1995, as implemented by the U.S. Food and Drug Administration defines SAE or reaction as any untoward medical occurrence that at any dose:

- results in death;
- is life-threatening; *(NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.)*
- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in persistent or significant disability/incapacity; or
- is a congenital anomaly/birth defect.

In addition, important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug reaction, when based on appropriate medical judgment that may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition.

Physical Examination.: A physical examination of the oral cavity, head, eyes, ears, nose, and throat, cardiovascular system, lungs, abdomen, extremities, skin, neuropsychiatric mental status and sensory/motor status, musculoskeletal system and general appearance will be performed during screening, weeks 4, 8, and 12.

Clinical Chemistry: ALT, Albumin, alkaline phosphatase, AST, bilirubin (total and direct), calcium, chloride, cholesterol, creatinine, GGT, glucose, phosphate, potassium, sodium, total protein, BUN, uric acid. Assessed at screening and weeks 4, 8 and 12.

Hematology: Hemoglobin, hematocrit, red blood cell count (RBC), reticulocytes, white blood cell count (WBC), platelets. Assessed at screening and weeks 4, 8 and 12

Urine drug tests: Urine drug tests will be used to assess candidates for recent use of amphetamines, barbiturates, benzodiazepines, cocaine, opiates, cannabinoids, phencyclidine, propoxyphene, and methadone. Assessed at screening and weeks 4, 8 and 12.

6 HYPOTHESES TO BE TESTED

There are no formal hypotheses being tested, as the study is primarily a safety and PK evaluation study.

7 SAMPLE SIZE CONSIDERATIONS

The cohort size of 6 subjects receiving the active drug is generally accepted for first-in-humans clinical trials that provide a reasonable sample size for PK parameter estimates (Shen et al). Administration of kindolor tosylate to 6 subjects in each dose group provides a 47%, 62%, 74%, or 82% probability of observing at least 1 occurrence of any AE with a true incidence rate for a given dose group of 10%, 15%, 20%, or 25%, respectively. Furthermore, it will be assumed that pooling the data for the subjects who received placebo (2 from each cohort) provides an adequately sized control group.

8 PROCEDURE FOR UNBLINDING DATA

This study is a double-blind study. If the treatment assignment for an individual subject needs to be unblinded during the trial, the PI will contact the unblinded sponsor or data management center staff for the treatment assignment. A note to the file will be prepared by the person who performed the unblinding to indicate when the subject was unblinded, why the subject was unblinded, and to whom the unblinding information was given.

Blinding and unblinding procedures will be performed in accordance with Fast-Track's SOPs CT017 Procedures for Unblinding Investigational Agent Identity for a Study or a Single Subject, CT024 Prepareation of Randomization Codes and Maintenance of Treatment Assignment Schedules, CT033 Security and Access to Clinical Trial Databases, and CT045 Development of Clinical Data Management Plans.

At the completion of the study, after the database has underdone edit checking and QA audit and is deemed ready to be locked, the treatment assignments will be uploaded to the main study database, and the database will be locked.

9 STATISTICAL CONSIDERATIONS

9.1 General Considerations

All data collected will be presented in summary tables and/or data listings. Descriptive statistics will be used to present study data. For categorical variables, the number and percentage of subjects in each category will be summarized. Continuous variables will be summarized with the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum values. All data will be presented in listings. Analyses will be performed using SAS v9.4.

9.2 Demographics and Baseline Characteristics

Demographics for the safety analysis set will be presented as summary statatistics for age (overall and by subgroups), gender, race/ethnicity, height, and weight by treatment group and all

groups combined. Baseline infectious disease presence or absences and COVID prsences or absence will be presented in tabular form. Baseline stool consistency and symptoms will be summarized. All of the above and medical history and physical examination results will be included in data listings.

9.3 Participant Accountability and Protocol Deviations

The disposition of all study subjects will be summarized including the total numbers screened, eligible, randomized, analysis set, withdrawn, and completed. Accountability data including study termination and reason will be provided in a listing for all subjects who were randomized. A listing of all Protocol Deviations will be provided.

9.4 Study Drug Exposure

Study drug is given once per patient. Patient listing will be provided with date and time of administration, whether there was any problem with administration and specification of the problem.

9.5 PK Analysis

PK parameters such as $AUC_{0\text{-defined time}}$, C_{max}, T_{max}, λz, and $t_{1/2}$ are presented as summary statistics including mean, standard deviation (SD), gerometric mean, median, minimum and maximum. These parameters are defined and will be calculated using WinNonLin 5.2 (Pharsight Corp, Mountain View, CA) using a non-compartmental analysis as follows:

AUC(0-t): Area under the plasma concentration-time curve from time 0 to the time (t) of last quantifiable concentration (Ct) calculated by the log/linear trapezoidal rule.

AUC(0-inf): Area under the plasma concentration-time curve from time 0 extrapolated to infinity. The terminal area from Ct to infinity will be calculated by using the approximation as $Ct/\lambda z$ thus AUC(0-inf) = AUC(0-t) + $Ct/\lambda z$.

Cmax: The maximum observed plasma concentration.

Tmax: The observed time to reach maximum plasma concentration.

λz: The terminal-phase exponential rate constant as calculated from the negative slope of the regression line for the terminal linear portion of the LN transformed plasma concentration versus time curve.

$t_{1/2}$: The apparent terminal exponential half-life, calculated as $\ln(2)/\lambda z$.

Concentration time curves by individual subject and by group geometric means ± SD will be presented.

9.6 Adverse Events and Serious Adverse Events

AEs will be coded using the most recent version of the Medical Dictionary of Regulatory

Activities (MedDRA) preferred terms and will be grouped by system, organ, and class (SOC) designation. The severity, frequency, and relationship of AEs to study drug will be presented by preferred term by SOC grouping. Listings of each individual AE including start date, stop date, severity, relationship, outcome, and duration will be provided. The duration of the event will be calculated by subtracting the start date of the event from the stop date of the event and adding the integer one. Thus, if an AE started and stopped on the same day, then the duration is 1 day. Or if the AE started one day and stopped the next day, the duration is 2 days.

GI AEs will also be summarized separately including stool consistency scores and presence/absence and severity of other symptoms according to the GI Signs and Symptoms checklist or endoscopy results if applicable. The GI AE scale scoring will be presented as summary statistics by categorical response. The presence, absence, and severity of other signs and symptoms of GI AEs indicative of possible gastric inflammation or erosion including endoscopy results will be presented as numbers and percentages, including if the GI AE triggered a study stopping criteria.

Serious Adverse Events (SAEs): A listing of all participants experiencing SAEs will be provided. This listing will include the subject ID, name of the SAE, treatment group, gender, age, onset day relative to last injection, and outcomes.

9.7 Clinical Laboratory Data

Clinical laboratory test results, urine drug screen results, and pregnancy test results will be reported as summary statistics for each assessment time point. Clinical chemistry, amylase, lipase, hematology, coagulation, urinalysis, FOBT, urine drug screen results, and pregnancy test results will be presented as summary statistics and change from baseline. In addition, change from baseline (shift tables) will also be presented for clinical chemistry, amylase, lipase, hematology, and coagulation data.

9.8 Vital Signs

Vital signs and ECG parameters will be presented as summary statistics and change from baseline. The proportions of ECG results considered clinically significant will also be provided. Urine output in mL/hour will be calculated over the two 24-hour period of collection and presented as summary statistics for both periods. All data will be presented by treatment group.

9.9 Concomitant Medications

A listing of all concomitant medications will be provided for the safety analysis set.

9.10 Handling of Missing Data

Adverse event data is not imputed. Missing dates are handled as follows:

- Missing day: The first day of the month will be used.
- Missing Month: The first month of the year will be used.
- Completely missing dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

9.11 Interim Analyses and Data Monitoring

An interim analysis of the safety data will be prepared as each cohort completes the study. As 2 placebo subjects will be included in each cohort, the safety data from all placebo subjects will be combined for each interim analysis.

10 VALIDATION OF PROGRAMMING CODE

All SAS code used to generate tables, listings, and figures will be validated and reviewed before being finalized. The validation process will be used to determine that the numbers are produced by a statistically valid method and that the execution of the computations is correct. Qualified personnel who have not previously been involved in the production of the original programming code will perform the validation procedures. Methods of validation include independent programming and comparison to data listings. PK parameters will be verified by visual inspection (Cmax and Tmax) and by confirming the plasma parameter input and output files are 100% congruent, as this data will be transferred to the study pharmacologist. Tables will be reviewed for accuracy, consistency with this plan, consistency within tables, and consistency with corresponding output. Once validation is complete, a quality control reviewer will perform a final review of the documents for accuracy and consistency. Upon completion of validation and quality review procedures, all documentation will be collected and filed in the study documentation files at Fast-Track.

11 References

Shen J, Swift B, Mamelok R, Pine S, Sinclair J, Attar M. Design and Conduct Considerations for First-in-Human Trials. Clin Transl Sci. 2019;12:6-19

12. TABLES, LISTINGS, AND FIGURE SHELLS

LIST OF TABLES

Table Shells

Screening and Baseline Assessments

Table 2: Subject Disposition - All Consented Subjects

	Treatment Group				
	Kindolor 100 mg	**Kindolor 300 mg**	**Kindolor xx mg**	**Placebo**	**All subjects**
	n (%)	**n (%)**	**n (%)**		**n (%)**
Subjects Screened					xxx
Subjects Eligible					xxx (xx.x%)[a]
Subjects Randomized	xx	xx	xx	xx	xx
Safety Analysis Set	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
PK Analysis Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects who Completed study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects who withdrew from the study early	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for early withdrawal (n, % of subjects withdrawn)					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to follow up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol deviation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study termination by sponsor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal of consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other reason	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Percent of subjects screened. Other percentages are percentage of subjects randomized.

Table 3: Demographic Characteristics

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo	All subjects
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Age (years)					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx	xx	xx	xx	xx
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)
Gender at Birth					
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race					
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
African-American or Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
American Indian or Alaskan Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
More than one race	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown or not reported	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity					
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not reported	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Height (cm)					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)

Table 3: Demographic Characteristics (Continued)

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo	All subjects
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Weight (kg)					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)
Body Mass Index (kg/m^2)					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)

Table 3: Baseline Characteristics

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo	All subjects
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Positive Infectious Diseases					
HAV-IgM	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
HBsAg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
HCV Ab	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
HIV Ab	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SARS-CoV-2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Frequency of Stools per Day					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)
Consistency of Stools per Day					
Type 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type 5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type 6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type 7	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Urgency of Stools					
No urgency	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat urgent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Urgent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very urgent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdominal Pain or Discomfort					
No discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild – moderate discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat severe discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bloating					
No discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild – moderate discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat severe discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo	All subjects
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Very severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Interference with performing normal, daily activities					
Not at all	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Some interference	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much interference	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Incapacitating	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 4: Pharmacokinetic Parameters

Analyte: DCUKA / 8-OH DCUKA

	Kindolor 100 mg	**Kindolor 300 mg**	**Kindolor 900 mg**	**Kindolor 1800 mg**
Parameter	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
$C_{max\ (ng/mL)}$				
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Geometric mean	xx.x	xx.x	xx.x	xx.x
Median	xx	xx	xx	xx
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
$t_{max\ (hr)}$				
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Geometric mean	xx.x	xx.x	xx.x	xx.x
Median	xx	xx	xx	xx
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
AUC_{0-t} (h*ng/mL)				
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Geometric mean	xx.x	xx.x	xx.x	xx.x
Median	xx	xx	xx	xx
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
AUC_{∞} (h*ng/mL)				
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Geometric mean	xx.x	xx.x	xx.x	xx.x
Median	xx	xx	xx	xx
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
λ_z				
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Geometric mean	xx.x	xx.x	xx.x	xx.x
Median	xx	xx	xx	xx
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
$t_{½\ (hr)}$				
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Geometric mean	xx.x	xx.x	xx.x	xx.x
Median	xx	xx	xx	xx
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx

Safety

Table 5: Overall Summary of Adverse Events

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Number of AEs	xx	xx	xx	xx
Number of SAEs	xx	xx	xx	xx
Number (%) of subjects with at least one AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number (%) of subjects with at least one SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number (%) of subjects with at least one AE related to study product	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of AEs by severity				
Mild	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Moderate	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Severe	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Life-threatening	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Number of AEs by relationship to study product				
At least possibly related	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Unrelated	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)

Table 6: Number and Percentage of Subjects with Adverse Events

MedDRA System Organ Class/	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
Preferred Term	(N=xx)	(N=xx)		
- Any Adverse Events -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC				
- Overall -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
[1] Fisher's exact test
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 4: Summary of Subjects with Adverse Events by Severity and Relationship – Kindolor 100 mg

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 8: Summary of Subjects with Adverse Events by Severity and Relationship – Kindolor 300 mg

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 9: Summary of Subjects with Adverse Events by Severity and Relationship – Kindolor 900 mg

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 10: Summary of Subjects with Adverse Events by Severity and Relationship – Kindolor 1800 mg

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 11: Summary of Subjects with Adverse Events by Severity and Relationship – Placebo

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 12: Number and Percentage of Subjects with Adverse Events by Maximum Severity - Kindolor

MedDRA SOC/ Preferred Term	Kindolor 100 mg (N=xx)				Kindolor 300 mg (N=xx)			
	Mild	Moderate	Severe	Life-threatening	Mild	Moderate	Severe	Life-threatening
- Any Adverse Events -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC								
- Overall -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

MedDRA SOC/ Preferred Term	Kindolor 900 mg (N=xx)				Kindolor 1800 mg (N=xx)			
	Mild	Moderate	Severe	Life-threatening	Mild	Moderate	Severe	Life-threatening
- Any Adverse Events -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC								
- Overall -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 13: Number and Percentage of Subjects with Adverse Events by Maximum Severity - Placebo

MedDRA SOC/ Preferred Term	Placebo (N=xx)			
	Mild	Moderate	Severe	Life-threatening
- Any Adverse Events -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC				
- Overall -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 14: Number and Percentage of Subjects with Adverse Events Leading to Withdrawal from the Study

MedDRA SOC/	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
Preferred Term	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
SOC				
- Overall -	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 15: Stool Consitency by Visit

		Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo	All subjects
Visit	**Characteristic**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Repeat for Treatment, Inpatient Follow-up, Clinic Discharge, Outpatient Follow-up and Earl termination	**Frequency of Stools per Day**					
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)
	Consistency of Stools per Day					
	Type 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Type 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Type 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Type 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Type 5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Type 6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Type 7	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Urgency of Stools					
	No urgency	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Somewhat urgent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Urgent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Very urgent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abdominal Pain or Discomfort					
	No discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild – moderate discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Somewhat severe discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Very severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Bloating					
	No discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild – moderate discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Somewhat severe discomfort	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Very severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Interference with performing normal, daily activities					
	Not at all	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Some interference	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

		Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo	All subjects
Visit	**Characteristic**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
	Much interference	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Incapacitating	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 16: Gastrointestinal Signs and Symptoms by Visit

		Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo	All subjects
Visit	**Symptoms Present**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Repeat for Treatment, Inpatient Follow-up, Clinic Discharge, Outpatient Follow-up and Earl termination	Epigastric pain/discomfort (dyspepsia)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Fatigue	xx.x	xx.x	xx.x	xx.x	xx.x
	Light headedness	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)	(xx-xx)
	Postural dizziness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Syncope	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Nausea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Hematemesis (vomiting blood)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Hematochezia (anal or rectal bleeding)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Positive FOBT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease in hematocrit of at least 10 % points	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease in hemoglobin by at least 20 g/dL	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase in BUN ≥ 40 mg/dL	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase in creatinine ≥ 1.8 mg/dL	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase in ALT ≥ 3 ULN	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase in AST ≥ 3 ULN	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 5: Summary of Blood Chemistries

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Repeat for each visit: Screening, Day -1, discharge and follow-up				
Test Name (units)				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
Change from baseline at discharge and follow-up				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx

Programmers note: table will include alanine aminotransferase, albumin, alkaline phosphatase, aspartate aminotransferase, bilirubin (total and direct), calcium, chloride, cholesterol, creatinine, GGT, glucose, phosphate, potassium, sodium, total protein, uric acid, amylase, lipase and BUN.

Table 18: Summary of Hematology Tests

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Repeat for each visit: Screening, Day -1, discharge and follow-up				
Test Name (units)				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
Change from baseline at discharge and follow-up				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx

Programmers note: Hemoglobin, hematocrit, red blood cell count (RBC), reticulocytes, white blood cell count (WBC), and platelets.

Table 19: Summary of Coagulation Tests

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Repeat for each visit: Screening, Day -1, discharge and follow-up				
Test Name (units)				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx

Programmers note: INR, Fibrinogen, prothrombin time (PT), and partial thromboplastin time (PTT).

Table 20: Summary of FOBT and Urinalysis Tests

		Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
Test	**Result**	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Repeat for each visit: Screening, Day -1, discharge and follow-up					
Test Name (units)					
	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
Change from baseline at discharge and follow-up					
	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
Fecal Occult Blood Test (FOBT)	Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Invalid	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Glucose	Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Programmers note: Repeat for collected tests. Continuous tests should be summarized usings mean, sd, range.

Table 21: Summary of Positive Pregnancy and Urine Drug Tests

	Number positive (%)			
	Kindolor 100 mg	**Kindolor 300 mg**	**Kindolor xx mg**	**Placebo**
Test	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Repeat for each visit: Screening, Day -1, discharge and follow-up				
Amphetamine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Barbiturates	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Benzodiazepines	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cocaine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Opiates	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
cannabinoids	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
phencyclidine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
propoxyphene	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
methadone	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy Test	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 22: Summary of Shift from Baseline – Chemistry Tests

				Post-Baseline		
Treatment Group	**Test**	**Visit**	**Baseline**	**Low**	**Normal**	**High**
	Lab test (Unit)	Repeat for each visit: discharge and follow-up	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 23: Summary of Shift from Baseline – Hematology Tests

				Post-Baseline		
Treatment Group	**Test**	**Visit**	**Baseline**	**Low**	**Normal**	**High**
	Lab test (Unit)	Repeat for each visit: discharge and follow-up	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 24: Summary of Shift from Baseline – Coagulation Tests

				Post-Baseline		
Treatment Group	**Test**	**Visit**	**Baseline**	**Low**	**Normal**	**High**
	Lab test (Unit)	Repeat for each visit: discharge and follow-up	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 25: Summary of Vital Signs

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Repeat for each visit: Screening, Day -1, Treatment, Inpatient Follow-up, Clinic Discharge, Outpatient Follow-up and Earl termination				
Test Name (units)				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
Change from baseline				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx

Programmers note: vital signs include heart rate (sitting), blood pressure (sitting), respiratory rate, oral temperature

Table 26: Summary of ECG Results

	Kindolor 100 mg	Kindolor 300 mg	Kindolor xx mg	Placebo
Result	**(N=xx)**	**(N=xx)**	**(N=xx)**	**(N=xx)**
Repeat for each visit: Screening, Day -1, Treatment, Inpatient Follow-up, Clinic Discharge, Outpatient Follow-up and Earl termination				
Parameter (units)				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
Change from baseline				
N	xx	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Min - Max	xx-xx	xx-xx	xx-xx	xx-xx
Interpretation				
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal, Not Clinically Significant	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal, Clinically Significant	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Listing Shells

Listing 1: Subject Disposition - All Subjects

Subject ID	Date of Consent	Eligible	Date of random-ization	Treatment Group	Safety Analysis Set	PK Analysis Set	Study Completion	(Day) Date of Study Completion or Early Withdrawal	Reason for Early Withdrawal
xxxx	mm/dd/yyyy	Y/N	mm/dd/yyyy		Yes	Yes	Yes	(xx) mm/dd/yyyy	xxxxxx
					No	No	No		

Note: Day is relative to Study Day 1.

Listing 2: Reasons not Eligible – Screen Failures

Subject ID	Criterion Type	Criterion
xxxx	Inclusion Criteria	
	Exclusion Criteria	

Listing 3: Protocol Deviations

Subject ID	Treatment	Deviation Date	Protocol Deviation	Other Details
xxxx		mm/dd/yyyy		

Note: Only subjects with protocol deviation are listed.

Listing 4: Demographics Data

Subject	Treatment	Gender at Birth	Age (yrs)	Ethnicity	Race
xxxx		Male	xx	Hispanic or Latino	American Indian or Alaska Native
		Female		Not Hispanic or Latino	Asian
				Unknown	Native Hawaiian or Other Pacific Islander
					Black or African American
					White
					Other
					Unknown

Listing 5: Medical History -Screening

Subject	Treatment	Medical History Term	Start Date	Ongoing
xxxx		xxxx		
			mm/dd/yyyy	No
				Yes

Listing 6: Physical Exam -Screening

Subject	Treatment	Exam Date	Any abnormal finding during the physical exam?	Describe
xxxx		mm/dd/yyyy	Yes	xxxxxxxx
			No	

Listing 7: Height/Weight-Screening

Subject ID	Treatment	Exam Date	Height (cm)	Weight (kg)	Body Mass Index (kg/m^2)
xxxx		mm/dd/yyyy	xxx	xx	

Listing 8: Genetic Tests -Clinic Intake

Subject ID	Group	Exam Date	Any Blood Collection Problems? /Specify
xxxx		mm/dd/yyyy	Y/xxxx

Listing 9: Infectious Disease Serology-Screening

Subject ID	Group	HBSAg	Hep C Antibody	HIV-1 antibody	HIV-2 antibody	HIV-1 p24	HIV-2 p24	COVID antigen
xxx		1, 2, 3	mm/dd/yyyy	mm/dd/yyyy	xx	xx		

Listing 10: Pregnancy Test/Birth Control Methods (Females only) -Screening and Day-1

Subject ID	Group	Pregnancy Test Performed?	Pregnancy Test Date	Pregnancy Result	Methods of birth control
xxx		Not Done	mm/dd/yyyy	Negative	
				Positive	

Programming note: Only indicate birth control methods that were indicated as Yes

Listing 11: Endoscopy

Subject ID	Group	Visit	Date	Was Overall Video Quality Acceptable?	Reason Not Acceptable	Any Microscopic Abnormalities?	Specify Microscopic Abnormalities	Any Macroscopic Abnormalities?	Specify Macroscopic Abnormalities
xxxx		Screening	mm/dd/yyyy	-30	xxx	xxx	xxx	xx	xx.x
		Day -1		-15					
				+15					
				+30					

Listing 12: GI Signs and Symptoms

Subject ID	Group	Visit	Date	Symptoms	Present?
xxxx		Screening	mm/dd/yyyy		
		Day -1			

Listing 13: Stool Consistency

Subject ID	Group	Visit	Date/ Time	Frequency of Stools per Day	Consistency of Stools per Day	Category/Symptom	Severity
xxxx		Screening	mm/dd/yyyy				
		Day -1					

Listing 14: Plasma Concentrations

Subject ID	Group	Nominal Timepoint	Date	Time	DCUKA (ng/mL)	8-OH DCUKA (ng/mL)
xxxx			mm/dd/yyyy	hh:mm	xx.x	xx.x

Note: Nominal timepoints include: 15 minutes prior to dosing, then at 0.25, 0.5, 1, 1.5, 2, 4, 8, 12, 24, and 48 hours after dosing.

Listing 15: Pharmacokinetic Parameters

Subject ID	Group	C_{max} (ng/mL)	t_{max} (hr)	AUC_{0-4} (h*ng/mL)	AUC_{0-8} (h*ng/mL)	AUC_{0-last} (h*ng/mL)	AUC_{∞} (h*ng/mL)	λ_z	$t_{½}$ (hr)
xxxx		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x

Listing 16: Adverse Events

Subject ID	Treatment Group	Adverse Event (Verbatim) S: SOC P: PT Term	Start Date/ Day	Stop Date/ Day	Duration in Days	Severity	Relation-ship	Actions Taken	Outcome	Serious
xxx		Verbatim	mm/dd/yyyy	mm/dd/yyyy	xx	1	1	1	1	Yes
		S: xxxx	xx	xx		2	2	2	2	No
		P: xxxx				3	3	3	3	
						4	4	4	4	
							5	5	5	
								6		

Notes: Day is relative to Study Day 1.
Severity: 1=Grade 1; 2= Grade 2; 3= Grade 3, 4= Grade 4.
Relationship: 1= Not related; 2=Unlikely related; 3=Possibly related; 4=Related
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment; 7=Other
Outcome: 1=Resolved without sequelae; 2= Ongoing; 3= Recovered with sequelae; 4=Fatal; 5=Unknown

Programmer's Note: If "Were any AEs reported?" checkbox=No, then display "None Reported" in the Adverse Event column and SOC/PT column. If an AE started and stopped the same day, the duration is 1 day.

Listing 17: Adverse Events Leading to Subject Withdrawal from Study

Subject ID	Treatment Group	Adverse Event (Verbatim) S: SOC P: PT Term	Start Date/ Day	Stop Date/ Day	Duration in Days	Severity	Relation -ship	Actions Taken	Outcome	Serious
xxx		Verbatim	mm/dd/yyyy	mm/dd/yyyy		1	1	1	1	Yes
		S: xxxx	xx	xx		2	2	2	2	No
		P: xxxx				3	3	3	3	
						4	4	4	4	
							5	5	5	
								6		

Notes: Day is relative to Study Day 1.
Severity: 1=Grade 1; 2= Grade 2; 3= Grade 3, 4= Grade 4.
Relationship: 1= Not related; 2=Unlikely related; 3=Possibly related; 4=Related
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment; 7=Other
Outcome: 1=Resolved without sequelae; 2= Ongoing; 3= Recovered with sequelae; 4=Fatal; 5=Unknown

Programmer's Note: If "Were any AEs reported?" checkbox=No, then display "None Reported" in the Adverse Event column and SOC/PT column. If an AE started and stopped the same day, the duration is 1 day.

Listing 18: Serious Adverse Events

Subject ID	Treatment Group	SAE Verbatim S: SOC P: PT	Start Date/ Day	Stop Date/ Day	SAE Category	Severity	Relationship
xxx		Verbatim	mm/dd/yyyy	mm/dd/yyyy	Death	1	1
		S: XXX	Xx	Xx	Life-threatening	2	2
		P: XX			Hospitalization	3	3
					Disability	4	4
					Congenital Anomaly/Birth Defect	5	5
					Required Intervention to Prevent Permanent Impairment / Damage		
					Other		

Subject ID No.	**SAE**	**Continued Study Participation**	**Study Drug Start Date**	**Date of last administration of study drug prior to SAE**	**SAE Abated after study drug stopped?**	**Continued study drug Administration**	**SAE reappeared after rechallenge?**	**Outcome**
xxx	Verbatim	Yes	mm/dd/yyyy	mm/dd/yyyy	Yes	Yes	Yes	1
		No			No	No	No	2
					n/a		n/a	3

Notes: Day is relative to Study Day 1.
Severity: 1=Grade 1; 2= Grade 2; 3= Grade 3, 4= Grade 4.
Relationship: 1= Not related; 2=Unlikely related; 3=Possibly related; 4=Related
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment; 7=Other
Outcome: 1=Resolved without sequelae; 2= Ongoing; 3= Recovered with sequelae; 4=Fatal; 5=Unknown

Listing 19: Blood Chemistries

Subject ID	Group	Visit	Visit Date	Test Name	Result	Units	Evaluation
xxxx			mm/dd/yyyy	ALT			WNL
				Albumin			Abnormal, NCS
				Alkaline phosphatase			Abnormal, CS
				AST			
				Total bilirubin			
				Direct bilirubin			
				BUN			
				Calcium			
				Chloride			
				Cholesterol			
				Creatinine			
				GGT			
				Glucose			
				Phosphate			
				Potassium			
				Sodium			
				xxxxx			
				xxxxx			

Listing 20: Hematology

Subject ID	Group	Visit	Visit Date	Test Name	Result	Units	Evaluation
xxxx		Screening	mm/dd/yyyy	Hematocrit			WNL
		Day 4		Hemoglobin			Abnormal, NCS
		Week 4		RBC			Abnormal, CS
		Week 8		WBC			
		Week 12		Platelets			
				xxxxxx			

Listing 21: Coagulation

Subject ID	Group	Visit	Visit Date	Test Name	Result	Units	Evaluation
xxxx		Screening	mm/dd/yyyy	Fibrinogen			WNL
				PT			Abnormal, NCS
				PTT			Abnormal, CS
				xxxx			

Listing 22: Urine Drug Screen

Subject ID	Group	Visit Date	Visit	AMP	Barb	Benzos	Coc	Opiates	Canab	Phen	Prop	Meth	Fen	Mor
xxxx		mm/dd/yyyy		P	P	P	P	P	P	P	P	P	P	P
				N	N	N	N	N	N	N	N	N	N	N
				UNK	UNK	UNK	UNK	UNK	UNK	UNK	UNK	UNK		

P=positive; N=negative
AMP=amphetamine, , Barb=barbiturates Benzos=benzodiazepines, Coc=cocaine, Canab=cannabinoids, Phen=phencyclidine, Prop=propoxyphene, Fen=Fentanyl, Mor=Morphine

Listing 23: Vital Signs

Subject ID	Group	Visit Date	Visit	Timepoint	Heart Rate (beats/min)	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)	Respiry Rate (breaths/ min)	Temperature (°F)
xxxx		mm/dd/yyyy			xxx	xxx	xxx		

Listing 24: Electrocardiogram

Subject ID	Group	Visit Date	Visit	Timepoint	Heart Rate (beats/min)	RR Interval (Sec)	QT Interval (msec)	QTcF (msec)	Interpretation
xxxx		mm/dd/yyyy			xxx	xxx	xxx		

Listing 25: Prior and Concomitant Medications

Subject ID	Group	Prior Med?	Verbatim Medication Name	Indication	Route	Frequency	Dose	Start Date	Stop Date	Continuing? /Used to Treat AE?
xxxx		Yes	xxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	dd/mmm/yyyy	dd/mmm/yyyy	Yes /No
xxxx		No	xxx							No

Figure Shells

LIST OF FIGURES

Figure 1: Mean (SD) Chemistry Values Over Time

X-axis – Days – Y Axis – mean standard deviation for each chemistry value over time – all groups

Figure 2: Mean (SD) Hematology Values Over time

X-axis – Days – Y Axis – mean standard deviation for each hematology value over time – all groups

Figure 3: Mean (SD) Vital Signs Over Time

X-axis – Days – Y Axis – mean standard deviation for each vital sign value over time – all groups

Figure 4: Mean (SEM) Plasma Concentrations Over Time

X-axis – Days – Y Axis – mean standard error of the mean for each plasma concentrations of DCUKAand 8-OH DCUKA values (on separate graphs) over time plotted on linear and log scales – all groups

Figure 5: Individual Subjects Plasma Concentrations Over Time

X-axis – Days – Y Axis – DCUKAand 8-OH DCUKA plasma concentrations for each subject