NOVOTECH
The Asia Pacific CRO

STATISTICAL ANALYSIS PLAN

A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Safety, Tolerability, and Pharmacokinetic Study of Escalating Single and Multiple Doses of CVN766 in Healthy Subjects

PROTOCOL NO.: CVN766-101

PRODUCT CODE: CVN766

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SAP APPROVAL

By my signature, I confirm that this SAP has been reviewed by and has been approved for use on the CVN766-101 study:

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List of Abbreviations

Abbreviation	Description
λz	Terminal Elimination Rate Constant
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Class
AUC	Area under the curve
AUC_{24}	Area under the plasma concentration-time curve from time 0 to 24 hours
$AUC_{0\text{-}inf}$	Area under the plasma concentration-time curve from time 0 to infinity
AUC_{tau}	Area under concentration-time curve over dosing interval
AUC_t	Area under the plasma concentration-time curve
BMI	Body mass index
BQL	Below the quantitation limit
CL/F	Apparent clearance after extravascular administration
CL/F_{ss}	Apparent clearance after extravascular administration at steady state
[redacted]	[redacted]
C_{max}	Maximum observed plasma concentration
C_{min}	Minimum observed plasma concentration
CNS	Central nervous system
CS	Clinically Significant
$C_{ss,max}$	Maximum observed plasma concentration at steady state
$C_{ss,min}$	Minimum observed plasma concentration at steady state
CSR	Clinical Study Report
C_{trough}	Pre-dose Trough Concentration
CV	Coefficient of Variation
DBP	Diastolic blood pressure
ECG	12-Lead Electrocardiogram
eCRF	Electronic Case Report Form
FE	Food Effect
FSH	Follicle-stimulating hormone
GCP	Good Clinical Practice
HIV	Human Immunodeficiency Virus
MAD	Multiple-ascending dose
MedDRA	Medical Dictionary for Regulatory Activities
N/A	Not Applicable
NCS	Not Clinically Significant
NK	Not Known
PI	Principal Investigator
PD	Pharmacodynamic
PK	Pharmacokinetic
PT	Preferred Term
QTcB	QT interval with Bazett's correction method
QTcF	QT interval with Fridericia's correction method
R_{acc}	Accumulation ratio
SAD	Single Ascending Dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBP	Systolic blood pressure
SD	Standard Deviation
S.I.	International System of Units

Abbreviation	Description
SOC	System Organ Class
SOP	Standard Operating Procedure
SRC	Safety Review Committee
$t_{1/2z}$	Terminal elimination half-life
TEAE	Treatment Emergent Adverse Event
T_{max}	Time to maximum concentration
$T_{ss, max}$	Time for C_{max} at steady state.
V_z/F	Apparent volume of distribution after extravascular administration
V_z/F_{ss}	Apparent volume of distribution after extravascular administration at steady state
WHO-DD	World Health Organization Drug Dictionary

1. INTRODUCTION

The following Statistical Analysis Plan (SAP) provides the outline for the statistical analysis of the data collected from the CVN766-101 study (protocol version 4.0 amendment 3 dated 19 May 2022).

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data. Any post hoc, or unplanned exploratory analyses performed will be clearly identified as such in the final CSR.

CVN766 is a highly selective orexin-1 receptor (Ox1R) antagonist and may have utility as treatment for psychiatric disorders including schizophrenia, panic disorder and anxiety, and addiction. The present study will be the first conducted in humans with CVN766 and will examine the compound's safety, tolerability, and PK in healthy subjects.

2. PROJECT OVERVIEW

2.1 Study Design

This is a Phase 1, randomized, double-blind, placebo-controlled, single- and multiple-dose ascending study in healthy subjects with concurrent PK sampling from blood plasma, urine, and cerebrospinal fluid. This study is formed by two parts: Part 1 (SAD) and Part 2 (MAD).

2.1.1 Part 1: SAD is the single-dose regimen and Fasted- Fed Crossover

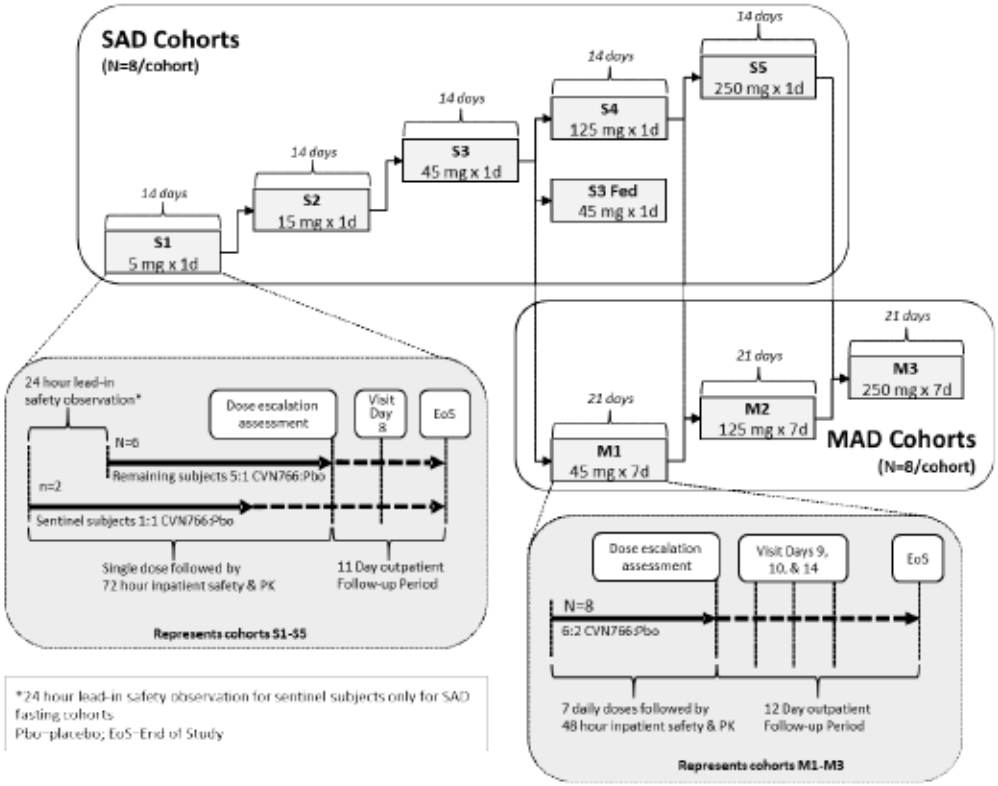
Approximately 40 healthy male or female subjects will be enrolled in 1 of 5 single-dose cohorts (designated as S1 through S5, respectively) in an ascending fashion. An optional Cohort 3a may be added in parallel to SC3 for additional safety and tolerability evaluation. Cohort S3a dose level will be consistent with Cohort S3 (45 mg planned) in a fasted condition only and without lumbar puncture, aligned with other SAD cohorts. Each cohort will consist of 8 subjects randomized to CVN766 or placebo, whereby 6 subjects will receive a single oral dose of CVN766 suspension, and 2 subjects will receive a matching placebo suspension under overnight fasted conditions. Sentinel dosing (1 subject to receive CVN766 and 1 subject to receive placebo) will be used in each cohort to ensure adequate safety and tolerability evaluation prior to administering CVN766 or placebo to the remainder of the subjects within the cohort. The planned dose levels will be 5, 15, 45, 125, and 250 mg CVN766. Each following dose level may be higher, lower, or remain the same as the preceding cohort. Additional cohort(s) may be added if deemed necessary by the SRG to fully characterize the safety and tolerability of CVN766.
To assess the effect of food on CVN766 bioavailability in suspension formulation, the single-dose administration will be repeated in a single cohort (S3) after ingestion of a standardized high-fat, high-calorie meal. Once the safety of the S3 cohort dose level has been assessed, the S3 cohort subjects will return to the clinic (no sooner than 14 days after their prior dose, or at least 4 half-lives, has lapsed based on preliminary PK data, whichever is longer). They will receive the same dose as before, administered after ingesting a standardized breakfast. Subjects will finish at least approximately 85% of their breakfast within 30 minutes and receive an investigational product 30 minutes (± 5 minutes) after beginning the meal. Sentinel dosing will not be required for subjects returning to the clinic for the fed regimen. If the CVN766 PK parameters in the fasted S3 cohort reveal poor absorption with inconclusive results, the fed cohort will be deferred until a higher dose level.
On Day 1, subjects will undergo safety monitoring and PK sampling from blood plasma through 72 hours post-dose and, for cohort S3 (fasted) only, from CSF via lumbar puncture at 3 hours post-dose

2.1.2 Part 2 MAD is a Multiple-Dose Regimen

Approximately 24 healthy male and female subjects aged 18 to 55 will be enrolled in 1 of the 3 multiple-dose cohorts (designated as M1 through M3, respectively) in an ascending fashion. The dose levels planned to be studied in the multiple-dose regimen are 45, 125, and 250 mg CVN766 for multiple-dose cohorts M1 through M3, respectively. Each multiple-dose cohort will consist of 8 subjects randomized to CVN766 or placebo, whereby 6 subjects will receive a daily oral dose of CVN766, and 2 subjects will receive matching placebo for 7 days. Dosing will be administered in the fasting state; the SRG can change this if exposure is higher in the fed state. The planned dosing duration for the multiple-dose cohorts is 7 days. However, the duration may be increased to ≤14 days if preliminary PK data suggest steady-state will not be achieved within 6 days of daily dosing.

On Day 1 subjects, will undergo safety monitoring and PK sampling from blood plasma through 24 hours post-dose and on Day 7, will undergo safety monitoring and PK sampling from blood plasma through 72 hours post-dose. Additionally, PK samples will be collected on Days 3, 4, 5 and 6 prior to the next planned dose. For cohort M1, on day 7 only, subjects will undergo PK sampling from CSF via lumbar puncture at 3 hours post dose and PK sampling from urine over 24 h on Day 1 and Day 7. CSF samples may also be taken from M2 and M3 cohorts at the SRG's discretion.

Figure 1: Study Design



2.2 Objectives

Primary objective(s)

• To characterize the safety and tolerability profile of escalating dose levels of CVN766 suspension when administered as a single oral dose or daily oral doses for 7 days in healthy subjects.

Secondary objective(s)

The secondary objectives of this study are:

• To characterize the single-dose PK profile of CVN766 in plasma, and CSF

• To characterize the multiple-dose PK profile of CVN766 in plasma, and CSF

• To assess the effect of food on the bioavailability of CVN766 in the current formulation

Exploratory objective(s)

The exploratory objectives of this study are:

- To explore possible drug metabolic enzyme and transporter polymorphisms that may contribute to variability in CVN766 PK, or safety

[redacted]

2.3 Endpoints

Primary endpoint(s)

The primary endpoints of this study will be the following:

- Percentage of subjects who experience at least one treatment-emergent adverse event (TEAE)
- Percentage of subjects with abnormal and clinically significant (CS) safety laboratory test results at least once post-dose
- Percentage of subjects with abnormal and CS electrocardiogram (ECG) test results at least once post-dose
- Percentage of subjects with abnormal and CS vital sign measurements at least once post dose

Secondary endpoints(s)

- Single-dose plasma PK parameters of CVN766 including time to maximum plasma concentration (T_{max}), area under the plasma concentration-time curve from time 0 to 24 (AUC_{24}) and time 0 to infinity (AUC_{inf}), and terminal elimination half-life ($t_{1/2z}$) Multiple-dose plasma PK parameters of CVN766 including C_{min}, C_{trough}, C_{max}, AUC from time 0 to the end of dosing interval (AUC_t), terminal elimination half-life ($t_{1/2z}$), accumulation ratio (R_{acc}), time to steady-state ($T_{ss,max}$), steady-state C_{max} ($C_{max,ss}$), and steady-state C_{min} ($C_{min,ss}$) Single-dose and multiple-dose CSF concentrations and CSF: plasma ratios of CVN766

Other endpoints(s)

- Change from baseline in safety laboratory and ECG test results and vital signs.
- Additional plasma PK parameters of CVN766: CL/F or CL/Fss and Vz/F or Vz/Fss [redacted]

2.4 Sample Size

Sample size is formed by a total of 64 healthy male and female subjects 18 to 55 years old. In SAD, up to 40 adult subjects. Five cohorts (Cohorts 1 to 5) of 8 subjects each (40 subjects in total) will receive a single dose of CVN766 or matching placebo orally.

In MAD, up to 24 adult subjects. Three cohorts (Cohorts 1 to 3) of 8 subjects each (24 subjects in total) will receive a daily dose of CVN766 orally.

Since there is no formal statistical hypothesis testing, no formal sample size calculation has been performed. The proposed sample sizes for each study part are typical for studies at this phase of development and are deemed sufficient to evaluate the study objectives for this Phase 1 study.

2.5 Randomization

In SAD, five cohorts (Cohorts 1 to 5) of 8 subjects each (40 subjects in total) will receive a single dose of CVN766 or matching placebo. Within each cohort, 6 subjects will be randomly assigned to receive CVN766, and 2 subjects will receive matching placebo. For each cohort, a sentinel group of 2 subjects will initially be randomized to receive CVN766 or placebo (1:1 ratio) on the same day to allow for the assessment of any acute adverse events (AEs). The remaining 6 subjects (5 CVN766 and 1 placebo) will be randomized and dosed at least 24 hours after the sentinel group, following a review of available safety data by the Sponsor and Principal Investigator (PI).

In MAD, three cohorts (Cohorts 1 to 3) of 8 subjects each (24 subjects in total), will be enrolled. Within each cohort, 6 subjects will be randomly assigned to receive CVN766, and 2 subjects will receive matching placebo.

3. STATISTICAL CONSIDERATIONS

Data will be handled and processed per the sponsor's representative (Novotech) Standard Operating Procedures (SOPs), which are written based on the principles of good clinical practice (GCP).

Each study part will be presented separately.

3.1 General Considerations

All data collected on the electronic case report form (eCRF) will be presented in the data listings and will be listed and sorted by treatment arm, participant number and visit, where applicable. All descriptive summaries will be presented by treatment group and nominal visit/time point (where applicable).

Unless otherwise stated, the following methods will be applied:

- Continuous variables: Descriptive statistics will include the number of non-missing values (n), arithmetic mean, standard deviation (SD), median, minimum, and maximum values.

  The minimum and maximum values will be displayed to the same decimal precision as the source data, the arithmetic mean, SD, and median values will be displayed to one more decimal than the source data for the specific variable.

  The appropriate precision for derived variables will be determined based on the precision of the data on which the derivations are based, and statistics will be presented in accordance with the above-mentioned rules.

- PK data: The actual blood sampling dates and times relative to dosing time will be listed by participant and nominal sampling time, with time deviation calculated, for all participants with available plasma concentration data, including participants excluded from the PK population. Individual (for each participant) and mean CVN766 concentrations over time will be displayed graphically in linear and semi-logarithmic plots of CVN766 concentrations versus time. The actual collection time will be used for individual plasma CVN766 concentration curves and the nominal time will be used for the plots of mean plasma CVN766 concentration curves.

  For PK concentration data, the number of non-missing values, number of below limit of quantification (BLQ) values, arithmetic mean, standard deviation, median, minimum, maximum, coefficient of variation (CV%), geometric mean and geometric coefficient of variation (geo CV%) values will be presented. For the calculation of summary statistics, unrounded data will be used and reported to three significant figures with the exception of n, n BLQ, and CV% which will be presented to the nearest integer and one decimal place, respectively.

  For PK parameter data, the number of non-missing values, arithmetic mean, standard deviation, median, minimum, maximum, coefficient of variation (CV%), geometric mean and geometric coefficient of variation (geo CV%) values will be presented. Individual PK parameters will be presented to three significant figures with the exception of λz which will be presented to four decimal places.

- Categorical variables: Descriptive statistics will include counts and percentages per category. The denominator in all percentage calculations will be the number of participants in the relevant analysis population with non-missing data, unless specifically stated otherwise. Percentages will be displayed to one decimal place. Proportions will be displayed in 3 decimal places.

- Repeat/unscheduled assessments: Only values collected at scheduled study visits/time points will be presented in summary tables. If a repeat assessment was performed, the result from the original assessment will be presented as the result at the specific visit/time point. All collected data will be included in the data listings.

- Assessment windows: All assessments will be included in the data listings and no visit windows will be applied to exclude assessments that were performed outside of the protocol specified procedure windows.

- Result display convention: Results will be center aligned in all summary tables and listings. Participant identifiers visit and parameter labels may be left-aligned if required.
- Date and time display conventions: The following display conventions will be applied in all outputs where dates and/or times are displayed:

  Date only: YYYY-MM-DD

  Date and time: YYYY-MM-DD HH:MM

If only partial information is available, unknown components of the date or time will be presented as 'NK' (not known), i.e., '2016-NK-NK'. Times will be reported in military time.

3.2 Key Definitions

The following definitions will be used:

- Baseline: The baseline value is defined as the last available valid (quantifiable continuous or categorical value), non-missing observation for each participant prior to first study drug administration. Repeat and unscheduled assessments will be included in the derivation of the baseline values.
- Change from Baseline: The change from baseline value is defined as the difference between the result collected/derived at a post-baseline visit/time point and the baseline value.

  The change from baseline value at each post-baseline visit/time point will be calculated for all continuous parameters using the following formula:

  Change from Baseline Value = Result at Visit/Time Point – Baseline Value

  The change from baseline value will only be calculated if the specific post-baseline visit/time point result and the baseline value for the parameter are both available and will be treated as missing otherwise.
- Study day: The study day of an event is defined as the relative day of the event starting with the date of the first study drug administration (reference date) as Day 1 (there will be no Day 0).

  The study day of events occurring before the first study drug administration will be calculated as:

  Study Day = (Date of Event - Date of First Study Drug Administration)

  For events occurring on or after Day 1, study day will be calculated as:

  Study Day = (Date of Event - Date of First Study Drug Administration) + 1

  Study days will only be calculated for events with complete dates and will be undefined for events that are 'Ongoing' at the end of the study.

  Relative days compared to an alternative reference point will be calculated similarly, but the alternative starting reference start date will be used instead of the date of the first study drug dosing.
- Actual Time from First Dose (hours) = (Date/Time of PK Sample collection) – (Date/Time of First Dose on Day 1)
- Actual Time from Last Dose (hours) = (Date/Time of PK Sample collection) – (Date/Time of Last Dose), where the last dose = Most Recent Previous Dose.
- Actual Time Deviation (hours) = (Actual PK Sample Collection Time Post Dose) – (Scheduled PK Sample Collection Time Post Dose).
- Prior Medications: Prior medications are defined as any medication where the use was stopped prior to the first administration of the study medication.
- Concomitant Medications: Concomitant medications are defined as any medication (other than the study drug) that was used at least once after the first administration of the study drug.

Medications that were stopped on the same date as the first study drug administration will be defined as concomitant medications. If a clear determination cannot be made (partial medication end dates) the medication will be classified as concomitant

- Treatment Emergent Adverse Events (TEAEs): are defined as adverse events that occurred within 30 days (onset date – last date of dose + 1 ≤ 30) after study drug administration.

3.3 Inferential Analyses

Descriptive statistics will be used to summarize the safety and PK data. No formal hypothesis testing is planned.

All analyses (unless otherwise specified) will be performed at a two-sided 10% level of significance.

- Dose Proportionality

Dose proportionality will be evaluated for C_{max}, AUC_{inf}, AUC_t, AUC_{24} (SAD) and steady state parameters AUC_{tau} and $C_{max,ss}$ (MAD). Data will be presented graphically and a statistical analysis using the power model will be conducted. The analysis will be divided into days:

SAD: C_{max}, AUC_{24}, AUC_t, AUC_{inf}

MAD Day 1: C_{max}, AUC_{24}

MAD Day 7: $C_{max,ss}$, AUC_{tau}.

The model will include the log_e-transformed CVN766 dose level as an independent variable. This model will be used to investigate the null hypothesis (H0: ß=1). Dose proportionality will be rejected (H1: ß not equal 1) if the 90% CI of the estimated slope falls outside the critical interval.

The power model will have the form:

Y = a*(dose)b

where Y is the PK parameter, and a and b are the coefficient and exponent, respectively, of the power equation.

By taking the natural logarithm (ln), the power model can be analyzed using linear regression and has the form:

ln(Y) = ln(a)+b*ln(dose) + error =α + β*ln(dose) + error,

where α is the intercept, and β is the slope, and ln(dose) is based on the dose size for each subject. Estimates of slope and intercept along with their 90% confidence intervals will be reported. A minimum of 3 values per dose must be available for a given parameter to estimate dose proportionality using the power model. For dose proportionality, the slope of the regression line (b) = 1 and for dose independence b = 0.

Apparent dose linearity and proportionality of PK Parameters will be assessed graphically as well. The scatter plots and power model regression line will be plotted together with the natural log-transformed PK parameters as the values on the y-axis, and the natural log-transformed dose level as the values on the x-axis. Regression/scatter plot for SAD and MAD in the log-log scale for the Hummel power analysis will be performed by day.

- Food Effect

The effect of fed/fasting state on PK and bioavailability of CVN766 will be analyzed. The analysis will be descriptively. In addition, a random effects mixed model on the log-transformed pharmacokinetic parameters (AUC_t, AUC_{inf}, AUC_{24}, and C_{max}) will be applied to explore the effect of food, where meal status (fed vs. fasted) will be included as a fixed effect and participant will be included as a random effect. The geometric mean for fed/fasted and their 90% CIs will be estimated from the model based on the least squares means. The ratio of the geometric means (geometric mean ratio) and its 90% CI of the

fed data compared to the fasted data will be obtained based on the exponential of the difference of least-squares means (LSM) from the model.

- Gender Effect

The effect of gender (male vs. female) on Dose Normalized PK parameters of CVN766 will be analyzed. A random effects mixed model on the log-transformed pharmacokinetic parameters:

SAD: C_{max}/Dose, AUC_{24}/Dose, AUC_t/Dose, AUC_{inf}/Dose and $t_{1/2z}$

MAD Day 1: AUC_{24}/Dose, C_{max}/Dose, AUC_t/Dose, $t_{1/2z}$ and $t_{max.}$

MAD Day 7: $C_{max,ss}$/Dose, AUC_{tau}/Dose, AUC_t/Dose, $t_{1/2z}$ and $t_{max.}$

will be applied to explore the effect of gender, where gender (male vs. female) will be included as a fixed effect and participant will be included as a random effect. The geometric mean for Male/Female and their 90% CIs will be estimated from the model based on the least squares means. The ratio of the geometric means (geometric mean ratio) and its 90% CI of the Male data compared to the Female data will be obtained based on the exponential of the difference of least-squares means (LSM) from the model.

Point estimates and 90% CIs for differences on the log scale will be exponentiated to obtain estimates for the ratios of geometric means and respective 90% CIs on the original scale.

For $t_{1/2z}$, a non-parametric analysis (Hodges-Lehmann estimate) will be used to produce the median difference between female and male. A p-value will be generated by the Wilcoxon signed-rank test.

3.4 Multiple Comparisons and Multiplicity Adjustments.

Not applicable for this study.

3.5 Handling of Missing Data

For the classification of Treatment emergent adverse event (TEAE), Medical History and Concomitant medication, the following will be applied in the following order:

a. If all dates/times (start and stop) missing, the event/medication will automatically be classified as a TEAE/Concomitant medication.

b. For AEs with a missing start date/time, if the event end date/time is prior to first study drug administration, the event will not be classified as a TEAE.

c. If only the AE start year/ medication end year is present and is the same or is after the first study drug administration year unit, the event/medication will be classified as a TEAE/Concomitant medication.

d. If the AE start month and year/medication end month and year are present and are the same or after the first study drug administration month and year units, the event/medication will be classified as a TEAE/Concomitant medication.

e. If start AEs, Concomitant Medication and Medical History Day is missing, it will be assigned as 1st Day of the Month. If AEs, Concomitant Medication and Medical History Month is missing, it will be assigned as 1st Month of the Year and if AEs, Concomitant Medication and Medical History Year is missing, Informed Consent Year will be used.

f. If end AEs, Concomitant Medication and Medical History Day is missing, it will be assigned as 31st . If AEs, Concomitant Medication and Medical History Month is missing, it will be assigned as 12.

For the PK analysis the following will be applied:

a. For the concentration descriptive summaries, concentrations may be excluded if sampling time deviation is considered large to affect the profile at the discretion of the pharmacokineticist.

b. Concentrations that are below limit of quantification (BLQ) prior to the first quantifiable value will be set equal to zero. Post dose BLQ concentrations, post T_{max}, will be set to missing.

c. Where there are no results (NR), these will be set to missing.

d. If more than 75% of values per nominal timepoint and treatment group are BLQ, then all descriptive statistics, except for nBLQ, will be denoted as not calculable (NC).

e. For the calculation and graphical representation (semi-log and log-log plots) of geometric descriptive statistics, 0 values will be set to missing.

f. For the purpose of calculating the non-compartmental PK parameters, concentrations that are BLQ prior to the first quantifiable value will be set equal to zero. BLQ values after measurable concentrations will be set to missing. Concentrations in the terminal phase, which is preceded by two BLQ values, will be set to zero.

g. For the calculation of summary statistics of PK parameters, all NR and NC values in a data series will be set to missing.

Conversion of categorical values

In some instances, continuous variables are expressed as a range (i.e., < 10). In such cases, values may be converted to the range boundary (upper or lower limit as applicable). As an example, a value of <10 may be converted to 10. Such substitutions will be clearly documented in the footnotes of relevant outputs.

3.6 Coding of Events and Medications

Medical history and AE verbatim terms will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) using the latest version available at the time of study commencement. Terms will be coded to the full MedDRA hierarchy, but the system organ class (SOC) and preferred terms (PT) will be of primary interest for the analysis.

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary using the latest version available at the time of study commencement. Medications will be mapped to the full WHO-DD Anatomical Therapeutic Chemical (ATC) class level 4 and reported to class level 3 and 4 hierarchy, but PTs will be of primary interest in this analysis.

3.7 Treatment Groups

The following treatment group labels will be used for all summary outputs.

Part 1 (SAD):

This representation as below will only be used for the descriptive summary of concomitant medication, medical history and AEs and will not be based on feeding status:

- S1: CVN766 5 mg
- S2: CVN766 15 mg
- S3 Fasted: CVN766 45 mg
- S3 Fed: CVN766 45 mg
- S4: CVN766 125 mg
- S5 CVN766 250 mg
- Overall CVN766
- Overall Placebo
- S3 Fed: Placebo
- Overall

Note: Overall CVN766 is the pooled group of all participants with active treatment. The assessments for the participants with active treatments in Cohort S3 Fed: CVN766 45 mg condition are not counted in 'Overall CVN766', and they will be counted under 'S3 Fed: CVN766 45 mg'. 'Overall Placebo' is the pooled group of all participants with placebo. The assessments for the participants with placebo in Cohort S3 fed condition are not counted in 'All Placebo', and they will be counted under 'A3/Placebo/Fed'. In demographic and baseline characterises summary tables, Cohort S3 fed condition is not needed as appropriate.

Part 2 (MAD):

- M1: CVN766 45 mg
- M2: CVN766 125 mg
- M3: CVN766 250 mg
- Overall CVN766
- Overall Placebo

- Overall

Note: Overall CVN766 is the pooled group of all participants with active treatment.

Overall Placebo is the pooled group of all participants with placebo.

4. ANALYSIS SETS

In this study 3 analysis populations are defined: Safety and PK.

Furthermore, any additional exploratory analysis not identified in the SAP will be identified in the final CSR as exploratory post hoc analyses, including analyses for additional study populations or subgroups of interest.

4.1 Population Descriptions

Safety Set

The Safety Analysis Set will consist of all subjects who are enrolled and receive study drug. Subjects in this analysis set will be used for demographic, baseline characteristics, and safety summaries.

PK Set

The PK set will consist of all subjects who receive study drug and have at least 1 measurable plasma concentration.

If any subjects are found to be non-compliant in dosing schedule or with incomplete data, a decision will be made on a case-by-case basis as to their inclusion in the analysis but will be presented in the subject listings.

5. PARTICIPANT DISPOSITION AND ANALYSIS POPULATIONS

Participant disposition and analysis population analysis will be based on Safety population. Participant disposition and analysis populations will be summarized descriptively as described in section 3.1 (categorical descriptive analysis).

Participant Disposition

Participant disposition will include the number of participants who completed the treatment/study as planned, participants withdrawn from the treatment /study, as well as the primary reason for early termination. Participant disposition will be summarized descriptively.

Analysis Populations

The number of participants included in each study populations will be summarized descriptively.

In addition, the inclusion of each participant into/from each of the defined analysis populations will be presented in the by-participant data listings.

6. PROTOCOL DEVIATIONS

Protocol deviations will be presented for each participant in the by-participant data listings, sorted by study part, dose level and participant ID based on the All-Enrolled population.

Prior to database lock, all protocol deviations will be reviewed by medical monitors and assigned a status of importance if qualifying as such.

Protocol deviations, including Minor and Important protocol deviations, will be categorized as noted in the Protocol deviation management plan version 4.0 amendment 3 dated 19 May 2022.

All protocol violations that impact the safety of the patients and/or the conduct of the study and/or its evaluation will be reported. These include:

- Patients who are dosed on the study despite not satisfying the inclusion criteria
- Patients who develop withdrawal criteria whilst on the study but are not withdrawn
- Patients who receive the wrong treatment or an incorrect dose
- Patients who receive an excluded concomitant medication
- Deviations from GCP.

The identification of these and other CSR-reportable deviations will be based on the inclusion/exclusion criteria or other criteria presented in the protocol.

7. DEMOGRAPHIC AND BASELINE INFORMATION

Demographic and baseline information analysis will be based on Safety population. Demographic and baseline information will be summarized descriptively as described in section 3.1.

7.1 Demographics

The following demographic parameters will be analyzed:

Continuous descriptive analysis:

- Age (years)
- Height (cm)
- Weight (kg)
- BMI (kg/m^2)

Categorical descriptive analysis:

- Sex
- Childbearing Potential
- Race
- Ethnicity

7.2 Medical /Surgical history

Medical / Surgical history will be coded using MedDRA® and will be presented in the by-participant data listings. Medical history to be obtained will include determining whether the subject has any significant conditions or diseases that stopped at or prior to signing the ICF.

7.3 Hepatitis panel and HIV Antibody Test

Hepatitis B Antigen (HBsAg), Hepatitis C Antibody (HCVAb), and Human Immunodeficiency Virus (HIV-1/HIV-2 Antibody) results will be presented in the by-participant data listings.

7.4 Alcohol, Urine Drug & Cotinine Screen Test

Urine Drug Test results will be presented in the by-participant data listings.

7.5 Follicle stimulating hormone (FSH) Test

FSH Test results will be presented in the data listings.

7.6 Pregnancy Test (Serum and Urine)

Serum and urine pregnancy test results will be presented in the by-participant data listings.

8. TREATMENT EXPOSURE

All study drug administration information (study drug administered (Yes/No), reason not administered, dose administered (mg), date and time of administration, vomiting (Yes/No), lot number/ bottle Number and date/time of first/last meal will be presented in the by-participant data listings under the Safety Set.

9. PRIOR AND CONCOMITANT MEDICATIONS

Concomitant medications will be coded using the most current version of the World Health Organization Drug Dictionary (WHO-DD) and summarized by Anatomical Therapeutic Chemical (ATC) class Level 3 and PT and will be presented alphabetically as noted in section 3.1 (categorical descriptive analysis) using Safety Set. All concomitant treatments, blood products, as well as nondrug interventions received by patients from screening until the end of study visit will be recorded on the eCRF.

The number and percentage of subjects using at least one concomitant medication will be displayed together with the number and percentage of subjects using at least one medication within each therapeutic class (ATC-Level 3) and preferred name A participant who used the same medication on multiple occasions will only be counted once in the specific category (PT). These will be summarized under the Safety population for dose levels defined in section 3.5 Prior medications will be presented in the by-participant data listings.

For food effect cohort, a concomitant medication starting in period 1 (Fasted) and continuing into the next period (Fed) is counted only in the onset period.

10. PHARMACOKINETICS

10.1 Collection of Plasma/Serum Samples for PK Analysis SAD

All PK analyses, summary tables and figures will be based on the PK set. All analyses will be summarized as described in section 3.1 (PK - continuous descriptive analysis). All listings will be based on the Safety set except for the PK parameter listings.

For SAD (Part 1, Cohorts 1, 2, 3a, 4, 5 and Cohort 3 FE), blood samples will be collected at Pre-dose (within 15 minutes prior to dosing) and at 0.5, 1, 1.5, 2, 3, 5, 8, 12, 16, 24-, 36-, 48-, and 72-hours post-dose. A blood sample will be collected prior to discharge in case of early termination.

Table 6 Collection of Blood Samples for PK Analysis in Single-Dose Cohorts

Sample Type	Dosing Day	Time Post-dose (hours).
Plasma	1	Pre-dose (within 15 minutes prior to dosing) and at 0.5, 1, 1.5, 2, 3, 5, 8, 12, 16, 24-, 36-, 48-, and 72-hours post-dose.

10.2 Collection of Plasma/Serum Samples for PK Analysis MAD

For MAD (Part 2), blood samples will be collected as follows: Day 1: Pre-dose (within 15 minutes prior to dosing) and at 0.5, 1, 1.5, 2, 3, 5, 8, 12, 16, and 24 (Day 2 pre-dose) hours post-dose. Day 3, Day 4, Day 5, and Day 6: Pre-dose (within 15 minutes prior to dosing). Day 7: Pre-dose (within 15 minutes prior to dosing) and at 0.5, 1, 1.5, 2, 3, 5, 8, 12, 16, 24, 36, 48, and 72 (a) hours post-dose. A blood sample will be collected prior to discharge in case of early termination.

Table 7 Collection of Blood Samples for PK Analysis in Multiple-Dose Cohorts

Sample Type	Dosing Day	Time Post-dose (hours).
Plasma	1	Pre-dose (within 15 minutes prior to dosing) and at 0.5, 1, 1.5, 2, 3, 5, 8, 12, 16, and 24 (Day 2 pre-dose) hours post-dose.
	3,4,5,6	Pre-dose (within 15 minutes prior to dosing)
	7	Pre-dose (within 15 minutes prior to dosing) and at 0.5, 1, 1.5, 2, 3, 5, 8, 12, 16, 24, 36, 48, and 72 [(a)] hours post-dose.

(a) If emerging PK data indicate the CVN766 $t_{½}$ is 15 hours (or less), the 72-hour timepoint is unnecessary.

[redacted]

10.5 Pharmacokinetic Parameters

Part 1 – Single Ascending Doses

The following pharmacokinetic parameters will, where possible, be determined from the plasma concentrations and CSF of analyte using non-compartmental methods via Phoenix WinNonlin Version 8.3 or higher.

Part 1 – Single Ascending Dose

Parameter	Definition
C_{max}	Observed maximum CVN766 concentration which is directly determined from the plasma concentration time profiles
T_{max}	Time to observed maximum observed CVN766 concentration. If the same C_{max} concentration occurs at different time points, T_{max} is assigned to the first occurrence of C_{max}.
T_{last}	Time to last observed CVN766 concentration.
AUC_{24}	The area under the plasma CVN766 concentration-time curve, from time 0 (time of dosing) to 24 hours, calculated by linear trapezoidal/ linear interpolation method
AUC_t	Area under the drug concentration-time curve, from time 0 (time of dosing) to the last measurable concentration using linear trapezoidal/ linear interpolation method
AUC_{inf}	The area under the plasma CVN766 concentration-time curve from time 0 (time of dosing) extrapolated to infinity. AUC_{inf} is calculated as the sum of AUC_t plus the ratio of the last measurable plasma concentration (C_{last}) to the elimination rate constant (λ_z), calculated by linear trapezoidal/ linear interpolation method.
$AUC_{\%extrap}$	The percentage of the AUC that has been extrapolated beyond the last observed data point, using the following formula, calculated by linear trapezoidal/ linear interpolation method $AUC_{\%extrap} = (AUC_{inf} - AUC_t/(AUC_{inf})*100$
λ_z	Apparent terminal elimination rate constant calculated by linear regression of the terminal linear portion of the log concentration vs. time curve.
$t_{½}$	Apparent plasma terminal half-life calculated as ln (2)/λ_z
CL/F	Apparent total plasma clearance, using the following formula Dose/AUC_{inf}.
V_z/F	Apparent volume of distribution based on the terminal phase, reported to 3 significant figures and calculated as: Dose/(λ_z×AUC_{inf}).
CSF:Plasma ratio	Ratio of the CVN766 concentration in CSF vs. the CVN766 concentration in plasma at 3h post dose.
DN_C_{max}	Dose-normalized C_{max} = Cmax/dose
DN_AUC_{24hr}	Dose-normalized AUC_{24hr} = AUC_{24hr}/dose
DN_AUC_t	Dose-normalized AUC_t = AUC_t/dose

DN_AUC_{inf}	Dose-normalized AUC_{inf}= AUC_{inf}/dose

Part 2 – Multiple Ascending Doses

All PK analyses, PK summary tables and figures will be based on the PK set. All analyses will be summarized as described in section 3.1 (PK - continuous descriptive analysis). All listings will be based on the PK set. All missing and BLQ handling of urine concentrations for PK analysis will be based on section 3.5.

Approximate attainment of steady state will be visually assessed by plotting mean C_{trough} concentrations.

The following pharmacokinetic parameters will, where possible, be determined from the plasma concentrations and CSF of analyte using non-compartmental methods via Phoenix WinNonlin Version 8.3 or higher.

Parameter at Day 1	**Definition**
C_{max}	Observed maximum CVN766 concentration in the dosing interval at Day 1
$C_{min,}$	Observed minimum CVN766 concentration in the dosing interval at Day 1
$C_{trough\ DayN}$	Plasma concentration at the end of the dosing interval at day N, where N is Day 2,3,4,5,6,or 7
T_{max}	Time to reach maximum CVN766 concentration at Day 1
T_{min}	Time of minimum observed CVN766 concentration at Day 1
AUC_t	Area under the drug concentration-time curve, from time 0 (time of dosing) to the last measurable concentration at steady state using 'linear trapezoidal/ linear interpolation method' when t is < 24h. Determined following Dose on Day 7
AUC_{24}	The area under the plasma CVN766 concentration-time curve, from time 0 to 24 hours, calculated by linear trapezoidal/ linear interpolation method. Determined following Dose on Day 1
CSF:Plasma ratio:	Ratio of the CVN766 concentration in CSF vs the CVN766 concentration in plasma at 3 h post dose
DN_$C_{max,ss}$	Dose-normalized $C_{max,ss}$ = $C_{max,ss}$/dose
DN_AUC_{24hr}	Dose-normalized AUC_{24hr}= AUC_{24hr}/dose
DN_AUC_t	Dose-normalized AUC_t = AUC_t/dose

Parameter at Day 7	Definition
$C_{max, ss}$	Observed maximum CVN766 concentration in the dosing interval at steady state at Day 7.
$C_{min,ss}$	Observed minimum CVN766 concentration in the dosing interval at steady state at Day 7.
$C_{trough\ DayN}$	Plasma concentration at the end of the dosing interval at day N, where N is Day 2,3,4,5,6,or 7
$C_{avg,ss}$	Average steady state CVN766 concentration, determined following Dose on Day 7, using the following formula $C_{avg,ss} = AUC_{tau}/ tau$ Where, tau = dosing interval
$T_{max, ss}$	Time to reach maximum CVN766 concentration in the dosing interval at steady state at Day 7.
$T_{min, ss}$	Time of minimum observed CVN766 concentration in the dosing interval at steady state at Day 7.
$T_{last, ss}$	Time of the last CVN766 concentration assessment in the dosing interval at steady state. Determined following Dose on Day 7
AUC_t	Area under the drug concentration-time curve, from time 0 (time of dosing) to the last measurable concentration at steady state using 'linear trapezoidal/ linear interpolation method' when t is < 24h. Determined following Dose on Day 7
AUC_{tau}	Area under the plasma CVN766 concentration-time curve over a dosing interval at steady state using the linear trapezoidal/ linear interpolation method. Determined following Dose on Day 7
AUC_{inf}	The area under the plasma CVN766 concentration-time curve from time 0 (time of dosing) extrapolated to infinity. AUC_{inf} is calculated as the sum of AUC_t plus the ratio of the last measurable plasma concentration (C_{last}) to the elimination rate constant (λ_z), calculated by linear trapezoidal/ linear interpolation method. Determined following dose on Day 1
λ_z or Kel	Apparent terminal elimination rate constant calculated by linear regression of the terminal linear portion of the log concentration vs. time curve. Determined following Dose on Day 7
$t_{½}$	Apparent plasma terminal half-life calculated as ln (2)/$\lambda_{z..}$ Determined following Dose on Day 1 and Day 7
CL/F_{ss}	Apparent total plasma clearance at steady state, using the following formula Dose/AUC_{tau}. Determined following Dose on Day 7
Vz/F_{ss}	Apparent terminal volume of distribution, calculated as: Dose/ ($\lambda_z \times AUC_{0\text{-}tau}$). Determined following Dose on Day 7
RA_{Cmax}	Accumulation ratio based on C_{max} in Part 2 calculated as $C_{max,ss}$ on Day 7/C_{max} on Day 1 for each individual.
RA_{AUC}	Ratio of the measure of systemic drug exposure over a specific dosing interval at steady state to the measure of systemic drug exposure over a specific dosing interval after single dose administration. It is calculated as $AUC_{tau\ Day\ 7}/AUC_{24\ Day\ 1}$
CSF:Plasma ratio:	Ratio of the CVN766 concentration in CSF vs the CVN766 concentration in plasma at 3 h post dose
DN_$C_{max,ss}$	Dose-normalized $C_{max,ss}$ = $C_{max,ss}$/dose
DN_AUC_t	Dose-normalized AUC_t = AUC_t/dose
DN_AUC_{tau}	Dose-normalized AUC_{tau} = AUC_{tau}/dose
DN_AUC_{inf}	Dose-normalized AUC_{inf} = AUC_{inf}/dose

C_{trough} determination for MAD cohorts:

C_{trough_Day1}	The pre-dose morning concentration observed on day 2 prior to the next dosing
C_{trough_Day2}	The pre-dose morning concentration observed on day 3 prior to the next dosing
C_{trough_Day3}	The pre-dose morning concentration observed on day 4 prior to the next dosing
C_{trough_Day4}	The pre-dose morning concentration observed on day 5 prior to the next dosing
C_{trough_Day5}	The pre-dose morning concentration observed on day 6 prior to the next dosing
C_{trough_Day6}	The pre-dose morning concentration observed on day 7 prior to the next dosing

C_{trough_Day1}, C_{trough_Day2}, C_{trough_Day3}, C_{trough_Day4}, C_{trough_Day5}, C_{trough_Day6} will be listed for each MAD cohort and dose level.

Additional pharmacokinetic parameters may be determined where appropriate.

Pharmacokinetic analysis will be carried out using actual doses and blood sampling times (post dose hourly sampling times for the specified days), where possible. If actual times are missing, nominal times may be used with sponsor approval.
Plasma, urine, and CSF concentrations of CVN766 will be used as supplied by the bioanalytical laboratory. The units of concentration and resulting PK parameters, with amount or concentration in the unit, will be presented as they are received from the bioanalytical laboratory.

If a PK parameter cannot be derived from a patient's concentration data, the parameter will be coded as NC (i.e., not calculated). NC values will not be generated beyond the day that a patient discontinues. If an individual patient has a known biased estimate of a PK parameter (due for example to a deviation from the assigned dose level and/or concomitant medication violation), this will be footnoted in summary tables and the parameter will not be included in the calculation of summary statistics or statistical analyses.

Pharmacokinetic Noncompartmental Analysis (NCA)

General Plasma NCA Pharmacokinetic Settings

The general settings in Phoenix WinNonlin® for generation of plasma PK parameters are as listed below.

- NCA Model Type: Plasma (200-202)
- Weighting: Uniform
- AUC Calculation Method: Linear trapezoidal/ linear interpolation method
- Dose Options Type: Extravascular
- Slopes Setting Fit Method: Best Fit/Visual Inspection
- Rsq_Adjusted Criteria for 'λ_z': 0.8
- AUC% extrapolation Criteria: 20

10.6 Urine PK Parameters MAD

All PK summary tables and figures will be based on the PK population. All analyses will be summarized as described in section 3.1 (PK - continuous descriptive analysis). All listings will be based on the safety population. All missing and BLQ handling of urine concentrations for PK analysis will be based on section 3.5.

Pharmacokinetic analysis will be carried out using actual doses, actual urine sampling times (start and end times), actual urine volumes, where possible. If actual times are missing, nominal times may be used

with sponsor approval. The following urine pharmacokinetic parameters will, where possible, be determined from the urine concentrations of CVN766 and the respective urine volumes within each collection interval by non-compartmental method using Phoenix WinNonlin software (Version 8.3 or higher, Certara, USA):

Note: PK urine samples and urine volumes will be collected at the following timepoints (± 15 minutes) on Day 1: 0 to 6, 6 to 12, and 12 to 24 hours post dose for MAD and on Days 7: 0 to 6, 6 to 12 and 12 to 24 hours for MAD Cohort 1.

PK concentration and parameter data will be analyzed descriptively as noted in section 3.1.

General Urine NCA Pharmacokinetic Settings

The general settings in Phoenix WinNonlin® for generation of urine PK parameters are as listed below.

- NCA Model Type: Urine (210-212)
- Weighting: Uniform
- AUC Calculation Method (if applicable): Linear trapezoidal/ linear interpolation method

10.7 Criteria for the Calculation of an Apparent Terminal Elimination Half-Life

The start of the terminal elimination phase for each participant will be defined by visual inspection and will generally be the first point at which there is no systematic deviation from the log linear decline in plasma concentrations.

Number of Data Points

At least 3 data points will be included in the regression analysis and not including C_{max}. The number of points and the beginning and end times of the terminal phase will be listed for each individual.

Plausibility

The data will be pharmacokinetically plausible.

Summary of Plasma / Urine PK Concentrations and PK Parameters

Plasma PK (concentration and PK parameters $Ae_{t1\text{-}t2}$, $Fe_{t1\text{-}t2}$, and CL_r) data for Part 1 (SAD) and Part 2 (MAD) will be summarized separately. All PK summary tables and figures will be based on the PK population, and PK listings will be based on PK population. All analyses will be summarized descriptively in general according to section 3.1

The actual blood sampling dates and times relative to dosing time will be listed by participant and nominal sampling time, with time deviation calculated, for all participants with available plasma concentration data, including participants excluded from the PK population. Individual values for PK concentration data will be reported to the same level of precision as received from the bioanalytical laboratory.

Summary of PK concentrations

For the concentration-time data/profile summary, the following will be applied:

- For the concentration descriptive summaries, concentrations may be excluded if sampling time deviation is considered too large to affect the profile at the discretion of the pharmacokineticist.
- Concentrations that are below limit of quantification (BLQ) will be set to 0 for the calculation of standard statistics (i.e. arithmetic mean) and set to missing for the calculation of geometric statistics. For PK parameters, all plasma concentrations will be set to BLQ if prior to first measurable concentration and treated as missing thereafter

Individual (for each participant) and mean (SD) concentrations over time for the analyte will be displayed graphically in linear and semi-logarithmic plots of the analyte concentrations versus time. The actual collection time will be used for individual plasma analyte concentration curves, and the nominal time will be used for the plots of mean plasma analyte concentration curves.

Summary of Plasma PK parameters

PK parameters will be determined for each analyte with intensive PK samplings. For the purpose of calculating the non-compartmental PK parameters, concentrations that are BLQ prior to the first measurable concentration value will be set equal to zero. BLQ values embedded between measurable concentrations will be set to missing. Concentrations that are BLQ in the terminal phase after the last measurable concentration will be set to missing.
It should be noted the imputation of BLQ for the determination of PK parameters is different from the BLQ imputation when PK concentrations are summarized. When PK parameters are estimated by a standard non-compartmental model, actual collection time will be used in the calculation of plasma PK parameters.

Goodness of Fit

- If data permits, the default 'best fit' method by Phoenix WinNonlin will be used for the selection of slopes to determine 'λ_z'. If data do not permit, then the slope selection will be done by visual inspection or by a manual method to determine λ_z.
- When assessing terminal elimination phases, the R^2 adjusted value will be used as a measure of the goodness of fit of the data points to the determined line.
- Regression-based parameters (λ_z or k_{el}, AUC_{inf}, $AUC_{\%extrap}$, $t_{1/2}$, CL/F or CL/Fss, and V_z/F or V_z/Fss) will only be calculated if the R^2 adjusted value of the regression line is greater than or equal to 0.8 If regression-based parameters cannot be calculated, they will be set to "NC", defined as "not calculated" in the data listings and summary tables as appropriate.

Calculation of AUC

- The minimum requirement for the calculation of AUC will be the inclusion of at least 3 consecutive plasma concentrations above the lower limit of quantification (LLOQ), with at least one of these concentrations following C_{max}.
- All AUC values will be calculated using linear trapezoidal/ linear interpolation method

Period of Estimation

- Time period used for the estimation of $t_{1/2}$, where possible, will be over at least 2 half lives.
- Where an elimination half-life is estimated over a time period of less than 2 half-lives, it will be flagged in the data listings at the discretion of the pharmacokineticist, and the robustness of the half-life value and regression-based parameters (λ_z or k_{el}, AUC_{inf}, $AUC_{\%extrap}$, $t_{1/2}$, CL/F or CL/Fss, and V_z/F or V_z/Fss) should be discussed in the study report.

Inferential Analyses

The following endpoints will be analyzed as described in sections 3.3:

- Dose proportionality
    - Dose proportionality - CVN766 SAD
        - AUC_{inf}
        - AUC_t
        - AUC_{24}
        - C_{max}
    - Dose proportionality - CVN766 MAD
        - MAD Day 1: C_{max}, AUC_{24}
        - MAD Day 7: $C_{max,ss}$, AUC_{tau}.
- Food-Effect Assessment (SAD: Cohort S3):

  The following parameters will be analyzed as described in sections 3.3:

    - AUC_t
    - AUC_{inf}
    - AUC_{24}
    - C_{max}
- Gender effect Assessment

  The following parameters will be analyzed as described in sections 3.3:

  SAD : C_{max}/Dose, AUC_{24}/Dose, AUC_t/Dose, AUC_{inf}/Dose, T_{max} and $t_{1/2z}$.

  MAD Day 1: AUC_{24}/Dose, C_{max}/Dose, AUC_t/Dose, $t_{1/2z}$ and t_{max}.

  MAD Day 7: $C_{max,ss}$/Dose, AUC_{tau}/Dose, AUC_t/Dose, $t_{1/2z}$ and t_{max}.

  Details are provided in section 3.3 of SAP.

11. SAFETY

Safety endpoints will be analyzed using the Safety population and will be summarized descriptively as described in section **Error! Reference source not found.**. Safety data will be summarized separately for Part 1 (SAD) and Part 2(MAD).

11.1 Adverse Events

All AEs including will be coded using latest MedDRA version. All AE summaries will be restricted to TEAEs only. AEs will be grouped by system organ class (SOC) and preferred term (PT) and summarized, by actual treatment group and overall. Summary tables will include the number of participants (%) experiencing an event and the number of events. Participants will be counted only once for each SOC and PT level; they will be sorted alphabetically and for PT tables only, they will be ordered with the highest first (categorical descriptive analysis).

For food effect cohort, an adverse event starting in one period and continuing into the next period is counted only in the onset period.

Assigned treatment	Definition
Treatment Period 1 (Fasting)	AE start date/time is on or after the dose date/time of treatment received in Period 1 and prior to the date/time of treatment received in period 2 (fed period) no matter when AE stops.
Treatment Period 2 (Fed)	AE start date/time is on or after the dose date/time of treatment received in Period 2 until the end of study.

For Part 1 (SAD) Cohort S3 food effect arm, TEAE will be further assigned to S3/Fasted (period 1) or S3/Fed (period 2) by using period 2 start date and TEAE's that start post first study drug administration of period 2 (Fed) will not be attributed to treatment during period 1 (Fasted). TEAE's that start post first study drug administration of period 1, but prior to first study drug administration of period 2, will be attributed to period 1 only. TEAEs that start post first study drug administration of period 1 (Fasted) and ongoing will be attributed to Onset period only

The TEAE summaries will include:

- Overall summary of TEAEs.
- TEAE summary by SOC and PT.
- TEAE summary of serious events by SOC and PT.
- TEAE summary by SOC, PT and Severity.
- TEAE summary by SOC, PT and relationship to study drug.
- TEAE summary of events leading to the study drug discontinuation by SOC and PT.
- Overall Frequency of TEAE by PT.
- Overall Frequency of related TEAE by PT.

11.2 Safety Laboratory Assessments

Blood and urine samples will be collected at the time points specified in the Schedule of Events (refer to the Protocol) to conduct hematology, chemistry, and urinalysis (including microscopic examinations) analyses. Clinical laboratory data will be summarized by the type of laboratory test. The number and percentage of subjects who experience abnormal (i.e., outside of reference ranges) and/or clinically significant abnormalities after study drug administration will be presented for each clinical laboratory

measurement. For each clinical laboratory measurement, descriptive statistics will be provided for baseline and all subsequent post-treatment scheduled visits.

Changes from baseline to the post-treatment visits will also be provided. Descriptive statistics of vital signs will also be provided in a similar manner. In addition, shift from baseline in CTCAE grade (where applicable) and by high/low flags (where CTCAE grades are not defined) will be presented by dose level.

The following tests will be performed within each of the specified test panels:

Hematology:	Serum Chemistry:	Urinalysis & Microscopic Urinalysis:
• RBC ($x10^{12}$/L)	• ALT (U/L)	• pH (4.5-8)
• WBC with differential (% and absolute; $x10^{9}$/L)	• Albumin (g/L)	• Specific gravity (1.002-1.030)
• Hemoglobin (g/L)	• Alkaline phosphatase (U/L)	• Protein (g/L)
• Hematocrit (L/L)	• Lipase (U/L)	• Glucose (mmol/L)
• Platelets ($x10^{9}$/L)	• AST (U/L)	• Blood
• PT/INR	• Total bilirubin (umol/L)	• Nitrite
	• Direct bilirubin (umol/L)	• Microscopic Analysis (only if positive dipstick results):
	• Total protein (g/L)	• RBC/high power field
	• Creatinine (umol/L)	• WBC/high power field
	• BUN/Urea (mmol/L)	• Epithelial cells, casts etc
	• Creatine kinase (U/L)	
	• GGT (U/L)	
	• Potassium (mmol/L)	
	• Sodium (mmol/L)	
	• Glucose (mmol/L)	
	• Chloride (mmol/L)	
	• Bicarbonate (mmol/L)	

	• Calcium (mmol/L)	

All laboratory data collected at scheduled and unscheduled visits will be included in the listings, but only results collected as scheduled visits will be included in the summary tables.

If required, the results (and the corresponding normal range cut-off values) for individual parameters may be converted to International System of Units (S.I.) units to summarize the data.

For all the parameters where a unit value has been reported, the parameter names that will be used in the outputs will comprise of the test name and the unit of measure, for example, 'Albumin (g/L)'. For the urinalysis parameters, the parameter name will be the reported test name only. Parameters will be sorted alphabetically within tables and listings.

For all parameters where a normal range limit value was reported, the normal range will be derived based on the available lower and upper limit values and any reported mathematical symbols. If both a lower and upper limit value is available, the normal range will be presented as '(Lower, Upper)'.

The reported results for each parameter with a defined normal range will be classified ('Low', 'Normal', 'High') in relation to the defined normal range limits. If a result is equal to the normal range cut-off value, the result will be considered 'Normal'.

The hematology and chemistry results tables will present summary statistics for each laboratory parameter within the specific test panel. For each parameter, summaries will be presented for the baseline and each scheduled post-baseline visit. In addition, summaries will be presented for the change from baseline values at each scheduled post-baseline visit (continuous descriptive analysis).

In particular, quantitative data will be summarized using simple descriptive statistics (mean, SD, median, minimum, and maximum) of actual values and changes from baseline for each nominal visit over time. The changes computed will be the differences from baseline. Qualitative data based on reference ranges will be described according to the categories (i.e., Low, Normal, High).

The decimal precision to which the summaries for each parameter will be based on the maximum number of decimals to which the reported result or the normal range limits are presented to in the raw data. The results and normal ranges will be displayed to the same decimal precision in the listings.

Additionally, counts (%) of number participants with values out of normal range at each scheduled time point will also be presented along with shift tables that will represent the changes in normal range categories across post-baseline time points (categorical descriptive analysis).

The urinalysis table will present counts and percentages of normal, abnormal clinically significant and clinically significant for the reported results at baseline and each post-baseline visit for all parameters (categorical descriptive analysis).

11.3 Vital Signs

The following vital signs measurements will be taken at the time points specified in the Schedule of Events (refer to the Protocol):

- Pulse (beats/min);
- Systolic Blood Pressure (SBP) (mmHg)
- Diastolic Blood Pressure (DBP) (mmHg)
- Respiratory Rate (breaths/min)
- Body Temperature (ºC)

All vital signs data collected at scheduled and unscheduled visits will be included in the listings, but only results collected as scheduled visits will be included in the summary tables.

Triplicate orthostatic vital signs (blood pressure and heart rate) will be recorded at baseline (Check-in Day -1) 15 minutes apart (the average will be used to determine eligibility).

The parameter names that will be used in the outputs will comprise of the test name and the unit of measure, for example, 'Systolic Blood Pressure (mmHg)'. Parameters will be sorted in the order that the measurements were collected in on the Vital Signs eCRF page within the tables and listings.

Vital signs measurements will present summary statistics for the results at the baseline and each scheduled post-baseline visit for each of the parameters in Supine and Standing position. In addition, summaries will be presented for the change from baseline values at each scheduled post-baseline visit in Supine and Standing position (continuous descriptive analysis). The average of triplicate vital signs in Supine and Standing position will be used as baseline for HR and BP.

In addition, vital signs and postural changes, the individual subject level at each time point between the two positions in which readings are taken (Supine vs Standing) will be reported. At each timepoint standard descriptive stats for HR, sBP and dBP postural data will be reported.

Further, a categorical tabulation for number (percentage) of subjects per time point (and overall categories for any post-exposure timepoint for each parameter separately and for the 2 BP measures together) for the following clinically changes will be created:

- Drop in dBP of ≥10mmHg when moving from supine to standing
- Drop in sBP of ≥20mmHg when moving from supine to standing
- Increase in HR of ≥30bpm when moving from supine to standing

The decimal precision to which the summaries for each parameter will presented will be based on the maximum number of decimals to which the results were reported on the eCRF.

11.4 12-Lead Electrocardiogram (ECG)

The following ECG measurements will be taken at the time points specified in the Schedule of Events (refer to the Protocol):

- Heart Rate (bpm)
- QT interval (msec)
- PR interval (msec)
- QRS interval (msec)
- RR Interval (msec)
- QTcF (msec)
- QTcB (msec)
- ECG clinical interpretation

All ECG data collected at scheduled and unscheduled visits will be included in the listings, but only results collected as scheduled visits will be included in the summary tables.

The parameter names that will be used in the outputs will comprise of the test name and the unit of measure, for example, 'Ventricular Rate (beats/min)'. Parameters will be sorted in the order that the measurements were collected in on the ECG eCRF page within the tables and listings.

ECG measurements will present summary statistics for the results at the baseline and each scheduled post-baseline visit for each of the parameters. In addition, summaries will be presented for the change from baseline values at each scheduled post-baseline visit (continuous descriptive analysis). The average of the replicate measurements should be determined after the derivation of the individual parameter at each time point.

If multiple tracings are done as part of one assessment, the mean of the three tracings per parameter and the worst clinical interpretation per timepoint will be summarized for each participant. All values will be listed including the mean value per parameter and the worst clinical interpretation. Changes from baseline will be calculated based on the mean values of the triplicates where appropriate. The summary of overall interpretation findings table will present counts and percentages for the reported results at baseline and each post-baseline visit/time point. Result categories will be ordered as 'Normal', 'Abnormal Not Clinically Significant (NCS)' and 'Abnormal Clinically Significant (CS)' (categorical descriptive analysis).

The decimal precision for each parameter will be based on the maximum number of decimals to which the results were reported on the eCRF.

11.5 CV Telemetry

By-participant data listings will be created for CV Telemetry at all time points collected in CRF.

11.6 Neurological Exam

By-participant data listings will be created for all Neurological examination parameters at all time points collected in CRF.

11.7 Physical Examinations

By-participant data listings will be created for all physical examination parameters at all time points collected in CRF

12. CHANGES TO THE PLANNED ANALYSIS

Changes to planned analysis include:

- The following endpoint has been added in relation to PK analysis: To potentially identify significative difference between gender of PK parameters in plasma.
- Standard descriptive stats for HR, sBP and dBP postural data will be reported using a categorical tabulation for number (percentage) of subjects per time point in relation to:
    - Drop in dBP of ≥10mmHg when moving from supine to standing
    - Drop in sBP of ≥20mmHg when moving from supine to standing
    - Increase in HR of ≥30bpm when moving from supine to standing
- For triplicate vital sign at Day -1/ baseline average value will be used.
- Pharmacodynamic Exploratory Endpoints will not be included in the SAP.
- To date, RNA/DNA Analysis has not been conducted, and no data is available for the SAP.
- No suicidal assessments were conducted as part of this study; therefore, this will not be included in data listings.
- It was decided that screen failure data will not be entered in the EDC, as it is the site/CRO practice for phase 1 studies because there are hundreds of SFs, and this data is not imperative for any analysis.

- **INTERIM AND FINAL ANALYSIS**

12.1 Final Analysis (End of Study)

No interim analysis is planned.

The final analysis will be conducted after all participants have completed the study, the clinical database has been locked, the analysis populations have been approved and the study has been unblinded.

The final analysis will be based on the final version of the SAP. Any deviations from the planned analysis will be documented in the CSR.

13. SOFTWARE

- SAS® Version 9.4 or higher (SAS Institute, Cary, North Carolina, USA).
- Phoenix WinNonlin® Version 8.3 or higher (Certara, USA).

14. TABLES

Table Number	Table Title	Population
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14.1.1.2	Summary of Participant Enrolment and Disposition MAD	Safety
14.1.2.1	Analysis Set SAD	Safety
14.1.2.2	Analysis Set MAD	Safety
14.1.3.1	Summary of Demographics and Baseline Characteristics SAD	Safety
14.1.3.2	Summary of Demographics and Baseline Characteristics MAD	Safety
14.1.4.1	Summary of Medical History SAD	Safety
14.1.4.2	Summary of Medical History MAD	Safety
14.2	**PK**	
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14.2.1.2	Summary of Plasma Concentrations (ng/mL) of CVN766 MAD	PK
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14.2.2.2	Summary of CSF Concentration (ng/mL) MAD	PK
14.2.3.1	Summary of Urine Concentrations (ng/mL) of CVN766 MAD	PK
14.2.4.1	Summary of Plasma Pharmacokinetic Parameters of CVN766 SAD	PK
14.2.4.2	Summary of Plasma Pharmacokinetic Parameters of CVN766 MAD	PK
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14.2.7.1	Food Effect Assessment of Plasma CVN766 Pharmacokinetic Parameters SAD	PK
14.2.8.1	Gender Effect Assessment of Plasma CVN766 Pharmacokinetic Parameters SAD	PK
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14.3.1.2	Summary of Concomitant Medication MAD	Safety
14.3.3	**Adverse Events**	
14.3.3.1.1	Summary of Overall Treatment Emergent Adverse Events SAD	Safety
14.3.3.1.2	Summary of Overall Treatment Emergent Adverse Events MAD	Safety
14.3.3.2.1	Summary of Treatment Emergent Adverse Events by SOC and PT SAD	Safety
14.3.3.2.2	Summary of Treatment Emergent Adverse Events by SOC and PT MAD	Safety
14.3.3.3.1	Summary of Serious Treatment Emergent Adverse Events by SOC and PT SAD	Safety

Table Number	Table Title	Population
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14.3.3.4.1	Summary of Treatment Emergent Adverse Events by SOC, PT and Severity SAD	Safety
14.3.3.4.2	Summary of Treatment Emergent Adverse Events by SOC, PT and Severity MAD	Safety
14.3.3.5.1	Summary of Treatment Emergent Adverse Events by SOC, PT and Relationship SAD	Safety
14.3.3.5.2	Summary of Treatment Emergent Adverse Events by SOC, PT and Relationship MAD	Safety
14.3.3.6.1	Summary of TEAE leading to the study discontinuation by SOC and PT SAD	Safety
14.3.3.6.2	Summary of TEAE leading to the study discontinuation by SOC and PT MAD	Safety
14.3.3.7.1	Summary of Overall Frequency of TEAE by PT SAD	Safety
14.3.3.7.2	Summary of Overall Frequency of TEAE by PT MAD	Safety
14.3.3.8.1	Summary of Overall Frequency of Related TEAE by PT SAD	Safety
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14.3.4	**Laboratory Parameters**	
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14.3.4.1.1.2	Summary of Hematology & Coagulation MAD	Safety
14.3.4.1.2.1	Summary of Hematology & Coagulation Shifts from Baseline SAD	Safety
14.3.4.1.2.2	Summary of Hematology & Coagulation Shifts from Baseline MAD	Safety
14.3.4.2.1.1	Summary of Serum Chemistry SAD	Safety
14.3.4.2.1.2	Summary of Serum Chemistry MAD	Safety
14.3.4.2.2.1	Summary of Serum Chemistry Shifts from Baseline SAD	Safety
14.3.4.2.2.2	Summary of Serum Chemistry Shifts from Baseline MAD	Safety
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14.3.5.1.1	Summary of Vital Signs SAD	Safety
14.3.5.1.2	Summary of Vital Signs MAD	Safety
14.3.5.2.1	Summary of Orthostatic Vital Signs SAD	Safety
14.3.5.2.2	Summary of Orthostatic Vital Signs MAD	Safety
14.3.5.3.1	Categorical Tabulation of Orthostatic Vital Signs SAD	Safety
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14.3.5.4.1.2	Summary of 12-Lead ECG MAD	Safety
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16.2.1.2.2	Participant Disposition MAD	Safety
16.2.2	**Protocol Deviations**	
16.2.2.1	Protocol Deviations SAD	Safety
16.2.2.2	Protocol Deviations MAD	Safety
16.2.4	**Demographic and Other Baseline Data**	
16.2.4.1.1	Demographics and Baseline Characteristics SAD	Safety
16.2.4.1.2	Demographics and Baseline Characteristics MAD	Safety
16.2.4.2.1	Medical/Surgical History SAD	Safety
16.2.4.2.2	Medical/Surgical History MAD	Safety
16.2.4.3.1	Hepatitis Panel SAD	Safety
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16.2.4.4.1	Alcohol Breath Test SAD	Safety
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16.2.4.5.1	Urine Drug Screen SAD	Safety
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16.2.4.6.1	Follicle-Stimulating Hormone Test SAD	Safety
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16.2.4.7.2	Pregnancy Test MAD	Safety
16.2.4.8.1	Eligibility Criteria SAD	Safety
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Listing Number	Listing Title	Population
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16.2.5.3.1	Meal Records SAD	Safety
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16.2.6.2.1	Urine Concentration of CVN766 MAD	PK
16.2.6.3.1	PK Plasma Parameter for CVN766 SAD	PK
16.2.6.3.2	PK Plasma Parameter for CVN766 MAD	PK
16.2.6.4.1	PK Urine Parameter for CVN766 MAD	PK
16.2.6.5.1	CSF Collection Concentration SAD	PK
16.2.6.5.2	CSF Collection Concentration MAD	PK
16.2.6.6.1	CV Telemetry SAD	PK
16.2.7	**Adverse Events**	
16.2.7.1.1	Adverse Events SAD	Safety
16.2.7.1.2	Adverse Events MAD	Safety
16.2.7.2.1	Serious Adverse Events SAD	Safety
16.2.7.2.2	Serious Adverse Events MAD	Safety
16.2.8	**Laboratory Parameters**	
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16.2.8.1.2	Hematology & Coagulation MAD	Safety
16.2.8.2.1	Serum Chemistry SAD	Safety
16.2.8.2.2	Serum Chemistry MAD	Safety
16.2.8.3.1	Urinalysis SAD	Safety
16.2.8.3.2	Urinalysis SAD	Safety
16.2.9	**Other Safety**	
16.2.9.1.1	Vital Signs SAD	Safety

Listing Number	Listing Title	Population
16.2.9.1.2	Vital Signs MAD	Safety
16.2.9.2.1	12-Lead ECG SAD	Safety
16.2.9.2.2	12-Lead ECG MAD	Safety
16.2.9.3.1	Neurological Exam SAD	Safety
16.2.9.3.2	Neurological Exam MAD	Safety
16.2.9.4.1	Physical Examination SAD	Safety
16.2.9.4.2	Physical Examination MAD	Safety
16.2.10	**Prior & Concomitant Medication**	
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16.2.10.1.2	Prior Medication MAD	Safety
16.2.10.2.1	Concomitant Medication SAD	Safety
16.2.10.2.2	Concomitant Medication MAD	Safety
16.2.11	**Comments**	
16.2.11.1	Comments	Safety

16. FIGURES

Figure Number	Figure Title	Population
14.2	**PK**	
14.2.1.1.1	Individual Plasma Concentrations of CVN766 vs Time Post-Dose (Linear) SAD	PK
14.2.1.1.2	Individual Plasma Concentrations of CVN766 vs Time Post-Dose (Linear) MAD	PK
14.2.1.1.3	Individual Plasma C_{trough} Concentrations of CVN766 vs Time Post-Dose (Linear) MAD	PK
14.2.1.2.1	Individual Plasma Concentrations of CVN766 vs Time Post-Dose (Semi-Log) SAD	PK
14.2.1.2.2	Individual Plasma Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD	PK
14.2.1.2.3	Individual Plasma C_{trough} Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD	PK
14.2.2.1.1	Mean (+/- SD) Plasma Concentrations of CVN766 vs Time Post-Dose (Linear) SAD	PK
14.2.2.1.2	Mean (+/- SD) Plasma Concentrations of CVN766 vs Time Post-Dose (Linear) MAD	PK
14.2.2.1.3	Mean (+/- SD) Plasma C_{trough} Concentrations of CVN766 vs Time Post-Dose (Linear) MAD	PK
14.2.2.2.1	Mean (+/- SD) Plasma Concentrations of CVN766 vs Time Post-Dose (Semi-Log) SAD	PK
14.2.2.2.2	Mean (+/- SD) Plasma Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD	PK
14.2.2.2.3	Mean (+/- SD) Plasma C_{trough} Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD	PK
14.2.3.1.1	Plasma C_{max} versus dose for CVN766 SAD (Log Scale)	PK
14.2.3.1.2	Plasma $C_{max,ss}$ versus dose for CVN766 MAD (Log Scale)	PK
14.2.3.2.1	Plasma AUC_{inf} versus dose for CVN766 SAD (Log Scale)	PK
14.2.3.3.1	Plasma AUC_{24} versus dose for CVN766 SAD (Log Scale)	PK
14.2.3.3.2	Plasma AUC_{24} versus dose for CVN766 MAD (Log Scale)	PK
14.2.3.4.1	Plasma AUC_t versus dose for CVN766 SAD (Log Scale)	PK
14.2.3.5.2	Plasma AUC_t versus dose for CVN766 MAD (Log Scale)	PK
14.2.3.5.1	Plasma AUC_{tau} versus dose for CVN766 MAD (Log Scale)	PK
14.2.3.6.1	Plasma t1/2z versus dose for CVN766 SAD (Log Scale)	PK
14.2.3.6.2	Plasma t1/2z versus dose for CVN766 MAD (Log Scale)	PK
14.2.4.1.1	Dose-normalized C_{max} versus dose for CVN766 SAD	PK
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14.2.4.2.1	Dose-normalized AUC_{inf} versus dose for CVN766 SAD	PK
14.2.4.3.1	Dose-normalized AUC_{24} versus dose for CVN766 SAD	PK
14.2.4.3.2	Dose-normalized AUC_{24} versus dose for CVN766 MAD	PK
14.2.4.4.1	Dose-normalized AUC_t versus dose for CVN766 SAD	PK
14.2.4.4.2	Dose-normalized AUC_t versus dose for CVN766 MAD	PK
14.2.4.5.1	Dose-normalized AUC_{tau} versus dose for CVN766 MAD	PK

Figure Number	Figure Title	Population
14.2.4.6.1	Dose-normalized t1/2z versus dose for CVN766 SAD	PK
14.2.4.6.2	Dose-normalized t1/2z versus dose for CVN766 MAD	PK

17. REFERENCES

1) Clinical Study protocol version 4.0 amendment 3 dated 19 May 2022.
2) Note of Amendment dated 26 September 2022.

Mock Tables

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GENERAL COMMENTS

- Where a count is 0, the percentage will not be shown (e.g. 0(0.0%) will be displayed as 0)
- Unless otherwise states, parameters will be listed in alphabetical order.
- The minimum and maximum values will be presented to the same number of decimal places as recorded in the electronic Case Report Form (eCRF)
- Mean, SD, and Median will be presented to one more decimal place than the raw data
- Percentages will be rounded to one decimal place, with the denominator being the number of subjects in the relevant population with non-missing data, unless otherwise specified
- Change from Baseline:
  Change from Baseline will be calculated as:
  Change from Baseline = post baseline value – baseline value
- Percentage change from Baseline
  % Change from Baseline will be calculated as:
  % Change from Baseline = (post baseline value – baseline value)/baseline value x 100
- Unscheduled visits will be excluded from summary tables but included in all by-participant listings.
- **Names and order of Treatment Groups for Table Summaries**
  - Group 1 = SAD
  - Group 2 = MAD
- **Names and order of Treatment Groups for Tables/Listings**
- SAD:
  - CVN766 5 mg
  - CVN766 15 mg
  - CVN766 45 mg (Fasted)
  - CVN766 45 mg (Fed)
  - CVN766 125 mg
  - CVN766 250 mg
  - Overall CVN766 (Table only)
  - Overall Placebo (Table only)
  - Placebo (Fed; Table only)
  - Overall (Table only)
  - Screening Failures (Listing 16.2.4.7 only)

Overall CVN766 is the pooled group of all participants with active treatment. The assessments for the participants with active treatments in Cohort S3 Fed: CVN766 45 mg condition are not counted in 'Overall CVN766', and they will be counted under 'S3 Fed: CVN766 45 mg'. 'Overall Placebo' is the pooled group of all participants with placebo. The assessments for the participants with placebo in Cohort S3 fed condition are not counted in 'All

Placebo', and they will be counted under 'A3/Placebo/Fed'. In demographic and baseline characterises summary tables, Cohort S3 fed condition is not needed as appropriate.

- MAD:
  - CVN766 45 mg
  - CVN766 125 mg
  - CVN766 250 mg
  - Overall CVN766
  - Overall Placebo
  - Overall

Overall CVN766 is the pooled group of all participants with active treatment. Overall Placebo is the pooled group of all participants with placebo.

- **Treatment Display for Summary Tables**

Summary tables will be generally displayed in the following format. *If extra dosing group is added due to protocol amendment, the extra dosing group will be added in the analysis without further amendment of this template document.*

If limited by the page space, columns have to be displayed in different pages.
Overall is not needed for PK analyses.

SAD

CVN766 5 mg (N=xx)	CVN766 15 mg (N=xx)	CVN766 45 mg (Fasted) (N=xx)	CVN766 45 mg (Fed) (N=xx)	CVN766 125 mg (N=xx)	CVN766 250 mg (N=xx)	Overall CVN766 (N=xx)	Overall Placebo (N=xx)	Placebo (Fed) (N=xx)	Overall (N=xx)

MAD

CVN766 45 mg (N=xx)	CVN766 125 mg (N=xx)	CVN766 240 mg (N=xx)	Overall CVN766 (N=xx)	Overall Placebo (N=xx)	Overall (N=xx)

- **Names and order of Treatment Groups for Listings**

SAD

- Cohort 1/ CVN766 5 mg
- Cohort 1/ Placebo

- Cohort 2/ CVN766 15 mg
- Cohort 2/ Placebo
- Cohort 3 (Fed)/ CVN766 45 mg
- Cohort 3 (Fed)/ Placebo
- Cohort 3 (Fasted)/ CVN766 45 mg
- Cohort 3 (Fasted)/ Placebo
- Cohort 4/ CVN766 125 mg
- Cohort 4/ Placebo
- Cohort 5/ CVN766 250 mg
- Cohort 5/ Placebo
- Screening Failures (Listing 16.2.4.7 only)

MAD

- Cohort 1/ CVN766 45 mg
- Cohort 1/ Placebo
- Cohort 2/ CVN766 125 mg
- Cohort 2/ Placebo
- Cohort 3/ CVN766 250 mg
- Cohort 3/ Placebo

- **Names of visits**
- **SAD Cohorts 1, 2, 3a, 4, 5.**
  - Visit 1 = Screening
  - Visit 2 = Day -1
  - Visit 3 = Day 1
  - Visit 4 = Day 2
  - Visit 5 = Day 3
  - Visit 6 = Day 4 / Discharge
  - Visit 7 = Day 8 / Outpatient Visit
  - Visit 8 = Day 14 / Follow up / Early Termination
- **SAD Cohorts 3**
  - Visit 1 = Screening (Listing only)
  - Visit 2 = Day -1
  - Visit 3 = Day 1
  - Visit 4 = Day 2
  - Visit 5 = Day 3

- Visit 6 = Day 4 / Discharge Day
- Visit 7 = Day 8
- Visit 8 = Day 21
- Visit 9 = Day 22
- Visit 10 = Day 23
- Visit 11 = Day 24
- Visit 12 = Day 28 / Discharge
- Visit 13 = Day 42 / Follow up / Early Termination

- **MAD Cohorts 1, 2, 3**
  - Visit 1 = Screening (Listing only)
  - Visit 2 = Day -1
  - Visit 3 = Day 1
  - Visit 4 = Day 2
  - Visit 5 = Day 3
  - Visit 6 = Day 4
  - Visit 7 = Day 5
  - Visit 8 = Day 6
  - Visit 9 = Day 7
  - Visit 10 = Day 8
  - Visit 11 = Day 9/ Inpatient discharge
  - Visit 12 = Day 10/ Outpatient visit
  - Visit 13 = Day 14/ Outpatient visit
  - Visit 14 = Day 21/ Follow up/ Early Termination

Table 14.1.1.1 Summary of Participant Enrolment and Disposition SAD (Safety Population)

	CVN766 5 mg (N=xx)	CVN766 15 mg (N=xx)	Etc.	Overall (N=xx)
Number of Participants who Completed the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Participants who did not Complete the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Primary Reason for Non-Completion				
Adverse Event	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%)
Failure to Meet Randomization Criteria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	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%)
Non-compliance with Study Drug	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%)
Pregnancy	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%)
Screen Failure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Site Terminated by Sponsor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study Terminated by Sponsor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Technical Problems	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Percentages are calculated (the denominator used for the calculation) based on the number of participants in the all randomized population in each treatment group (N).

Programing Note:
Source Listing: 16.2.1.2.1
Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 45 mg (Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo, Placebo (Fed) and Overall.

Table 14.1.1.2 Summary of Participant Enrolment and Disposition MAD (Safety Population)

Programing Note:
Same as Table 14.1.1.1
Source Listing: 16.2.1.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.1.2.1 Analysis Set SAD (Safety Population)

	CVN766 5 mg (N=xx)	etc.	Overall (N=xx)
All Enrolled	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pharmacokinetic Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Safety Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Programing Note:
Source Listing: 16.2.1.1.1
Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 45 mg (Fed) CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo, Placebo (Fed) and Overall.

Table 14.1.2.2 Analysis Set MAD (Safety Population)

Programing Note:
Same as Table 14.1.2.1
Source Listing: 16.2.1.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.1.3.1 Summary of Demographics and Baseline Characteristics SAD (Safety Population)

Parameter	Statistic	CVN766 5 mg (N=xx)	etc.	Overall (N=xx)
Age (years) at Screening	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	SD	xx.x	xx.x	xx.x
	Median	x.x	x.x	x.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Sex n(%)	Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Undifferentiated	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Childbearing Potential n(%)*	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Is subject current smoker?	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race n (%)	Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity n(%)	Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Not Reported	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Unknown			
	Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Parameter	Statistic	CVN766 5 mg (N=xx)	etc.	Overall (N=xx)

Source Listing: 16.2.4.1.1

SD: Standard Deviation. Percentages are calculated (the denominator used for the calculation) based on the number of participants in the all randomized population in each treatment group (N).
*For childbearing potential, percentages are based on the number of female participants.

Table 14.1.3.1 Summary of Demographics and Baseline Characteristics SAD (Safety Population)

Parameter	Statistic	CVN766 5 mg (N=xx)	etc.	Overall (N=xx)
Weight (kg) at Screening	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	SD	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Height (cm) at Screening	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	SD	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Body Mass Index(kg/m^2) at Screening	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	SD	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx

Source Listing: 16.2.4.1.1

SD: Standard Deviation. Percentages are calculated (the denominator used for the calculation) based on the number of participants in the all randomized population in each treatment group (N).
*For childbearing potential, percentages are based on the number of female participants.

Programing Note:
Source Listing: 16.2.4.1.1
Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 45 mg (Fed) CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo, Placebo(Fed) and Overall.

Table 14.1.3.2 Summary of Demographics and Baseline Characteristics MAD(Safety Population)

Programing Note:
Same as Table 14.1.3.1
Source Listing: 16.2.4.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.1.4.1 Summary of Medical History SAD (Safety Population)

Parameter	CVN766 5 mg (N=xx)	etc.	Overall (N=xx)
Subjects with at least one Medical History	xx	xx	xx
	xx.x	xx.x	xx.x
Subjects with at least one ongoing Medical History	xx.x	xx.x	xx.x
	xx.x	xx.x	xx.x
Ongoing Medical History	xx	xx	xx
SOC1	xx	xx	xx
PT1			
SOC2			
PT1			
PT2			
Etc…			
Past (not ongoing) Medical History			
SOC1			
PT1			
SOC2			
PT1			
PT2			
Etc…			

Programing Note:
Source Listing: 16.2.4.2.1
Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 45 mg (Fed) CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo, Placebo(Fed) and Overall.

Table 14.1.4.1 Summary of Medical History MAD(Safety Population)

Programing Note:
Same as Table 14.1.4.1
Source Listing: 16.2.4.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.2.1.1 Summary of Plasma Concentrations (ng/mL) of CVN766 SAD (PK Population)

Analyte:xxx

Treatment	Visit	Timepoints	n	nBLQ	Mean	SD	CV%	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 5 mg (N=xx)	Day 1	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		1h										
		1.5h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		2h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		3h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		5h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		8h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		12h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		16h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 2	24h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		36h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 3	48h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 4	72h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
CVN766 15 mg (N=xx)	Day 1	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x

Source Listing: 16.2.6.1.1
BLQ = Below Limit of Quantitation; CV% = Coefficient of Variation; SD = Standard Deviation.
BLQ is set as 0 for standard statistics (such as arithmetic mean),and set as missing for geometric statistics.

Programing Note:

Add following treatment rows;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 45 mg (Fed), CVN766 125 mg, CVN766 250 mg.

Table 14.2.1.2 Summary of Plasma Concentrations (ng/mL) of CVN766 MAD (PK Population)

Analyte:xxx

Treatment	Visit	Timepoint	n	nBLQ	Mean	SD	CV%	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (N=xx)	Day 1	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		0.5h										
		1h										
		1.5h										
		…..										
	Day 2	24h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 3	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 4	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 5	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 6	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 7	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		0.5h										
		1h										
		…										
		16h										
	Day 8	24h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		36h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 9	48h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 10	72h	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
CVN766 125 mg (N=xx)	Day 1	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	…		xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x

BLQ = Below Limit of Quantitation; CV% = Coefficient of Variation; SD = Standard Deviation.
BLQ is set as 0 for standard statistics (such as arithmetic mean), and set as missing for geometric statistics.

Programing Note:
Source Listing: 16.2.6.1.2;
Add following treatment rows;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Table 14.2.2.1 Summary of CSF Concentration (ng/mL) SAD (Pharmacokinetic Population)

Analyte: xxx

Treatment	Visit	Timepoint	n	nBLQ	Mean	SD	CV%	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (Fasted) (N=xx)	Day 1	3h post-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x

BLQ = Below Limit of Quantitation; CV% = Coefficient of Variation; SD = Standard Deviation.
BLQ is set as 0 for standard statistics (such as arithmetic mean), and set as missing for geometric statistics.

Programing Note:
Source Listing: 16.2.6.5.1;
Add following treatment;
CVN766 45 mg (Fasted).

Table 14.2.2.2 Summary of CSF Concentration (ng/mL) MAD (Pharmacokinetic Population)

Treatment	Visit	Timepoint	n	nBLQ	Mean	SD	CV%	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (N=xx)	Day 7	3h Post-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x

BLQ = Below Limit of Quantitation; CV% = Coefficient of Variation; SD = Standard Deviation.
BLQ is set as 0 for standard statistics (such as arithmetic mean), and set as missing for geometric statistics.

Programing Note:
Source Listing: 16.2.6.5.2;
Add following treatment;
CVN766 45 mg

Table 14.2.3.1 Summary of Urine Concentrations (ng/mL) of CVN766 MAD (Pharmacokinetic Population)

Analyte: xxx

Treatment	Visit	Timepoints	n	nBLQ	Mean	SD	CV%	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (N=xx)	Day 1	Pre-dose	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		0-6 Hours	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		6-12 Hours	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		12-24 Hours	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Day 7	0-6 Hours	xx	xx	xx.x	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
		…….										

BLQ = Below Limit of Quantitation; CV% = Coefficient of Variation; SD = Standard Deviation.
BLQ is set as 0 for standard statistics (such as arithmetic mean), and set as missing for geometric statistics.

Programing Note:
Source Listing: 16.2.6.2.1;
Add following treatment rows;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Table 14.2.4.1 Summary of Plasma Pharmacokinetic Parameters of CVN766 SAD (Pharmacokinetic Population)

Analyte: xxx
Visit: Day 1

Treatment	Parameter	n	n NC	Mean	SD	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 5 mg (N=xx)	C_{max} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	T_{max} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	T_{last} (unit)	xx	xx	xx	xx	xx	xx	xx	xx	xx.x
	AUC_{24} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	AUC_t (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	AUC_{inf} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$AUC_{\%extrap}$ (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	λ_z (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$t_{½}$ (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	CL/F (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	$V_{z/F}$ (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	CSF:Plasma (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	DN_C_{max} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	DN_AUC_{24hr} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	DN_AUC_t (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	DN_AUC_{inf} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
CVN766 15 mg (N=xx)	C_{max}(unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	T_{max}(unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
…	…									

Source Listing: 16.2.6.3.1
N/A: = Not Applicable NC = Not Calculable; SD = Standard Deviation.

Programing Note:

Add following treatment rows;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Table 14.2.4.2 Summary of Plasma Pharmacokinetic Parameters of CVN766 MAD (Pharmacokinetic Population)

Analyte: xxx
Day 1

Treatment	Parameter	n	n NC	Mean	SD	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (N=xx)	C_{max}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$C_{min,}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	$C_{trough\ DayN}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	T_{max}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	T_{min}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	AUC_t	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	AUC_{24}	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	CSF:Plasma	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	DN_$C_{max,ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	DN_AUC_{24hr}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	DN_AUC_t	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
CVN766 125 mg (N=xx)	C_{max}(unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	C_{min} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
…	…									

Source Listing: 16.2.6.3.1
N/A: = Not Applicable NC = Not Calculable; SD = Standard Deviation.

Analyte: xxx
Day 7

Treatment	Parameter	n	n NC	Mean	SD	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (N=xx)	$C_{max,\ ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$C_{min,ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	$C_{trough\ DayN}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$C_{avg,ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$T_{max,\ ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$T_{min,\ ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x

Treatment	Parameter	n	n NC	Mean	SD	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
	$T_{last,\ ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	AUC_t	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	AUC_{tau}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	AUC_{inf}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	λ_z or Kel	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$t_{½}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	CL/F_{ss}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Vz/F_{ss}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	RA_{Cmax}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	RA_{AUC}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	CSF:Plasma	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$DN\_C_{max,ss}$	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	DN_AUC_t	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	DN_AUC_{tau}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	DN_AUC_{inf}	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
CVN766 125 mg (N=xx)	C_{max}(unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	$C_{min,ss}$(unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
…	…									

Source Listing: 16.2.6.3.1
N/A: = Not Applicable NC = Not Calculable; SD = Standard Deviation.

Programing Note:
Source Listing: 16.2.6.3.2
Add following treatment rows;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.
Repeat: Day 1, Day 7

Table 14.2.5.1 Summary of Urine Pharmacokinetic Parameters of CVN766 MAD (Pharmacokinetic Population)

Analyte: xxx
Visit: Day 1

Treatment	Parameter	n	n NC	Mean	SD	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (N=xx)	Ae_{t1-t2} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Fe_{t1-t2} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	CLr (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x

Analyte: xxx
Visit: Day 7

Treatment	Parameter	n	n NC	Mean	SD	Median	Minimum	Maximum	Geometric Mean	Geometric CV%
CVN766 45 mg (N=xx)	Ae_{t1-t2} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x
	Fe_{t1-t2} (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	N/A	xx.x
	CLr (unit)	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x

Programing Note:
Source Listing: 16.2.6.4.1
Add following treatment;
CVN766 45 mg
Include Visit = Day 1 and Day 7

Table 14.2.6.1 Statistical Analysis of Dose Proportionality for CVN766 SAD (Pharmacokinetic Population)

Analyte: xxxx

Parameter	n	Intercept Estimate	Slope Estimate	Slope 90% CI
AUC_{inf}	xx	x.xx	xxx.xx	(x.xx, x.xx)
AUC_{t}	xx	x.xx	xxx.xx	(x.xx, x.xx)
AUC_{24}	xx	x.xx	xxx.xx	(x.xx, x.xx)
C_{max}	xx	x.xx	xxx.xx	(x.xx, x.xx)

Source Listing: 16.2.6.3.1
CI = Confidence Interval.
Power Model: Ln(PK)=intercept + Ln(dose)

Dose proportionality can generally be concluded if the 90% CIs around the slope estimate (i.e., β1) include the value of 1 and is supported by the descriptive and graphical interpretation.

Programing Note:
Include only the following cohorts;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 125 mg, CVN766 250 mg.

Table 14.2.6.2 Statistical Analysis of Dose Proportionality for CVN766 MAD (Pharmacokinetic Population)

Analyte: xxx
Day 1

Parameter	n	Intercept Estimate	Slope Estimate	Slope 90% CI
AUC_{24}	xx	x.xx	xxx.xx	(x.xx, x.xx)
C_{max}	xx	x.xx	xxx.xx	(x.xx, x.xx)

Source Listing: 16.2.6.3.2
CI = Confidence Interval.
Power Model: Ln(PK)=intercept + Ln(dose)

Analyte: xxx
Day 7

Parameter	n	Intercept Estimate	Slope Estimate	Slope 90% CI
AUC_{tau}	xx	x.xx	xxx.xx	(x.xx, x.xx)
$C_{max,ss}$	xx	x.xx	xxx.xx	(x.xx, x.xx)

Source Listing: 16.2.6.3.2
CI = Confidence Interval.
Power Model: Ln(PK)=intercept + Ln(dose)

Dose proportionality can generally be concluded if the 90% CIs around the slope estimate (i.e., β1) include the value of 1 and is supported by the descriptive and graphical interpretation.

Table 14.2.7.1 Food Effect Assessment of Plasma CVN766 Pharmacokinetic Parameters SAD(Pharmacokinetic Population)

Analyte:xxxx

Parameter (Unit)/ Statistics	CVN766 45 mg Fasted (N=xx)	CVN766 45 mg Fed (N=xx)
AUC_t(Unit)		
n	xx.xx	xx.xx
Geometric LS Mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx xx.xx, xx.xx)
Ratio of Geometric LS Means (Fed/Fasting)		xx.xx
90% CI for Ratio of Geometric LS Means (Fed/Fasting)		(xx.xx, xx.xx)
AUC_{inf} (Unit)		
n	xx.xx	xx.xx
Geometric LS Mean	xx.xx	xx.xx
Ratio of Geometric LS Means (Fed/Fasting)		xx.xx
90% CI for Ratio of Geometric LS Means (Fed/Fasting)		(xx.xx, xx.xx)
AUC_{24} (Unit)		
n	xx.xx	xx.xx
LS Mean (SE)	xx.xx (xx.xxx)	xx.xx (xx.xxx)
Geometric LS Mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx xx.xx, xx.xx)
Ratio of Geometric LS Means (Fed/Fasting)		xx.xx
C_{max} (Unit)		
n	xx.xx	xx.xx
Geometric LS Mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx xx.xx, xx.xx)
Ratio of Geometric LS Means (Fed/Fasting)		xx.xx
90% CI for Ratio of Geometric LS Means (Fed/Fasting)		(xx.xx, xx.xx)

Source: Listing 16.2.6.3.1
LS = Least Square, SE = Standard Error, CI = Confidence Interval.

Programming Note:

- ANOVA model will be used
  - Fixed Effect: food status (fed, fasted)

- Random Effect: Subject

Table 14.2.8.1 Gender Effect Assessment of Plasma CVN766 Dose Normalized Pharmacokinetic Parameters SAD (Pharmacokinetic Population)

Analyte:xxxx
Visit: Day 1

			Gender	
Treatment	Parameter	Statistics	Male	Female
Pooled CVN766	AUC24/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	Cmax/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	AUCt/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	AUCinf/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	T1/2z	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	Tmax	n	xx	xx
		Hodges-Lehmann estimate (Median)	xx.xx	xx.xx
		Hodges-Lehmann CI		xx.xx (xx.xx, xx.xx)

Source: Listing 16.2.6.3.1
LS = Least Square, SE = Standard Error, CI = Confidence Interval.

Programming Note:

- ANOVA model will be used
  - Fixed Effect: Gender (Male, Female)
  - Random Effect: Subject

Programing Note:
Include only the following cohorts;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 125 mg, CVN766 250 mg

Table 14.2.8.2 Gender Effect Assessment of Plasma CVN766 Pharmacokinetic Parameters MAD (Pharmacokinetic Population)

Analyte:xxxx
Day 1

			Gender	
Treatment	Parameter	Statistics	Male	Female
Pooled CVN766	AUC24/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	Cmax/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	AUCt/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	T1/2z	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	Tmax	n	xx	xx
		Hodges-Lehmann estimate (Median)	xx.xx	xx.xx
		Hodges-Lehmann CI		xx.xx (xx.xx, xx.xx)

Analyte:xxxx
Day 7

			Gender	
Treatment	Parameter	Statistics	Male	Treatment
	Cmax,ss/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	AUCtau/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	AUCt/Dose	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	T1/2z	n	xx	xx
		Geometric LS mean (90% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
		Geometric mean ratio(90% CI) (female vs male)		xx.xx (xx.xx, xx.xx)
	Tmax	n	xx	xx

	Hodges-Lehmann estimate (Median)	xx.xx	xx.xx

Source: Listing 16.2.6.3.2
LS = Least Square, SE = Standard Error, CI = Confidence Interval.

Programming Note:

- ANOVA model will be used
  - Fixed Effect: Gender (Male, Female)
  - Random Effect: Subject

Table 14.3.1.1 Summary of Concomitant Medications SAD (Safety Population)

Anatomical Therapeutic Class (ATC) [Level 3] Preferred Term (PT)	CVN766 5 mg (N=xx) n (%) m	etc.	Overall (N=xx) n (%) m
Subjects with at least one Concomitant Medication	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
ATC 3	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
PT 1	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
PT 2	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
….	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
ATC 3	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
PT 1	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
PT 2	xx (xx.x%) x	xx (xx.x%) x	xx (xx.x%) x
……			

Source: Listing 16.2.10.2.1

Concomitant medications are defined as any medication (other than the study drug) that was used at least once after the first administration of the study drug.
ATC class and preferred names within ATC class are presented in alphabetical order.
If a participant has multiple occurrences of a concomitant medication, the participant is presented only once in the participant count (n) column for a given ATC and PT. Occurrences are counted each time in the mentions/occurrence (m) column.
Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).
World Health Organization-Drug Dictionary (WHO-DD) Version xx, YYYY

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed) CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo, Placebo (Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.2.2 Summary of Concomitant Medications MAD (Safety Population)

Programing Note:
Same as Table 14.3.1.1
Source: Listing 16.2.10.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.3.1.1 Summary of Overall Treatment Emergent Adverse Events SAD (Safety Population)

	CVN766 5 mg (N=xx) n (%) m	etc.	Overall (N=xx) n (%) m
Number of Participants Reporting at least one:			
TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Severe TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Treatment Related TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Serious TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
TEAE leading to study drug withdrawal[1]	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
TEAE leading to discontinuation from study	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Life threatening TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
TEAE leading to death	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

Source: Listing 16.2.7.1.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication. If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (m) column.

Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).
[1]Action taken = drug withdrawn

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo, Placebo(Fed)and Overall.
Overall CVN766 will not contain CVN766 45 mg(Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.3.1.2 Summary of Overall Treatment Emergent Adverse Events MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.1.1
Source: Listing 16.2.7.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall

Table 14.3.3.2.1 Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term SAD (Safety Population)

System Organ Class (SOC) *Preferred Term (PT)*	CVN766 5 mg (N=xx) n (%) m		Overall (N=xx) n (%) m
		etc.	
Participants with at least one TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
SOC1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…..			
SOC2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
….			

Source: Listing 16.2.7.1.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication.
If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (M) column.
SOC / PTs will be presented in decreasing order of 'overall' column.

Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg (Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.3.2.2 Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.2.1
Source: Listing 16.2.7.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.3.3.1 Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term SAD (Safety Population)

System Organ Class (SOC) *Preferred Term (PT)*	CVN766 5 mg (N=xx) n (%) m		Overall (N=xx) n (%) m
		etc.	
Participants with at least one Serious TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
SOC1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…..			
SOC2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
….			

Source: Listing 16.2.7.2.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication.
If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (M) column.
SOC / PTs will be presented in decreasing order of 'overall' column.
Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 cohort

Table 14.3.3.3.2 Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.3.1
Source: Listing 16.2.7.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.3.4.1 Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity - SAD (Safety Population)

System Organ Class (SOC) *Preferred Term (PT)* *Severity*	CVN766 5 mg (N=xx) n (%) m		Overall (N=xx) n (%) m
		etc.	
Participants with at least one TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Mild	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Moderate	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Severe	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Life-threatening	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Death	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
SOC1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Mild	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Moderate	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Severe	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Life-threatening	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Death	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Mild	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Moderate	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Severe	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Life-threatening	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Death	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…..			

Source: Listing 16.2.7.1.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication.
If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (M) column.
SOC / PTs will be presented in decreasing order of 'overall' column.
Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).
Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 cohort

Table 14.3.3.4.2 Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.4.1
Source: Listing 16.2.7.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.3.5.1 Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship SAD (Safety Population)

System Organ Class (SOC) *Preferred Term (PT)* *Relationship*	CVN766 5 mg (N=xx) n (%) m		Overall (N=xx) n (%) m
		etc.	
Participants with at least one TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Not Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
SOC1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Not Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Not Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…..			

Source: Listing 16.2.7.1.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication.
If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (M) column.
SOC / PTs will be presented in decreasing order of 'overall' column.

Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 Cohort

Table 14.3.3.5.2 Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.5.1
Source: Listing 16.2.7.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.3.6.1 Summary of TEAE leading to the study discontinuation by SOC and PT SAD (Safety Population)

System Organ Class (SOC) *Preferred Term (PT)*	CVN766 5 mg (N=xx) n (%) m		etc.	Overall (N=xx) n (%) m
Participants with at least one TEAE Leading to Study Discontinuation	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
SOC1	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
…				
SOC2	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
PT2	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
PT3	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
PT4	xx (xx.x%) xx	xx (xx.x%) xx		xx (xx.x%) xx
….				

Source: Listing 16.2.7.1.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication.
If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (M) column.
SOC / PTs will be presented in decreasing order of 'overall' column.

Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (fed) from S3 Cohort

Table 14.3.3.6.2 Summary of TEAE leading to the study discontinuation by SOC and PT MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.6.1
Source: Listing 16.2.7.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.3.7.1 Summary of Overall Frequency of TEAE by PT SAD (Safety Population)

Preferred Terms (PTs)	CVN766 5 mg (N=xx) n (%) m	etc.	Overall (N=xx) n (%) m
Participants with at least one TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT5	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…….			

…..

Source: Listing 16.2.7.1.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication.
If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (M) column.
SOC / PTs will be presented in decreasing order of 'overall' column.

Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg(Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.3.7.2 Summary of Overall Frequency of TEAE by PT MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.7.1
Source: Listing 16.2.7.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.3.8.1 Summary of Overall Frequency of Related TEAE by PT SAD (Safety Population)

	CVN766 5 mg (N=xx) n (%) m		Overall (N=xx) n (%) m
		etc.	
Participants with at least one TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Not Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
PT1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Not Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…..			
PT2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Not Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Related	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

…..

Source: Listing 16.2.7.1.1

Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that occurred following the first administration of study medication.
If a participant has multiple occurrences of a TEAE, the participant is presented only once in the Participant count (n) column for a given System Organ Class and Preferred Term. Occurrences are counted each time in the mentions/Occurrence (M) column.
SOC / PTs will be presented in decreasing order of 'overall' column.

Percentages are calculated (the denominator used for the calculation) based on the number of participants in the safety population in each treatment group (N).

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 45 mg (Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg (Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.3.8.2 Summary of Overall Frequency of Related TEAE by PT MAD (Safety Population)

Programing Note:
Same as Table 14.3.3.8.1
Source: Listing 16.2.7.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.4.1.1.1 Summary of Hematology and Coagulation SAD (Safety Population)

Lab Category: Hematology

Parameter: Basophils (unit)

		Actual Value						Change from Baseline[1]					
Treatment	Visit	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
CVN766 5 mg (N=xx)	Baseline[1]	xx	xx.x	xx.x	xx.x	xx	xx	N/A					
	Day 1	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 2	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 3	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 4	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 8	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 14/ ET	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
CVN766 15 mg (N=xx)	Baseline[1]	xx	xx.x	xx.x	xx.x	xx	xx	N/A					
	Day 1	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 2	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 3	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 4	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 8	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 14/ ET	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
….	….												

Source: Listing 16.2.8.1.1

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable, SD = Standard Deviation, ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg(Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Repeat for Lab Category: Coagulation and its parameters.

Table 14.3.4.1.1.2 Summary of Hematology and Coagulation MAD (Safety Population)

Programing Note:
Same as Table 14.3.4.1.1.1
Source: Listing 16.2.8.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.4.1.2.1 Summary of Hematology and Coagulation Shifts from Baseline SAD (Safety Population)

Lab Category: Hematology
Parameter: Hemoglobin (unit)

					Post-Baseline		
Treatment	Visit	Visit(n)[2]	Result Classification	Baseline[1] n(%)	Low n(%)	Normal n(%)	High n(%)
CVN766 5 mg (N=xx)	Day 1	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 2	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 3	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	…..						
	Day 14/ET	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…	…	…					

Source: Listing 16.2.8.1.1

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
Number of participants at each visit (n) will be used as the denominator for the calculation of all percentages.
[2] Number of participants with non-missing values at that visit.
Participant with both baseline and post-baseline values included.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg(Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.
Repeat for Lab Category: Coagulation and its parameters.

Table 14.3.4.1.2.2 Summary of Hematology and Coagulation Shifts from Baseline MAD (Safety Population)

Programing Note:
Same as Table 14.3.4.1.2.1
Source: Listing 16.2.8.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.4.2.1.1 Summary of Summary of Chemistry SAD (Safety Population)

Parameter: Alanine Aminotransferase (ALT) (unit)

		Actual Value						Change from Baseline[1]					
Treatment	Visit	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
CVN766 5 mg (N=xx)	Baseline[1]	xx	xx.x	xx.x	xx.x	xx	xx	N/A					
	Day 1	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 2	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 3	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 4	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 8	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 14/ ET	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
CVN766 15 mg (N=xx)	Baseline[1]	xx	xx.x	xx.x	xx.x	xx	xx	N/A					
	Day 1	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 2	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 3	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 4	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 8	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
	Day 14/ ET	xx	xx.x	xx.x	xx.x	xx	xx	Xx	xx.x	xx.x	xx.x	xx	xx
….	….												

Source: Listing 16.2.8.2.1

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable, SD = Standard Deviation, ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg(Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.4.2.1.2 Summary of Summary of Chemistry MAD (Safety Population)

Programing Note:
Same as Table 14.3.4.2.1.1
Source: Listing 16.2.8.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.4.2.2.1 Summary of Chemistry Shifts from Baseline SAD (Safety Population)

Parameter: Alanine Aminotransferase (ALT) (unit)

					Post-Baseline		
Treatment	Visit	Visit(n)[2]	Result Classification	Baseline[1] n(%)	Low n(%)	Normal n(%)	High n(%)
CVN766 5 mg (N=xx)	Day 1	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 2	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 3	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	…..						
	Day 14/ET	xx	Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…	…	…					

Source: Listing 16.2.8.2.1
[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
Number of participants at each visit (n) will be used as the denominator for the calculation of all percentages.
[2] Number of participants with non-missing values at that visit.
Participant with both baseline and post-baseline values included.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg(Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.4.2.2.2 Summary of Chemistry Shifts from Baseline MAD (Safety Population)

Programing Note:
Same as Table 14.3.4.2.2.1
Source: Listing 16.2.8.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.4.3.1 Summary of Urinalysis SAD (Safety Population)

Parameter: Glucose (unit)

Treatment	Visit	Visit(n)[2]	Normal	Abnormal, Not Clinically Significant	Abnormal, Clinically Significant
CVN766 5 mg (N=xx)	Baseline	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	…				
CVN766 15 mg (N=xx)	Baseline	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
….	Day 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%)

Source: Listing 16.2.8.3.1

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall.
Overall CVN766 will not contain CVN766 45 mg(Fed).
Overall Placebo will not contain Placebo (Fed) from S3 Cohort.

Table 14.3.4.3.2 Summary of Urinalysis MAD (Safety Population)

Parameter: Glucose (unit)

Treatment	Visit	Visit(n)[2]	Normal	Abnormal, Not Clinically Significant	Abnormal, Clinically Significant
CVN766 45 mg (N=xx)	Baseline	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	……				
CVN766 125 mg (N=xx)	Baseline	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
….	Day 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Source: Listing 16.2.8.3.2

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
Number of participants at each visit (n) will be used as the denominator for the calculation of all percentages.
[2] Number of participants with non-missing values at that visit.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.5.1.1 Summary of Vital Signs SAD (Safety Population)

Position: Supine Measurements
Parameter: Heart rate (beats/min)

			Actual Value						Change from Baseline[1]					
Treatment	Visit	Timepoint	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
CVN766 5 mg (N=xx)	Baseline[1]		xx	xx.x	xx.x	xx.x	xx	xx	N/A					
	Day 1	0.5 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		1 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		2 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		4 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		8 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		12 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 2	24 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		36 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 3	48 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		60 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 4	72 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 8		xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	ET		xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
….	….	….												

Source: Listing 16.2.9.1.1
[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable. SD = Standard Deviation.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 Cohort
Repeat for Position: Supine, Standing

Table 14.3.5.1.2 Summary of Vital Signs MAD (Safety Population)

Programing Note:
Same as Table 14.3.5.1.1
Source: Listing 16.2.9.1.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.
Repeat for Position: Supine, Standing

Table 14.3.5.2.1 Summary of Orthostatic Vital Signs SAD (Safety Population)

Parameter: Heart rate (beats/min)

			Orthostatic Change					
Treatment	Visit	Timepoint	n	Mean	SD	Median	Minimum	Maximum
CVN766 5 mg (N=xx)	Baseline[1]		xx	xx.x	xx.x	xx.x	xx	xx
	Day 1	0.5 hours	xx	xx.x	xx.x	xx.x	xx	xx
		1 hours	xx	xx.x	xx.x	xx.x	xx	xx
		2 hours	xx	xx.x	xx.x	xx.x	xx	xx
		4 hours	xx	xx.x	xx.x	xx.x	xx	xx
		8 hours	xx	xx.x	xx.x	xx.x	xx	xx
		12 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 2	24 hours	xx	xx.x	xx.x	xx.x	xx	xx
		36 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 3	48 hours	xx	xx.x	xx.x	xx.x	xx	xx
		60 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 4	72 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 8		xx	xx.x	xx.x	xx.x	xx	xx
	ET		xx	xx.x	xx.x	xx.x	xx	xx
….	….	….						

Source: Listing 16.2.9.1.1
[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable. SD = Standard Deviation.
ET = Early Termination.
Orthostatic Change = value of parameter in standing – value of parameter in supine.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (fed) from S3 cohort

Table 14.3.5.2.2 Summary of Orthostatic Vital Signs MAD (Safety Population)

Parameter: Heart rate (beats/min)

			Orthostatic Change					
Treatment	Visit	Timepoint	n	Mean	SD	Median	Minimum	Maximum
CVN766 45 mg (N=xx)	Baseline[1]		xx	xx.x	xx.x	xx.x	xx	xx
	Day 1	0.5 hours	xx	xx.x	xx.x	xx.x	xx	xx
		1 hours	xx	xx.x	xx.x	xx.x	xx	xx
		2 hours	xx	xx.x	xx.x	xx.x	xx	xx
		4 hours	xx	xx.x	xx.x	xx.x	xx	xx
		8 hours	xx	xx.x	xx.x	xx.x	xx	xx
		12 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 2	24 hours	xx	xx.x	xx.x	xx.x	xx	xx
		36 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 3	48 hours	xx	xx.x	xx.x	xx.x	xx	xx
		60 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 4	72 hours	xx	xx.x	xx.x	xx.x	xx	xx
	Day 8		xx	xx.x	xx.x	xx.x	xx	xx
	ET		xx	xx.x	xx.x	xx.x	xx	xx
….	….	….						

Source: Listing 16.2.9.1.1
[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable. SD = Standard Deviation.
ET = Early Termination.
Orthostatic Change = value of parameter in standing – value of parameter in supine.

Programing Note:

CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.5.3.1 Summary of Categorical analysis of Orthostatic Vital Signs SAD (Safety Population)

Category: Drop in dBP of ≥10mmHg from Supine to Standing

		TRTA	TRTB	TRTC	
		N=xxx	N=xxx	N=xxx	
Visit	Timepoint	n (%)	n (%)	n (%)	….
Day 1	0.5 hours	xx	xx	xx	xx
	1 hours	xx	xx	xx	xx
	2 hours	xx	xx	xx	xx
	4 hours	xx	xx	xx	xx
	8 hours	xx	xx	xx	xx
	12 hours	xx	xx	xx	xx
	24 hours	xx	xx	xx	xx
	36 hours	xx	xx	xx	xx
	48 hours	xx	xx	xx	xx
	60 hours	xx	xx	xx	xx
	72 hours	xx	xx	xx	xx
…					

Source: Listing 16.2.9.1.1

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 Cohort

Repeat for Category: Drop in dBP of ≥10mmHg from Supine to Standing, Drop in sBP of ≥20mmHg when moving from supine to standing, Increase in HR of ≥30bpm when moving from supine to standing

Table 14.3.5.3.2 Summary of Categorical analysis of Orthostatic Vital Signs MAD (Safety Population)

Category: Drop in dBP of ≥10mmHg from Supine to Standing

		TRTA	TRTB	TRTC	
		N=xxx	N=xxx	N=xxx	
Visit	Timepoint	n (%)	n (%)	n (%)	….
Day 1	0.5 hours	xx	xx	xx	xx
	1 hours	xx	xx	xx	xx
	2 hours	xx	xx	xx	xx
	4 hours	xx	xx	xx	xx
	8 hours	xx	xx	xx	xx
	12 hours	xx	xx	xx	xx
	24 hours	xx	xx	xx	xx
	36 hours	xx	xx	xx	xx
	48 hours	xx	xx	xx	xx
	60 hours	xx	xx	xx	xx
	72 hours	xx	xx	xx	xx
…					

Source: Listing 16.2.9.1.2

Programing Note:

CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.
Repeat for Category: Drop in dBP of ≥10mmHg from Supine to Standing, Drop in sBP of ≥20mmHg when moving from supine to standing, Increase in HR of ≥30bpm when moving from supine to standing

Table 14.3.5.4.1.1 Summary of 12-Lead ECG SAD (Safety Population)

Parameter: Heart Rate (bpm)

			Actual Value						Change from Baseline[1]					
Treatment	Visit	Timepoint	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
CVN766 5 mg (N=xx)	Baseline[1]		xx	xx.x	xx.x	xx.x	xx	xx	N/A					
	Day 1	0.5 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		…….												
		……												
	Day 2	24 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 3		xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 4		xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 8		xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	ET		xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
CVN766 15 mg (N=xx)	Baseline[1]		xx	xx.x	xx.x	xx.x	xx	xx	N/A					
	Day 1	0.5 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
		…….												
		……												
	Day 2	24 hours	xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
	Day 3		xx	xx.x	xx.x	xx.x	xx	xx	xx	xx.x	xx.x	xx.x	xx	xx
….	….	….												

Source: Listing 16.2.9.2.1

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
For multiple tracings done as part of one assessment, the mean of the three tracings are summarized for each participant.
N/A = Not Applicable, SD = Standard Deviation, ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall

Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 Cohort

Table 14.3.5.4.1.2 Summary of 12-Lead ECG MAD (Safety Population)

Programing Note:
Same as Table 14.3.5.2.1.1
Source: Listing 16.2.9.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo and Overall.

Table 14.3.5.4.2.1 Summary of 12-Lead ECG Interpretation SAD (Safety Population)

Treatment	Visit	Visit(n)[2]	Timepoint	Normal	Abnormal, Not Clinically Significant	Abnormal, Clinically Significant	Not Done
CVN766 5 mg (N=xx)	Baseline[1]	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 1	xx	0.5 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			……				
	Day 2	xx	24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 3	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 4	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 8	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 14/ ET	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
CVN766 15 mg (N=xx)	Baseline[1]	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 1	xx	0.5 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
			……..				
	Day 2	xx	24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 3	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 4	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 8	xx		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
….	….		….				

Source: Listing 16.2.9.2.1

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
Worst of the three tracings are summarized for each participant.

Number of participants at each visit (n) will be used as the denominator for the calculation of all percentages.
[2] Number of participants with non-missing values at that visit.
Participant with both baseline and post-baseline values included.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Placebo(Fed) and Overall
Overall CVN766 will not contain CVN766 45 mg(Fed)
Overall Placebo will not contain Placebo (Fed) from S3 cohort

Table 14.3.5.4.2.2 Summary of 12-Lead ECG Interpretation MAD (Safety Population)

Programing Note:
Same as Table 14.3.5.4.2.1
Source: Listing 16.2.9.2.2
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall CVN766, Overall Placebo Overall.

Listing 16.2.1.1.1 Analysis Populations SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Safety Population	Pharmacokinetic Population
XXX	Yes	Yes
XXX	Yes	Yes
XXX	Yes	Yes
XXX	No	No
….		

Programing Note:

Repeat for following treatments;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.1.1.2 Analysis Populations MAD (Safety Population)

Programing Note:
Same as Listing 16.2.1.1.1
Repeat for following treatments ;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.1.2.1 Participant Disposition SAD (*Safety Population*)

Treatment: CVN766 5 mg

	Informed Consent			Re-consent							
Subject ID	Date (YYYY-MM-DD)	Version	Protocol Version	Date (YYYY-MM-DD)	Version	Protocol Version	Did the Participant Complete the Study?	Study Completion/ Early Termination Date (YYYY-MM-DD)	Primary Reason for Non-completion	Reason for Consent Withdrawal	Date for Consent Withdrawal (YYYY-MM-DD)
XXX	YYYY-MM-DD	1.2	1.2	N/A			Yes	YYYY-MM-DD			
XXX	YYYY-MM-DD	Other: xx.x	Other: xx.x	N/A			Yes	YYYY-MM-DD			
XXX	YYYY-MM-DD	1.2	1.2	YYYY-MM-DD	Other: xx.x	Other: xx.x	No	YYYY-MM-DD	Withdrawal by Subject	xxxxxxxxxxxxxx	YYYY-MM-DD
XXX	YYYY-MM-DD	1.2	1.2	YYYY-MM-DD	Other: xx.x	Other: xx.x	Yes	YYYY-MM-DD			
….											

N/A = Not Applicable.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.1.2.2 Participant Disposition MAD (*Safety Population*)

Programing Note:
Same as Listing 16.2.1.2.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.2.1 Protocol Deviation SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Date of Deviation (YYYY-MM-DD)	Type of Deviation	Deviation Description	Important Deviation
XXX	YYYY-MM-DD	YYYYYYYYYYYYYY	XXXXXXXXXXXX	No
XXX	YYYY-MM-DD	YYYYYYYYYYYYYY	XXXXXXXXXXXX	No
….				

Programing Note:

Repeat for following treatments ;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.2.2 Protocol Deviation MAD (Safety Population)

Programing Note:
Same as Listing 16.2.2.1
Repeat for following treatments ;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.1.1 Demographics and Baseline Characteristics SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Date of Birth (YYYY-MM-DD)	Age at Informed Consent (years)	Sex	Childbearing Potential[1]	Reason not of Childbearing Potential	Smoking Status	Race	Ethnicity	Height at screening (cm)	Weight at screening (kg)	Body Mass Index at screening (kg/m^2)
XXX	YYYY-MM-DD	xx	Female	No	Other - xxxxxxx	Yes	Asian	xxxxx	xxx	xx.x	xx.x
XXX	YYYY-MM-DD	xx	Male	N/A		No	Asian	xxxxx	xxx	xx.x	xx.x
….											

N/A = Not Applicable.
[1] only for female participants.

Programing Note:

Repeat for following treatments;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.1.2 Demographics and Baseline Characteristics MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.1.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.2.1 Medical/Surgical History SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Medical History Term/ System Organ Class /Preferred Term	Start Date (YYYY-MM-DD)	End Date (YYYY-MM-DD)	Is the Subject currently taking medication for this condition?
XXX	XXXXXXXXXX/ YYYYYYYYY/ ZZZZZZZZZ	YYYY-MM-DD	YYYY-MM-DD	Xxx
	XXXXXXXXXX/ YYYYYYYYY/ ZZZZZZZZZ	YYYY-MM-DD	Ongoing	xxx
…..				

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Repeat for following treatments;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.2.2 Medical/Surgical History MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.2.1

Repeat for following treatments;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.3.1 Hepatitis Panel SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Collection Date/ Time (YYYY-MM-DD/ HH:MM)	Test Name	Result
XXX	Screening	YYYY-MM-DD/ HH:MM	Hepatitis B Surface Antigen (HBsAg)	Negative
			Hepatitis C Antibody (HCVAb)	Negative
			HIV-1 Antibody/HIV-2 Antibody	Negative
…..				

Programing Note:
Repeat for following treatments;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall Placebo.

Listing 16.2.4.3.2 Hepatitis Panel MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.3.1
Repeat for following treatments;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg, Overall Placebo.

Listing 16.2.4.4.1 Alcohol Breath Test SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Was Alcohol (Breath Test) Performed? (Yes/No – Reason)	Collection Date/ Time (YYYY-MM-DD/ HH:MM)	Result
XXX	Screening	Yes	YYYY-MM-DD/ HH:MM	xxxx
XXX	Screening	No- xxxx	YYYY-MM-DD/ HH:MM	xxxx
…..				

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.4.2 Alcohol Breath Test SAD MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.4.1
Repeat for following treatments;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.5.1 Urine Drug Screen SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Was subject abstained from caffeine consumption since 24hrs? (Yes/No)	Was Urine Drug Screen Test performed? (Yes/No-Reason)	Collection Date/ Time (YYYY-MM-DD/ HH:MM)	Test Name	Result
XXX	Screening			YYYY-MM-DD/ HH:MM	….	Negative
					….	Negative
					….	Negative
…..						

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.5.2 Urine Drug Screen MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.5.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.6.1 Follicle-Stimulating Hormone Test SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Collection Date/ Time (YYYY-MM-DD/ HH:MM)	Was Sample collected For FSH Test	Result (unit)
XXX	Screening	YYYY-MM-DD/ HH:MM	Yes	
			Yes	
			No	
…..				

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.6.2 Follicle-Stimulating Hormone Test MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.6.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.7.1 Pregnancy Test SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Was Sample Collected for Pregnancy test? (Yes/No)	Assessment Date/ Time (YYYY-MM-DD/ HH:MM)	Type of test	Result
XXX	Screening		YYYY-MM-DD/ HH:MM	xx	Xx
….					

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable. CS = Clinically Significant, NCS = Not Clinically Significant.
ET = Early Termination

Programing Note:
Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.7.2 Pregnancy Test MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.7.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.8.1 Eligibility Criteria SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Participant Eligible	Category Failed (Inclusion/ Exclusion)	Inclusion/ Exclusion Criterion not met
XXX	Screening	No	Inclusion and Exclusion	Exclusion: xx, xx; Inclusion xx, xx
	Day -2	Yes		
	Day -1	Yes		
….	….			

Programing Note:
Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.4.8.2 Eligibility Criteria MAD (Safety Population)

Programing Note:
Same as Listing 16.2.4.8.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.5.1.1 Participant Randomization SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Randomization Date (YYYY-MM-DD)	Randomization Number	Randomized Treatment Received
XXX	YYYY-MM-DD	XXX	…
XXX	YYYY-MM-DD	XXX	…
XXX	YYYY-MM-DD	XXX	…
….			

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.5.1.2 Participant Randomization MAD (Safety Population)

Programing Note:
Same as Listing 16.2.5.1.1
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.5.2.1 Study Drug Administration SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Study Drug Administered/ No - Reason	Date/ Time of Administration (YYYY-MM-DD/ HH:MM)	Dose (mg)	Was the full dose administered?	Was study drug given as per protocol?	Was subject fasting?
XXX	Day 1	Yes	YYYY-MM-DD/ HH:MM	xx	Yes	Yes	Yes
	Day 2	Yes	YYYY-MM-DD/ HH: MM	xx	Yes	Yes	Yes
	Day 3	No - xxxxxxxx					
...	.....						

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.5.2.2 Study Drug Administration MAD (Safety Population)

Programing Note:
Same as Listing 16.2.5.2.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.5.3.1 Meal Records SAD (Safety Population)

Treatment: CVN766 45 mg

Subject ID	Visit	Study Meal Administered/ No - Reason	Date/ Time of Administration (YYYY-MM-DD/ HH:MM)	Was full meal consumed?	Percentage consumed (%)	Reason full meal not consumed
XXX	Day 1	Break fast	YYYY-MM-DD/ HH:MM	Yes	xx	xx
	Day 1	Lunch	YYYY-MM-DD/ HH:MM	Yes	xx	xx
	Day 1	Dinner	YYYY-MM-DD/ HH:MM	Yes	xx	xx
	Day 1	Snack	YYYY-MM-DD/ HH:MM	Yes	xx	xx
	Day 2	Break fast	YYYY-MM-DD/ HH: MM	Yes	xx	xx
...	.....					

Programing Note:
Add following treatment;
CVN766 45 mg

Listing 16.2.6.1.1 Plasma Concentrations for CVN766 SAD (PK Population)

Analyte XXX (Unit)
Treatment: CVN766 5 mg

Subject ID	Visit	Timepoint	Was Pharmacokinetic Sample Collected – Reason Not Collected	Date and Time of Pharmacokinetic Sample Collection (YYYY-MM-DD/ HH:MM)	Actual Time (h)	Time Deviation (h)	Concentration (unit)
XXX	Day 1	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xx.xx	xx.xx	xxx
		30 minutes	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		1 hour	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		1.5 hour	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		2 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		3 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		5 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		8 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		12 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		16 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		24 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		36 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		48 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		72 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
XXX	Day 1	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
…	…	….					

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg

Listing 16.2.6.1.2 Plasma Concentrations for CVN766 MAD (PK Population)

Subject ID	Visit	Timepoint	Was Pharmacokinetic Sample Collected – Reason Not Collected	Date and Time of Pharmacokinetic Sample Collection (YYYY-MM-DD/ HH:MM)	Actual Time (h)	Time Deviation (h)	Concentration (unit)
XXX	Day 1	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		30 minutes	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		1 hour	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		1.5 hour	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		2 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		3 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		5 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		8 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		12 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		16 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
	Day 2	24 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
	Day 3	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
	Day 4	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
	Day 5	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
	Day 6	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
	Day 7	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		30 minutes	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		1 hour	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		1.5 hour	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		2 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		3 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		5 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		8 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		12 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		16 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		24 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		36 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		48 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
		72 hours	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
XXX	Day 1	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx
…	…	….					

Programing Note:
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.6.2.1 Urine Concentration of CVN766 MAD (PK Population)

Analyte XXX (Unit)
Treatment: CVN766 45 mg

Subject ID	Visit	Timepoint	Was PK Urine Sample Collected – Reason Not Collected	Start Date/ Time of Collection (YYYY-MM-DD/ HH:MM)	End Date / Time of Collection (YYYY-MM-DD/ HH:MM)	Duration of Sample (hours)	Total Volume Collected (mL)	Concentration (unit)	Urine Excretion (Ae) (unit)	Reason for Exclusion from Summary of Urine XXXXXXXX Excretion
XXX	Day 1	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		0-6 Hours	No: Reason	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		6-12 Hours	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		12-24 Hours	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
	Day 7	0-6 Hours	No: Reason	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		6-12 Hours	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		12-24 Hours	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
XXX	Day 1	Pre-Dose	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		0-6 Hours	No: Reason	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		6-12 Hours	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
		12-24 Hours	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	xxx.xx	xxx	xx.xx	
…	…									

Programing Note:

Add following treatment columns;
CVN766 45 mg

Listing 16.2.6.3.1 PK Plasma Parameters for CVN766 SAD (Pharmacokinetic Population)

Analyte XXX (Unit)
Treatment: CVN766 5 mg

Subject ID	Visit	C_{max} (unit)	t_{max} (unit)	Tlast	AUC_t (unit)	AUC_{24} unit)	AUC_{inf} (unit)	$\%AUC_{ext}$	$t_{½}$ (unit)	λ_z	CL/F (unit)	V_z/F (unit)	CSF:Plasma ratio	DN_C_{max}	DN_AUC_{24hr}	DN_AUC_t	DN_AUC_{inf}
XXX	Day 1	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
XXX	Day 1	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
….																	

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.6.3.2 PK Plasma Parameters for CVN766 MAD (Pharmacokinetic Population)

Analyte XXX (Unit)
Treatment: CVN766 45 mg
Visit: Day 1

Subject ID	Visit	C_{max} (unit)	C_{min} (unit)	C_{trough} (unit)	t_{max} (unit)	t_{min} (unit)	AUC_t (unit)	AUC_{24} unit)	CSF:Plasma ratio	DN_C_{max}	DN_AUC_{24hr}	DN_AUC_t
XXX	Day 1	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
XXX	Day 1	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
….												

Analyte XXX (Unit)
Treatment: CVN766 45 mg
Visit: Day 7

Subject ID	Visit	$C_{max,ss}$ (unit)	$C_{mix,ss}$ (unit)	C_{trough} (unit)	$C_{avg,ss}$ (unit)	$T_{max,ss}$ (unit)	$T_{min,ss}$ unit)	AUC_t (unit)	AUC_{tau} (unit)	AUC_{inf} (unit)	λ_z (unit)	$CL_{ss}/F,_s$ (unit)	$V_{z,ss}/F,_s$ (unit)	RAC_{max}	RA_{AUC}	CSF:Plasma ratio	$DN\_C_{max,s}$	DN_AUC_{24h}	DN_AUC$_t$	DN_AUC$_t$
XXX	Day 1	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
XXX	Day 1	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
….																				

Programing Note:
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.6.4.1 PK Urine Parameters for CVN766 MAD (Pharmacokinetic Population)

Analyte XXX (Unit)
Treatment: CVN766 45 mg
Visit: Day 1

Subject ID	Visit	Ae_{t1-t2} (unit)	Fe_{t1-t2} (unit)	CLr (unit)
XXX	Day 1	xx.x	xx.x	xx.x
XXX	Day 1	xx.x	xx.x	xx.x
….				

Programing Note:
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.6.5.1 CSF Concentration SAD (Pharmacokinetic Population)

Subject ID	Visit	Was PK CSF Sample Collected – Reason Not Collected	Scheduled Date/ Time of Collection (YYYY-MM-DD/ HH:MM)	Actual Time (h)	Time Deviation (h)	CSF : Plasma ratio	Concentration (unit)
XXX	Day 1	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xxx.x	xxx	xxx
		No: Reason					
XXX	Day 1	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx	xxx
		Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx	xxx
…	…			xxx.xx	xx.xx	xxx	xxx

Programing Note:
Add following treatment columns;
CVN766 45 mg (Fasted).

Listing 16.2.6.5.2 CSF Collection MAD (Pharmacokinetic Population)

Subject ID	Visit	Was PK CSF Sample Collected – Reason Not Collected	Scheduled Date/ Time of Collection (YYYY-MM-DD/ HH:MM)	Actual Time (h)	Time Deviation (h)	CSF: Plasma ratio	Concentration (unit)
XXX	Day 1	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xxx.x	xxx	xxx
		No: Reason					
	Day 7					xxx	xxx
XXX	Day 1	Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx	xxx
		Yes	YYYY-MM-DD/ HH:MM	xxx.xx	xx.xx	xxx	xxx
…	…			xxx.xx	xx.xx	xxx	

Programing Note:
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.6.6.1 CV Telemetry SAD (Pharmacokinetic Population)

Treatment: CVN766 5 mg

Test: CV Telemetry

Subject ID	Visit	Time Point	Were CV Telemetry performed? if No- reason	Start Date/time of Monitoring (YYYY-MM-DD/ HH:MM)	End Date/time of Monitoring (YYYY-MM-DD/ HH:MM)	Assessment Value	Abnormality Description
XXX	Screening		Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	Normal	
	Day -1			YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	Abnormal CS	xxxx
	Day 1	4 hours post-dose	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	
		8 hours post-dose	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	
	Day 2	24 hours post-dose	Yes	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	xx	
….							

N/A = Not Applicable.

Programing Note:
Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.7.1.1 Adverse Events SAD (Safety Population)

Treatment CVN766 5 mg

Subject ID	Adverse Event Verbatim/ System Organ Class/ Preferred Term	Start Date/ Time/ (YYYY-MM-DD/ HH:MM)	End Date/ Time/ (YYYY-MM-DD)	Pre-treatment event?	Severity	SAE/ Reason	Relationship to Study Treatment	Action Taken	Concomitant Medication/ Other Action	Outcome	Subject Discontinued due to AE	TEAE
XXX	XXXXXXXXXXXXXXXXXX ZZZZZZZZZZZZZZZZZZ YYYYYYYYYYYYYYYYYY	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	No	Mild	Yes/Death	Related	N/A	Yes, CM1/No	Recovered/ Resolved	No	Yes
XXX	XXXXXXXXXXXXXXXXXX ZZZZZZZZZZZZZZZZZZ YYYYYYYYYYYYYYYYYY	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM		Mild	Yes/hospitalization	Unrelated	Dose not changed	No/ Yes, CM1/No	Recovering / Resolving	No	Yes

….

SAE = Serious Adverse Event. TEAE = A treatment-emergent adverse event.

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.7.1.2 Adverse Events MAD (Safety Population)

Programing Note:
Same as Listing 16.2.7.1.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.7.2.1 Serious Adverse Events SAD (Safety Population)

Treatment: CVN766 5 mg
SAE Reason: Hospitalization

Subject ID	Adverse Event Verbatim/ System Organ Class/ Preferred Term	Start Date/ Time/ (YYYY-MM-DD/ HH:MM)	End Date/ Time/ (YYYY-MM-DD)	Severity	SAE/ Reason	Relationship to Study Treatment	Action Taken	Concomitant Medication/ Other Action	Outcome	Subject Discontinued due to AE	TEAE
XXX	XXXXXXXXXXXXXXXXXX ZZZZZZZZZZZZZZZZZZ YYYYYYYYYYYYYYYYYY	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	Mild (Grade 1)	…	Related	N/A	Yes, CM1/No	Recovered/ Resolved	No	Yes
XXX	XXXXXXXXXXXXXXXXXX ZZZZZZZZZZZZZZZZZZ YYYYYYYYYYYYYYYYYY	YYYY-MM-DD/ HH:MM	YYYY-MM-DD/ HH:MM	Mild (Grade 1)	…	Unrelated	Dose not changed	No/ Yes, CM1/No	Recovering / Resolving	No	Yes

….

SAE = Serious Adverse Event. TEAE = A treatment-emergent adverse event.

Medical Dictionary for Regulatory Activities (MedDRA) Version xx.x

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.7.2.2 Serious Adverse Events MAD (Safety Population)

Programing Note:
Same as Listing 16.2.7.2.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.8.1.1 Hematology and Coagulation SAD (Safety Population)

Treatment: CVN766 5 mg

Lab Category: Hematology

Parameter: Hemoglobin (unit)

Subject ID	Visit	Collection Date/ Time (YYYY-MM-DD/ HH:MM)	Actual Value	Change from Baseline[1]	Reference Range	High/Low Flag	Clinically Significant
XXX	Screening	YYYY-MM-DD/ HH:MM	xx	N/A	xx, xx		
	Day -1	YYYY-MM-DD/ HH:MM	xx	N/A	xx, xx	H	NCS
	Day 1	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx		
	Day 2	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx		
	Day 3	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx		
	…						
….	Day 14/ET	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx		

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable. H = Above Normal Range, L = Below Normal Range. CS = Clinically Significant, NCS = Not Clinically Significant.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.8.1.2 Hematology and Coagulation MAD (Safety Population)

Programing Note:
Same as Listing 16.2.8.1.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.8.2.1 Serum Chemistry SAD (Safety Population)

Treatment: CVN766 5 mg

Parameter: Sodium (unit)

Subject ID	Visit	Collection Date/ Time (YYYY-MM-DD/ HH:MM)	Actual Value	Change from Baseline[1]	Reference Range	High/Low Flag	Clinically Significant	Comments
XXX	Screening	YYYY-MM-DD/ HH:MM	xx	N/A	xx, xx			
	Day -1[1]	YYYY-MM-DD/ HH:MM	xx	N/A	xx, xx	H	NCS	xxxxxxxx
	Day 1	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx			
	Day 2	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx			
	Day 3	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx			
	…							
….	Day 14/ET	YYYY-MM-DD/ HH:MM	xx	xx	xx, xx			

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable. H = Above Normal Range, L = Below Normal Range. CS = Clinically Significant, NCS = Not Clinically Significant.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.8.2.2 Serum Chemistry MAD (Safety Population)

Programing Note:
Same as Listing 16.2.8.2.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.8.3.1 Urinalysis SAD (Safety Population)

Treatment: CVN766 5 mg

Parameter: Glucose (unit)

Subject ID	Visit	Collection Date/ Time (YYYY-MM-DD/ HH:MM)	Actual Value	Reference Range	Abnormal Flag	Clinically Significant
XXX	Day -1[1]	YYYY-MM-DD/ HH:MM	Trace	xx, xx	Abnormal	NCS
	Day 7	YYYY-MM-DD/ HH:MM	xxxxxxx	xx, xx		NCS
….						

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
H = Above Normal Range, L = Below Normal Range. CS = Clinically Significant, NCS = Not Clinically Significant.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.8.3.2 Urinalysis MAD (Safety Population)

Programing Note:
Same as Listing 16.2.8.3.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.9.1.1 Vital Signs SAD (Safety Population)

Treatment: CVN766 5 mg

Parameter: Heart Rate (bpm)
Test: Supine

Subject ID	Visit	Time Point	Assessment Date/ Time (YYYY-MM-DD/ HH:MM)	Actual Value	Change from Baseline[1]	Vital Signs Assessment
XXX	Screening		YYYY-MM-DD/ HH:MM	xx	N/A	xx
	Day -1		YYYY-MM-DD/ HH:MM	xx	N/A	xx
	Day 1	Pre-Dose [1]	YYYY-MM-DD/ HH:MM	xx	N/A	xx
….		0.5 hour	YYYY-MM-DD/ HH:MM	xx	xx	xx
		1 hour	YYYY-MM-DD/ HH:MM	xx	xx	xx
		2 hours	YYYY-MM-DD/ HH:MM	xx	xx	xx
		4 hours	YYYY-MM-DD/ HH:MM	xx	xx	xx
		6 hours	YYYY-MM-DD/ HH:MM	xx	xx	xx
		8 hours	YYYY-MM-DD/ HH:MM	xx	xx	xx
		12 hours	YYYY-MM-DD/ HH:MM	xx	xx	xx
	Day 2		YYYY-MM-DD/ HH:MM	xx	xx	xx
	Day 3		YYYY-MM-DD/ HH:MM	xx	xx	xx
	Day 4		YYYY-MM-DD/ HH:MM	xx	xx	xx
	Day 8		YYYY-MM-DD/ HH:MM	xx	xx	xx
	/ET		YYYY-MM-DD/ HH:MM	xx	xx	xx
….						

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
N/A = Not Applicable. CS = Clinically Significant, NCS = Not Clinically Significant.
ET = Early Termination.

Programing Note:

Add following treatment columns;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.
Repeat for: Supine, Standing.

Listing 16.2.9.1.2 Vital Signs - MAD (Safety Population)

Programing Note:
Same as Listing 16.2.9.1.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.
Repeat for: Supine, Standing.

Listing 16.2.9.2.1 12-Lead ECG SAD (Safety Population)

Treatment: CVN766 5 mg

Parameter: QTcF (msec)

Subject ID	Visit	Time Point	Tracing	Assessment Date/ Time (YYYY-MM-DD/ HH:MM)	Actual Value	Average value	Change from Baseline[1]	Overall ECG Clinical Interpretation	Abnormal Description
XXX	Screening			YYYY-MM-DD/ HH:MM	xx		N/A	Normal	
	Day -1			YYYY-MM-DD/ HH:MM	xx		N/A	Normal	
	Day 1	Pre-Dose[1]	1	YYYY-MM-DD/ HH:MM	xx	xx	N/A	Abnormal, NCS	xxxxxxxxxx
			2	YYYY-MM-DD/ HH:MM	xx			Normal	
			3	YYYY-MM-DD/ HH:MM	xx			Abnormal, CS	xxxxxxxxxx
		0.5 hours	1	YYYY-MM-DD/ HH:MM	xx	xx	xx	Normal	
			2	YYYY-MM-DD/ HH:MM	xx				
			3	YYYY-MM-DD/ HH:MM	xx				
….		1 hour	1	YYYY-MM-DD/ HH:MM	xx	xx	xx	Normal	
			2	YYYY-MM-DD/ HH:MM	xx		xx	Normal	
			3	YYYY-MM-DD/ HH:MM	xx		xx	Normal	
		…….		YYYY-MM-DD/ HH:MM	xx		xx	Normal	
	Day 2			YYYY-MM-DD/ HH:MM	xx	xx	xx	Normal	
	…			YYYY-MM-DD/ HH:MM	xx		xx	Normal	
	Day 14/ET			YYYY-MM-DD/ HH:MM	xx		xx	Normal	
….									

[1] Baseline is defined as the last available, valid, non-missing observation prior to first study drug administration.
[2] Mean value of ECG tracings at the timepoint. The worst of the ECG clinical interpretations will be presented with the mean value.
N/A = Not Applicable. CS = Clinically Significant, NCS = Not Clinically Significant.
ET = Early Termination.

Programing Note:
Add following treatment;

CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.
Display all ECG parameter.

Listing 16.2.9.2.2 12-Lead ECG MAD (Safety Population)

Programing Note:
Same as Listing 16.2.9.2.1
Add following treatment columns;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.
Display all ECG parameter.

Listing 16.2.9.3.1 Neurological Exam SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Was the Neurological Exam performed? (Yes/No – Reason)	Date/ Time of Examination (YYYY-MM-DD/ HH:MM)	Body System	Result
XXX	Day -1	Yes	YYYY-MM-DD/ HH:MM	Light Touch/ Power in Limbs/ Brief Cranial Nerve Examination	Normal/ Abnormal NCS/ Abnormal CS/ Not Done
	Day 1	Yes	YYYY-MM-DD/ HH:MM	…	xx
	Day 2	No – xxx	YYYY-MM-DD/ HH:MM	…	xx
	Day 3	…	YYYY-MM-DD/ HH:MM	…	xx
	Day 4	….	YYYY-MM-DD/ HH: MM	….	xx
...	……				

Programing Note:
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.9.3.2 Neurological Exam MAD (Safety Population)

Subject ID	Visit	Was the Neurological Exam performed? (Yes/No – Reason)	Date/ Time of Examination (YYYY-MM-DD/ HH:MM)	Body System	Result
XXX	Day -1	Yes	YYYY-MM-DD/ HH:MM	Light Touch/ Power in Limbs/ Brief Cranial Nerve Examination	Normal/ Abnormal NCS/ Abnormal CS/ Not Done
	Day 1	Yes	YYYY-MM-DD/ HH:MM	…	xx
	Day 7	No – xxx	YYYY-MM-DD/ HH:MM	…	xx
	Day 9	…	YYYY-MM-DD/ HH:MM	…	xx
	Day 14	….	YYYY-MM-DD/ HH: MM	….	xx
	E/T				
….	….	….			

Programing Note:
Same as Listing 16.2.9.3.1
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.9.4.1 Physical Examination SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Visit	Assessment Date (YYYY-MM-DD)	Exam Type/Body System	Result	Description of Abnormality
XXX	Screening	YYYY-MM-DD	Complete Physical examination		
			Head, Eyes, Ears, Nose, Throat	Normal	
			Respiratory	Normal	
			…	Normal	
			Respiratory	Normal	
			Other - XXXXXXXX	Normal	
	…….				
XXX	Day 1	YYYY-MM-DD	Symptom Directed Physical Examination		
			…Respiratory	Normal	
			…..		
	…….				
	Day 14/ ET	YYYY-MM-DD	Symptom Directed Physical Examination		
			General Appearance	Normal	
			Head and Neck	Normal	
			Eyes/Ears/Nose/Throat	Normal	
			…		
			Respiratory	Abnormal, NCS	ZZZZZZZZZZZZ
			Other - XXXXXXXX	Normal	
…					

CS = Clinically Significant, NCS = Not Clinically Significant.
ET = Early Termination

Programing Note:
Type = Complete Physical Examination and Symptom-directed Physical Examination
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.9.4.2 Physical Examination MAD (Safety Population)

Programing Note:
Same as Listing 16.2.9.4.1
Repeat for following treatments;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.10.1.1 Prior Medication SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Concomitant Medication Therapy/ Anatomical Therapeutic Class (ATC) [Level 3]/ Preferred Term (PT)	Active Ingredients	Indication	Start Date (YYYY-MM-DD) End Date (YYYY-MM-DD)	Dose	Unit	Frequency	Route
XXX	XXXXXXXXXXXXXXXXXXXXX/ ZZZZZZZZZZZZZZZZZZZZZ/ YYYYYYYYYYYYYYYYYYYY	xxxxxxxx, yyyyyyyy	zzzzzzzz	YYYY-MM-DD/ YYYY-MM-DD	XX	Unit	YYYYYY	ZZZZZ
	XXXXXXXXXXXXXXXXXXXXX/ ZZZZZZZZZZZZZZZZZZZZZ/ YYYYYYYYYYYYYYYYYYYY	xxxxxxxx, yyyyyyyy	zzzzzzzz	YYYY-MM-DD/ YYYY-MM-DD	XX	Unit	YYYYYY	ZZZZZ
…	…							

Prior medications are defined as any medication where the use was stopped prior to the first administration of the study medication.

World Health Organization-Drug Dictionary (WHO-DD) Version xx, YYYY

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.10.1.2 Prior Medication MAD (Safety Population)

Programing Note:
Same as Listing 16.2.10.1.1
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Listing 16.2.10.2.1 Concomitant Medication SAD (Safety Population)

Treatment: CVN766 5 mg

Subject ID	Concomitant Medication Therapy/ Anatomical Therapeutic Class (ATC) [Level 3]/ Preferred Term (PT)	Active Ingredients	Indication	Start Date (YYYY-MM-DD) End Date (YYYY-MM-DD)	Dose	Unit	Frequency	Route
XXX	XXXXXXXXXXXXXXXXXXXXX/ ZZZZZZZZZZZZZZZZZZZZZ/ YYYYYYYYYYYYYYYYYYYY	xxxxxxxx, yyyyyyyy	zzzzzzzz	YYYY-MM-DD/ YYYY-MM-DD	XX	Unit	YYYYYY	ZZZZZ
	XXXXXXXXXXXXXXXXXXXXX/ ZZZZZZZZZZZZZZZZZZZZZ/ YYYYYYYYYYYYYYYYYYYY	xxxxxxxx, yyyyyyyy	zzzzzzzz	YYYY-MM-DD/ Ongoing	XX	Unit	YYYYYY	ZZZZZ
…	…							

Concomitant medications are defined as any medication (other than the study drug) that was used at least once after the first administration of the study drug.

World Health Organization-Drug Dictionary (WHO-DD) Version xx, YYYY

Programing Note:

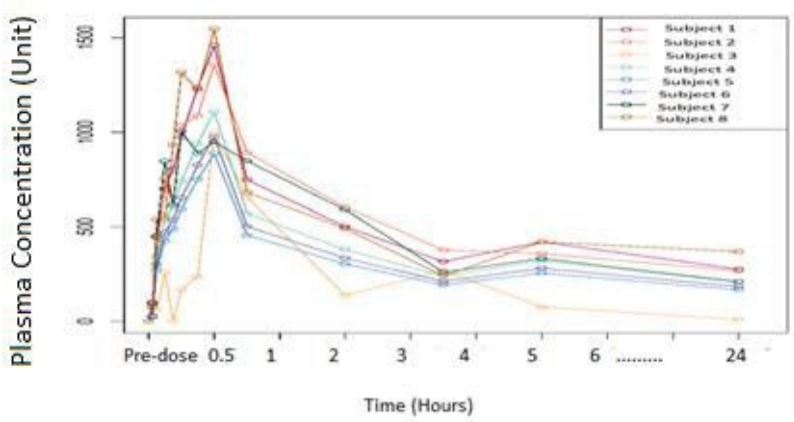
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Listing 16.2.10.2.2 Concomitant Medication MAD (Safety Population)

Programing Note:
Same as Listing 16.2.10.2.1
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.1.1.1 Individual Plasma Concentrations of CVN766 vs Time (Linear) SAD (Pharmacokinetic Population)

Treatment: CVN766 5 mg



Source Listing: 16.2.6.1.1

Programming Note:
The x-axis will represent the study time in hours (0 – 72 hours).
The y-axis will represent the Plasma Concentrations (unit). The y-axis will be on the linear scale.
All participants per treatment group (one page for each treatment group) will be represented on a single page. Each subject will be presented as a distinct line type.

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.1.1.2 Individual Plasma Concentrations of CVN766 vs Time (Linear) MAD (Pharmacokinetic Population)

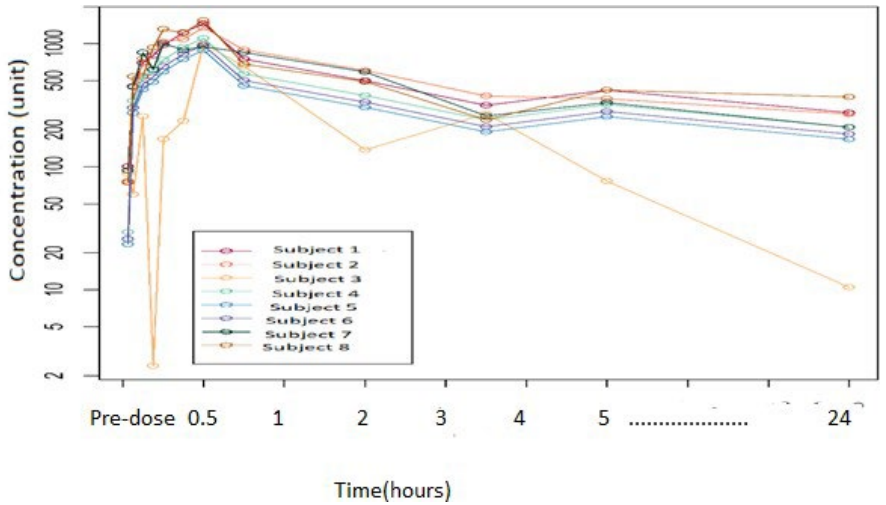
Programing Note:
Same as Figure 14.2.1.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.
Repeat for following days: Day 1, Day 7

Figure 14.2.1.1.3 Individual Plasma Ctrough Concentrations of CVN766 vs Time Post-Dose (Linear) MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.1.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.1.2.1 Individual Plasma Concentrations of CVN766 vs Time (Semi-Log) SAD (Pharmacokinetic Population)

Treatment: CVN766 5 mg



Source Listing: 16.2.6.1.1

Programming Note:
The x-axis will represent the study time in hours (0 – 72 hours).
The y-axis will represent the Plasma Concentrations (unit). The y-axis will be on the semi-log scale.
All participants per treatment group (one page for each treatment group) will be represented on a single page. Each subject will be presented as a distinct line type.

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.1.2.2 Individual Plasma Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD (Pharmacokinetic Population)

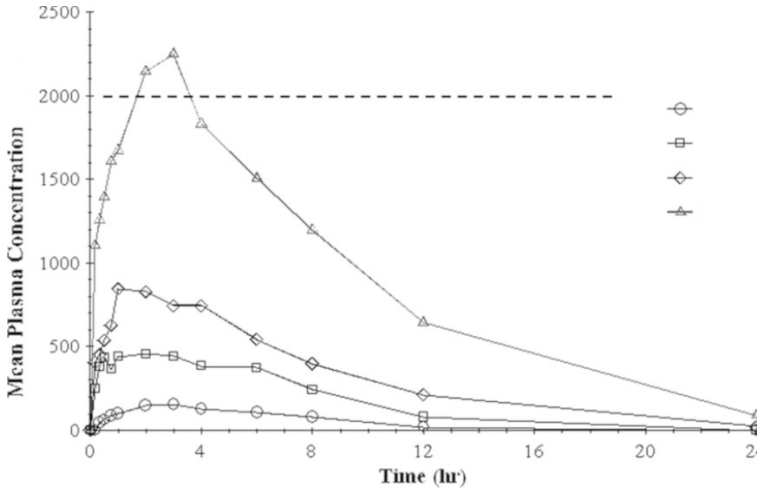
Programing Note:
Same as Figure 14.2.1.2.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.
Repeat for: Day 1, Day 7

Figure 14.2.1.2.3 Individual Plasma Ctrough Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.1.2.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.2.1.1 Mean (+/- SD) Plasma Concentrations of CVN766 vs Time Post-Dose (Linear) SAD (Pharmacokinetic Population)

Treatment: CVN766 5 mg



Source Listing: 16.2.6.1.1

Programming Note:
The x-axis will represent the study time in hours (0 –72 hours).
The y-axis will represent the mean (+/-SD) Plasma Concentrations (unit). The y-axis will be on the linear scale.
Each dose level for the active treatment will be presented as a distinct line type. Placebo will be excluded.

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.2.1.2 Mean (+/- SD) Plasma Concentrations of CVN766 vs Time (Linear) MAD (Pharmacokinetic Population)

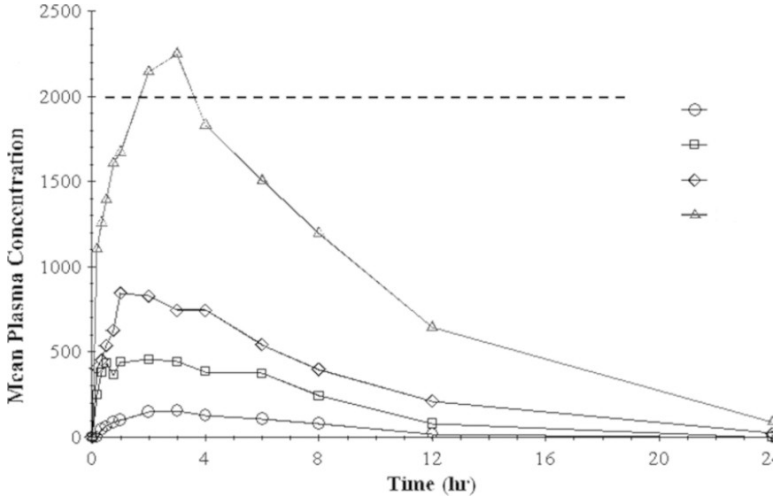
Programing Note:
Same as Figure 14.2.2.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.
Repeat for: Day 1, Day 7

Figure 14.2.2.1.3 Mean (+/- SD) Plasma Ctrough Concentrations of CVN766 vs Time Post-Dose (Linear) MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.2.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.2.2.1 Mean (+/- SD) Plasma Concentrations of CVN766 vs Time (Semi-Log) SAD (Pharmacokinetic Population)

Treatment: CVN766 5 mg



Source Listing: 16.2.6.1.1

Programming Note:
The x-axis will represent the study time in hours (0 –72 hours).
The y-axis will represent the mean (+/-SD) Plasma Concentrations (unit). The y-axis will be on the logarithmic scale.
All treatments will be represented on a single page. Each treatment group will be presented as a distinct line type.

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 45 mg(Fed), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.2.2.2 Mean (+/- SD) Plasma Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.2.2.1;
Source Listing: 16.2.6.1.2;

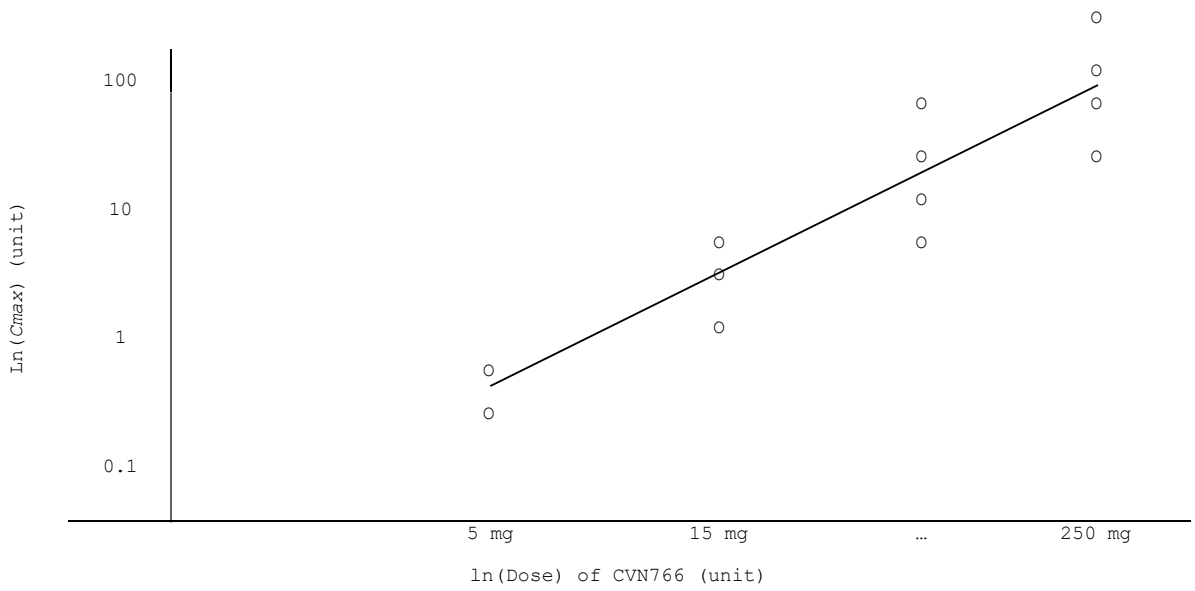
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.
Repeat for: Day 1, Day 7

Figure 14.2.2.2.3 Mean (+/- SD) Plasma Ctrough Concentrations of CVN766 vs Time Post-Dose (Semi-Log) MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.2.2.1;
Source Listing: 16.2.6.1.2;
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.1.1 Plasma Cmax versus dose for CVN766 SAD (Log Scale)(Pharmacokinetic Population)

Pharmacokinetic parameter: Cmax (unit)



Source Listing: 16.2.6.1.1

O Original values
____ = Power Model Curve

Programming Note:
The x-axis represents ln(dose) from 5 mg to 250 mg.
The y-axis will represent the Cmax on a ln scale.

Programing Note:

Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.1.2 Plasma Cmax,ss versus dose for CVN766 MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.2.1 Plasma AUCinf versus dose for CVN766 SAD (Log Scale) (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.3.1 Plasma AUC24 versus dose for CVN766 SAD (Log Scale) (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.3.2 Plasma AUC24 versus dose for CVN766 MAD (Log Scale) (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.4.1 Plasma AUCt versus dose for CVN766 SAD (Log Scale) (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.4.2 Plasma AUCt versus dose for CVN766 MAD (Log Scale) (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.5.1 Plasma AUCtau versus dose for CVN766 MAD (Log Scale) (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.6.1 Plasma t1/2z versus dose for CVN766 SAD (Log Scale) (Pharmacokinetic Population)

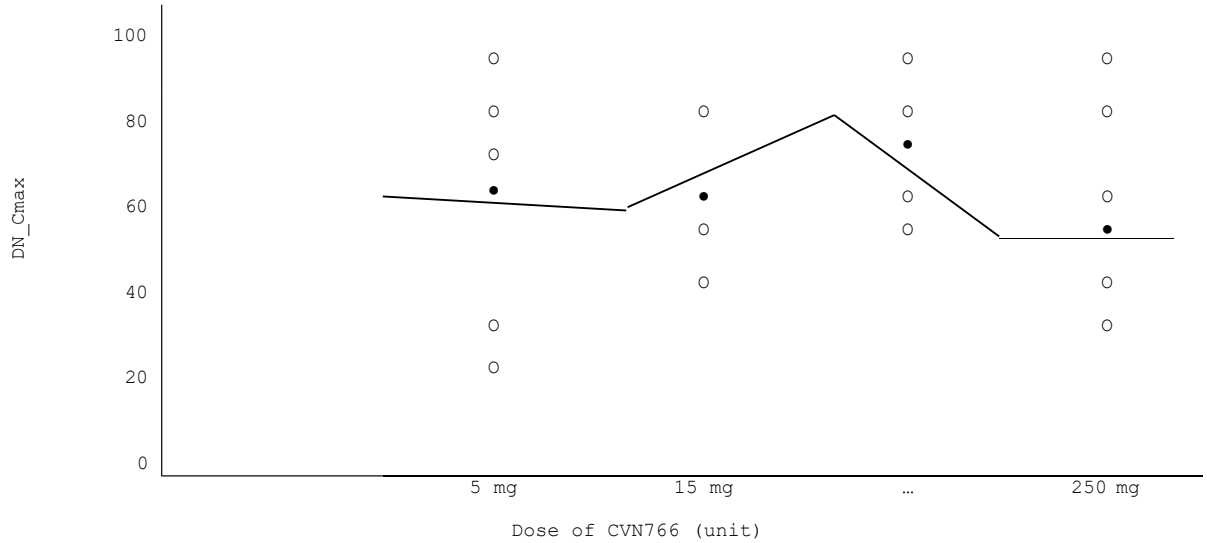
Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg(Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.3.6.2 Plasma t1/2z versus dose for CVN766 MAD (Log Scale) (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.3.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.1.1 Dose-normalized Cmax versus dose for CVN766 SAD (Pharmacokinetic Population)

Pharmacokinetic parameter: Cmax



Source Listing: 16.2.6.1.1

O Original values
____●____ Geometric Means

Programming Note:
The x-axis represents dose from 5 to 250 mg.
The y-axis will represent the dose normalized Cmax.

Programing Note: *Add following treatment;* *CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 125 mg, CVN766 250 mg.*

Figure 14.2.4.1.2 Dose-normalized Cmax,ss versus dose for CVN766 MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.2.1 Dose-normalized AUCinf versus dose for CVN766 SAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.3.1 Dose-normalized AUC24 versus dose for CVN766 SAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.3.2 Dose-normalized AUC24 versus dose for CVN766 MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.4.1 Dose-normalized AUCt versus dose for CVN766 SAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.4.2 Dose-normalized AUCt versus dose for CVN766 MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.5.1 Dose-normalized AUCtau versus dose for CVN766 MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.6.1 Dose-normalized t1/2z versus dose for CVN766 SAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.1
Add following treatment;
CVN766 5 mg, CVN766 15 mg, CVN766 45 mg (Fasted), CVN766 125 mg, CVN766 250 mg.

Figure 14.2.4.6.2 Dose-normalized t1/2z versus dose for CVN766 MAD (Pharmacokinetic Population)

Programing Note:
Same as Figure 14.2.4.1.1
Source Listing: 16.2.6.1.2
Add following treatment;
CVN766 45 mg, CVN766 125 mg, CVN766 250 mg.

Cerevance_CVN766-101_SAP_v1.0_2022_10_20

Final Audit Report 2022-10-21

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By:	[redacted]
Status:	Signed
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