

Reporting and Analysis Plan J2A-MC-GZGD (1.0)

A Multiple Dose Study in Healthy Participants to Investigate the Safety, Tolerability, and Pharmacokinetics of LY3502970

NCT05051566

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## REPORTING AND ANALYSIS PLAN

### A Multiple Dose Study in Healthy Participants to Investigate the Safety, Tolerability, and Pharmacokinetics of LY3502970

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## 2 List of Abbreviations

ADaM	analysis data model
AE	adverse event
AESI	adverse event of special interest
ATC	anatomical therapeutic chemical
AUC	area under the curve
BLQ	below the limit of quantification
BMI	body mass index
BP	blood pressure
CDISC	Clinical Data Interchange Standards Consortium
CHMP	Committee for Medicinal Products for Human Use
CI	confidence interval
COVID-19	Coronavirus disease 2019
CSR	clinical study report
CV%	coefficient of variation
CVw%	Intra-participant variability
D	'substantial' decrease from baseline for vital signs parameters
DP	decimal place
ECG	electrocardiogram
Frel	relative bioavailability
GMR	geometric mean ratio
h	hour
H	flag used for value that is above normal reference range
HR	heart rate
I	'substantial' increase from baseline for vital signs parameters
	increase in QTcF interval from baseline

ICH	International Council for Harmonisation
IMP	investigational medicinal product
ISF	Investigator Site File
L	flag used for value that is below normal reference range
LLOQ	lower limit of quantification
Max	maximum
MedDRA	Medical Dictionary for Regulatory Activities
Min	minimum
n	number of participants with an observation
N	number of participants in the dataset
NA	not applicable
NC	not calculated
NR	not reportable/no result
NS	no sample
PI	principal investigator
PK	pharmacokinetic
PT	preferred term
QC	quality control
QD	Once a day
RAP	reporting analysis plan
SAE	serious adverse event
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2

SD	standard deviation
SDTM	study data tabulation model
SF	significant figure
SI	substantial increase in QTcF interval from baseline
SOC	system organ class
SOP	standard operating procedure
TEAE	treatment-emergent adverse event
TFL	tables, figures and listings
TDL	The doctor's laboratory
WHO	World Health Organisation

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### 3 Introduction

This document details the following for Quotient Sciences (Quotient) Study QSC202755 (J2A-MC-GZGD).

- Criteria to be used for the definition of the populations and analysis sets relating to safety and pharmacokinetic (PK) data
- Handling of missing data
- Proposed tables, figures and listings (TFLs) for demographic, dosing, PK and safety data
- Methods for PK parameter estimation and the formal statistical analysis

This document has been compiled according to the Quotient standard operating procedure (SOP) "Production of Reporting and Analysis Plans" and has been written based on information contained in the final v2.0 study protocol dated 07 Jun 2021.

#### 3.1 Responsibilities

The Data Sciences Department at Quotient will be responsible for the production of the following items using Quotient SOPs, except where otherwise agreed upon and noted within the RAP: Clinical Data Interchange Standards Consortium (CDISC), study data tabulation model (SDTM) and analysis data model (ADaM) datasets; PK parameter estimation and output; including all summary tables, figures and data listings, and formal statistical analysis; and the clinical study report (CSR).

Quotient will provide two sets of tables, data listings and figures during the study:

- Post database lock TFLs (draft) for Lilly to review and
- Post-review TFLs (final) for reporting purposes.

Quotient will be responsible for the quality control (QC) of all deliverables prior to the client review ([Section 13.2](#)).

#### 3.2 Definitions

##### 3.2.1 Participant Definitions

During the clinical phase of the study, an evaluable participant is defined as a participant who received at least 1 full dose of prototype formulation and have a baseline and at least 1 postbaseline evaluable PK sample. This will be monitored during the clinical phase to identify any requirement for replacement participants. This definition will not be used during the reporting phase including the identification of analysis populations and datasets.

An enrolled participant is defined as a participant who signed the informed consent, qualified per the inclusion/exclusion criteria and were assigned a subject number and treatment. In the test periods of both study parts, a randomized participant is defined as a participant who signed the informed consent, qualified per the inclusion/exclusion criteria and were randomized and assigned to a treatment sequence in tests Period 1 and Period 2.

##### 3.2.2 Definition of Treatments

Throughout the reporting of the study, the treatments will be reported as detailed in [Table 1](#) below:

**Table 1 Study Treatments (Part A and Part B)**

IMP Name	Dose	Route of Administration	TFL Label
<b>Part A only</b>			
LY3502970 Capsule for Dose Titration	CCI QD (as 1 capsule)	Oral	CCI CAP
			CCI CAP
			CCI CAP
LY3502970 Reference Capsule	CCI QD	Oral	CCI CAP
LY3502970 Prototype X Tablet	CCI QD	Oral	CCI P TAB X
<b>Part B only</b>			
LY3502970 Capsule for Dose Titration	CCI QD (as 1 capsule)	Oral	CCI CAP
			CCI CAP
			CCI CAP
LY3502970 Reference Capsule	CCI QD	Oral	CCI CAP
LY3502970 Prototype X Tablet	CCI QD	Oral	CCI P TAB X
LY3502970 Prototype X Tablet Fed	CCI QD	Oral	CCI P TAB X FED
LY3502970 Prototype X Tablet + Proton Pump Inhibitor Tablet	CCI QD LY3502970+ 40 mg QD PPI	Oral	CCI P TAB X + PPI

QD=One Daily, CAP=Capsule, TAB=Tab, PPI=Proton Pump Inhibitor Capsule, All doses given fasted unless indicated

### 3.2.3 Definition of Visits

For clinical data in both Part A and Part B, visits will be referred to as Study Day throughout this document and will be referred to as Screening, Day -2 (Pre-admission), Day -1 (Baseline), Day 1 through to Day 41 and Follow-up (Between Day 43 and 53). Additionally a visit variable for reporting will be defined to reflect the Dosing Day within each period, Dosing Day 1 to Dosing Day 6, to allow reporting of data in the crossover period e.g. in Part A to allow data to be reported for each prototype relevant to the number of days dosed with each prototype.

Time points within these days are detailed in the schedule of assessments in [Appendix 1](#) (Part A) and [Appendix 2](#) (Part B) respectively.

Baseline is defined as nominally the last measurement recorded prior to the first dose of investigational medicinal product (IMP).

## 4 Objectives

The objectives and endpoints of the study are detailed in [Table 2](#).

**Table 2 Study Objectives and Endpoints (Part A and Part B)**

Objectives Endpoints	Objectives Endpoints
<b>Primary</b>	<b>Primary</b>
<ul style="list-style-type: none"> <li>To characterize and compare the PK of different prototype formulations of LY3502970 after multiple oral doses in healthy participants compared to the reference formulation</li> </ul>	<ul style="list-style-type: none"> <li>Primary PK parameters for analysis will include C<sub>max</sub>, AUC, and t<sub>max</sub></li> </ul>
<b>Secondary</b>	<b>Secondary</b>
<ul style="list-style-type: none"> <li>To assess the safety and tolerability of prototype formulations in healthy participants</li> <li>For options 1 and 2 of Part B, to characterize and compare the PK of 1 prototype formulation of LY3502970 under different administration conditions (fasted, fed, PPI) after multiple oral doses in healthy participants</li> </ul>	<ul style="list-style-type: none"> <li>Incidence of TEAEs and SAEs</li> <li>Primary PK parameters for analysis will include C<sub>max</sub>, AUC, and t<sub>max</sub></li> </ul>

## 5 Study Design

### 5.1 Brief Description

Study GZGD is a Phase 1, single-site, randomized, partially participant-blind, crossover study in healthy participants to be conducted in 2 parts.

#### 5.1.1 Part A (Initial Formulation Evaluation)

Part A will evaluate the safety, tolerability, and PK of multiple oral doses of LY3502970 formulation prototypes in healthy participants. There will be a dose titration period from Day 1 through Day 18, where participants will receive increasing doses of LY3502970 capsule for dose titration. Within-treatment dose escalation will be every 6 days and will reach a maximum dose of CCI once daily (QD) on Day 19. On Days 19 to 24, participants will receive LY3502970 reference capsule (CCI QD) before entering the test phase, from Day 25 to Day 36. During the test phase, the participants will be administered LY3502970 prototype tablet (CCI QD) formulations as per their randomization. The participants will crossover on Day 31 and receive the other prototype formulation through Day 36. PK and safety assessments will be performed according to the Schedule of Activities (SoA) [Appendix 1](#). Following the final dose on Day 36, a terminal PK period will be used to collect additional PK samples through the morning of Day 41. Participants should follow local guidance and clinical research unit (CRU) precautions to minimize risk for Coronavirus Disease 2019 (COVID-19) infection. On Day 41, the investigator or qualified designee will review all available inpatient safety data before discharging participants from the CRU after the morning procedures are completed, provided they are deemed medically fit by the investigator. Participants will complete the study after the safety follow-up visit, which will occur between 7 and 17 days after last dose.

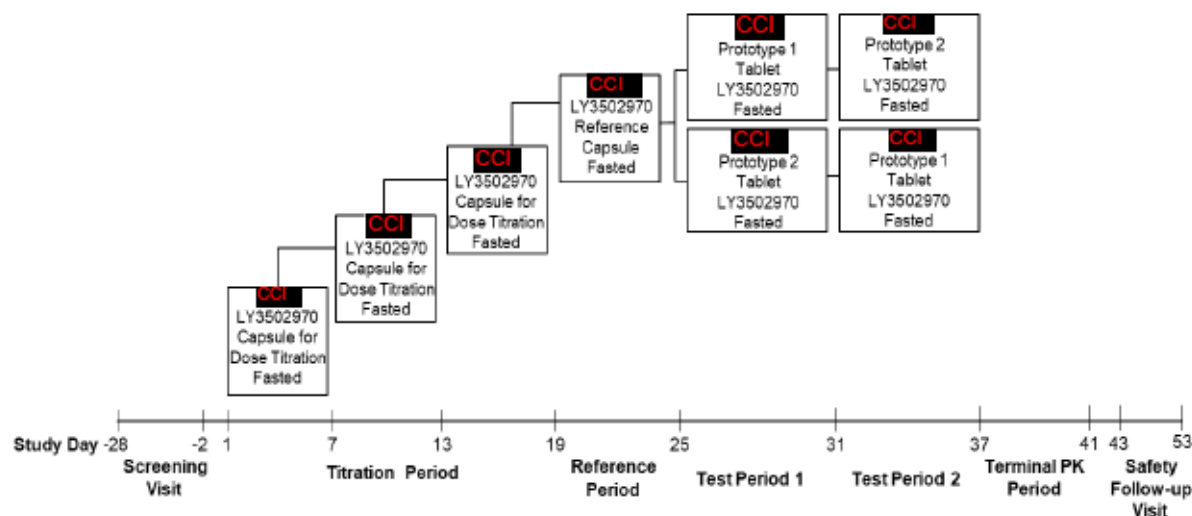


Figure 1 Schema Part A

### 5.1.2 Part B (Secondary Evaluation)

Depending on the results of Part A, Part B may further evaluate 1 of the formulations used in Part A with regard food and proton pump inhibitor (PPI) or Part B may be used to evaluate additional prototype formulations. As in Part A, treatment escalation will occur every 6 days during a titration period and will reach a maximum dose of CCI QD on Day 19. Based on the results of Part A, the sponsor will identify which 1 of 5 interventions (options) may be used for secondary evaluation of LY3502970 (CCI QD) from Day 19 to 36. These options include treatment with LY3502970 in a fasted or fed state and a fasted state with a co-administered PPI or evaluation of additional formulations in manner similar to Part A. Each option will begin with a 6-day reference period (CCI QD), followed by two 6-day test periods (CCI QD) as presented in the Schema (Figure 2). PK and safety assessments will be performed according to the SoA (Section 1.3). Following the final dose (CCI QD) on Day 36, a terminal PK period will be used to collect additional PK samples. Participants will remain at the CRU for the entire study. On Day 41, the investigator or qualified designee will review all available inpatient safety data before discharging participants from the CRU after the morning procedures are completed, provided they are deemed medically fit by the investigator. Participants will complete the study after the safety follow-up visit, which will occur between 7 and 17 days after last dose.

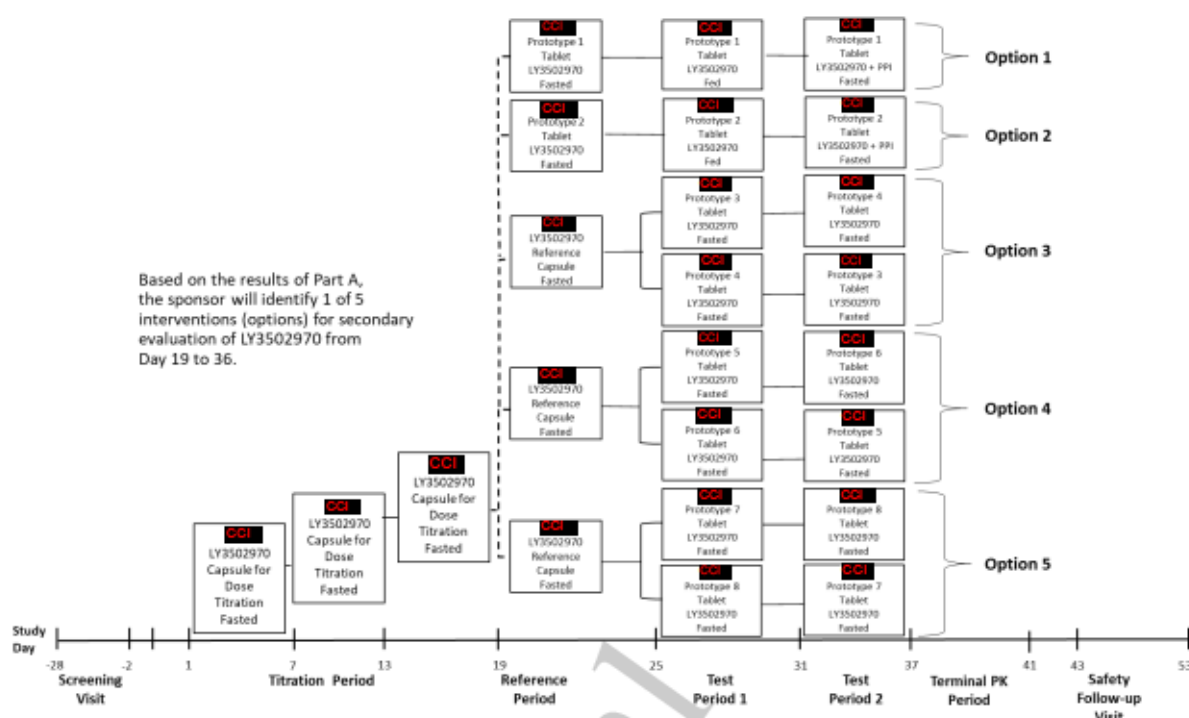


Figure 2 Schema Part B

## 5.2 Criteria for In-Study Decisions and Formulation Selection

Access to safety, tolerability, and PK data is scheduled to occur once approximately 10 evaluable participants have completed Part A of the study. The purpose of this review is to guide optimal formulation selection for Part B.

In-study decisions for formulation to be dosed will be made by the project team, and will always include the investigator, the sponsor's medical monitor or the sponsor's medically qualified designee who is familiar with the study protocol and IB, and a PK expert, where appropriate. The following in-study decisions will be made during this study:

- Formulation selection for Part B
- Whether to dose PPI
- Selection of prandial status

The decisions for Part B will only be made after a review of the available data collected from Part A. For the Part B decisions to occur, data should be available from approximately 10 participants who have received both prototype formulations and completed the planned safety assessments up to Day 40. If data are not available for 10 participants, the principal investigator, scientific lead and sponsor will make a decision as to whether the data available are sufficient to support the formulation selection decision.

The following data are required:

- Demography
- Adverse events
- Plasma concentrations of LY3502970

- PK parameter estimates, including figures and tables

Within-cohort dose escalations during the titration phase will be driven by emerging real-time safety data and assessed by the investigator on an individual participant basis. The decision to proceed with the next incremental dose will be documented in the source.

### 5.3 Study Sample Size

It is planned that 24 participants (12 for each part), will be assigned, randomly where applicable, to study intervention such that approximately 10 evaluable participants in each part complete the study. The sample size for the study was chosen to provide sufficient data for evaluating safety and/or PK parameters.

To enable the minimum number of evaluable participants to be met, participants who discontinue early may be replaced after consultation with the investigator and sponsor. The replacement participant will be assigned to the same treatment as the discontinued participant. Participants withdrawn from the study due to IMP safety reasons will not be replaced.

### 5.4 Randomization (including Replacement Participants)

Parts A and B (Options 3, 4 and 5) of the study are randomized; therefore, a randomization schedule will be produced for each part. The original randomization schedules and proof of quality control procedures will be held by the Data Sciences department at Quotient Sciences until the study is archived, at which time the randomization materials will be retained in the Investigator Site File (ISF).

Participants will be randomized immediately prior to dosing on Day 25.

In both study parts, participant numbers will be randomized to a study intervention sequence so that 12 participants are assigned to 1 of 2 sequences (i.e. Prototype 1/Prototype2, or Prototype 2/Prototype1 in Part A). The assignment will be balanced with 6 participants assigned to each treatment sequence.

Participant numbers will be allocated on the morning of dosing according to the code 001 to 024 using the lowest number available. Replacement participants will be allocated participant numbers 901 to 924, where the last 2 digits are the same as those of the original participant (e.g., if Participant 005 withdraws, the replacement will have participant number 905 and will receive any regimens which Participant 005 did not receive in addition to any regimens which are required to make the required comparison of interest).

### 5.5 Blinding Issues

Participants will be blinded (e.g., with a blindfold or similar method) to the various LY3502970 formulations in Parts A and B (Options 3, 4, and 5) from Days 25 to 37. For Options 1 and 2 in Part B, participants will not be blinded.

Returned study intervention should not be re-dispensed to the participants.

## 6 Populations and Analysis Sets

### 6.1 Safety Population and Safety Analysis Set

Separate safety populations will be defined for each study part, and will include all participants who have received at least 1 dose of IMP.

The safety analysis set will be defined on a treatment basis, and will include all relevant data from the participants included in the safety population who have received that treatment.

The safety population will be confirmed by Quotient with approval from Lilly after database lock, and will be summarised in the analysis populations table, which confirms the number of subject included in each population. The safety population will also be used to determine the participants to be included in the safety analysis set.

The safety analysis set will be confirmed by Quotient with approval from Lilly at the same time as the safety population and will be summarised for the analysis of demographic and baseline characteristics, and all safety data.

## 6.2 Pharmacokinetic Population and Pharmacokinetic Analysis Set(s)

The PK population will be defined separately for study parts A and B and will include all randomized (or entered into the next Period where the part is not randomized) participants who received at least 1 full dose of both the reference (baseline) formulation (i.e., either the reference capsule in the randomised components or the fasted prototype in the non-randomised component) and at least 1 prototype formulation in tests periods and have at least 1 post-baseline evaluable PK sample from the test period and who satisfy the following criteria for at least 1 profile:

- No missing samples or invalid post-dose analytical results at critical time points (e.g. around C<sub>max</sub>, T<sub>last</sub> etc)
- No relevant protocol deviations that may impact the study objectives with respect to the PK endpoints
- No relevant AEs such as vomiting occurring at any time during the PK sampling Day in question that suggest that the whole dose was not available for absorption for a particular participant

The PK analysis set will be defined on a per-treatment basis and will include all relevant data from the participants included in the PK population who have received that treatment.

Individual participants(i.e. treatments) will be excluded from the PK analysis set where deemed appropriate such as if the participant's data for the treatment affected did not meet the bullet point criteria above for at least one individual profile (i.e. day), or other study emergent point related to PK analysis or interpretation.

Individual participant profiles (i.e. days) will be flagged and excluded from the PK summary statistics where deemed appropriate such as if the profile in the treatment affected did not meet the bullet point criteria above, or other study emergent point related to PK analysis or interpretation.

All enrolled participants will be used for the PK data listings. The PK population will be used for the analysis populations table. The PK analysis set will be used for the provision of PK summary tables and figures as well as the formal statistical analysis.

## 7 Participant Disposition, Demographics and Baseline Characteristics

No formal statistical testing will be performed on participant disposition, or on demographic or baseline data. Summaries of participant disposition and analyses populations will be based on all enrolled participants and summaries of all other data described in this section will be based on the safety analysis set unless otherwise stated.

Separate summary tables and listings will be provided for each study part.

### 7.1 Screening Failures

Data for participants who have failed screening will be databased but will not be cleaned and therefore will not be included in the SDTM or ADaM datasets or any of the tables, figures or data listings or the CSR.

### 7.2 Participant Disposition and Withdrawals

For each study part, the number and percentage of participants enrolled, dosed, randomised (if applicable), completed and discontinued will be presented by sequence and overall. If any participants discontinued from the study early then the number of participants for each reason for discontinuation will be presented by sequence and overall. However, if none of the participants discontinued from the study early, then the reasons for discontinuation will not be populated in the summary table. A participant may be discontinued from the study early for 1 reason only.

Participant disposition and withdrawal data will be listed including details of informed consent.

Protocol deviations and any violations of the inclusion/exclusion criteria will also be listed.

### 7.3 Analysis Populations

A summary table will be produced for each study part detailing the number and percentage of participants in each Safety and PK population overall. The reasons for exclusion from each population will also be included in the summary table. However, if none of the participants were excluded from a population, then the reasons for exclusion will not be populated in the summary table. A participant may be excluded from a population for more than 1 reason. The denominator for the percentage is the number of participants enrolled in the respective sequence.

Details of participants included and excluded in the different analysis populations will be listed.

### 7.4 Analysis Sets

In each study part, a summary table will be produced detailing the number and percentage of participants in each of the safety/PK analysis set for each treatment. The table will be based on the relevant population the analysis set is derived from (i.e., the safety/PK population). Separate tables will be presented for the safety (analysis set only) and PK (analysis set). The reasons for exclusion from each analysis set will also be included in the summary. However, if none of the participants were excluded from an analysis set, then the reasons for exclusion will not be populated in the summary table. A participant may be excluded from the analysis set for more than 1 reason. The denominator for the percentage is the number of participants in each population.

Details of participants included and excluded in the different analysis sets will be listed.

### 7.5 Demographic Characteristics and Lifestyle Details

Demographic data (date of birth, ethnicity, race, sex, height [cm], weight [kg] and body mass index [BMI; kg/m<sup>2</sup>]) will be recorded at screening. Age will be calculated using the following formula:

$$\text{Age (years)} = \frac{\text{Date of Informed Consent} - \text{Date of Birth}}{365.25}$$

and will be rounded down to the nearest year (using the SAS Software floor function).

In each study part, summary statistics (number of participants with an observation [n], mean, standard deviation [SD], median, minimum and maximum) will be presented for age, height, weight and BMI at screening by sequence and overall. The number and percentage of participants will be presented by sequence and overall for race and sex. The denominator for the percentage is all participants in the safety analysis set. If any values are missing, a "missing" row will be presented on the table.

Lifestyle details (i.e., smoking history [does the participant smoke, use e-cigarettes or use nicotine replacement products?] and alcohol consumption) will be summarised by sequence and overall as a categorical variable.

Demographic and life style data for all enrolled participants will be listed.

Separate tables will be produced for the Safety and PK populations.

## 7.6 Medical/Surgical History

In each study part, medical history will be recorded for each participant at the screening visit. All medical history data will be listed by participant and will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.0 (or more recent version) for System Organ Class (SOC) and Preferred Term (PT).

**Prior and Concomitant Medication**  
Medications (product name) will be coded in each study part using the World Health Organization (WHO) Drug Dictionary Global Drug Reference version 2021 Mar (or more recent), using the following Anatomical Therapeutic Chemical (ATC) classification codes;

- Product name
- Preferred name
- Drug code
- Therapeutic subgroup (ATC 2nd level code)
- Chemical subgroup (ATC 4th level code)

Prior medications are defined as medications that start and stop prior to the first dose of IMP. All other medications will be defined as concomitant medications including those that start prior to the first dose of IMP and continue thereafter. Any medications with an unknown start or stop date will be assumed to be concomitant medications unless a partial start or stop date indicates otherwise.

All medications, including coded terms, and the underlying indication for which the medication was given, will be listed. One combined data listing of prior and concomitant medications will be provided. All prior medications as defined above will be flagged with a "#" symbol. Within this flagged group medications that started after screening and stopped before dosing of IMP will also be flagged using a "\*" symbol.

## 7.8 Other Baseline Characteristics

All other baseline characteristics, as listed below, at screening and baseline (Day-1) (unless otherwise stated) for each study part, will be listed by participant for all enrolled participants:

- Serum pregnancy test for female participants (Screening only)
- Urine pregnancy test for female participants (Baseline, Day -1 only)
- Follicle stimulating hormone for female participants (Screening only)
- Serum Calcitonin (Screening only)
- Serology (Screening only)
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Antibody (Screening, day before admission and discharge – See footnote in schedule of assessments)
- SARS-CoV-2 Antigen (Screening, day before admission and discharge – See footnote in schedule of assessments)
- Urine drug screen
- Ethanol breath test

## 8 Efficacy

Efficacy is not evaluated in this study.

## 9 Pharmacokinetics

### 9.1 Pharmacokinetic Parameter Estimation and Reporting

The PK parameters (Table 3) for LY3502970 in plasma will be estimated where possible and appropriate for each participants profile (i.e. treatment) by non-compartmental analysis methods using Phoenix WinNonlin software (v8.0 or a more recent version, Certara USA, Inc., USA). Additional parameters may be calculated if required, depending on the data. The version of any software used for the analysis will be documented in the CSR.

#### 9.1.1 Definition of Pharmacokinetic Parameters

Plasma PK parameter definitions are provided in [Table 3](#).

**Table 3 Plasma PK Parameter Definitions and Rounding Specifications**

Parameter	Definition	Unit	DP or SF	No. of DP/SF
Tmax	Time of maximum observed concentration	h	DP	2
Cmax	Maximum observed concentration	mass unit/mL	SF	same specification as BioA
AUC(0-24)	Area under the curve from time 0 to 24 hours post dose	mass unit.h/mL	SF	3
AUC(0-last)	Area under the curve from time 0 to the time of last measurable concentration	mass unit.h/mL	SF	3
AUC(0-inf)	Area under the curve from time 0 extrapolated to infinity (terminal period only)	mass unit.h/mL	SF	3
AUCextrap	Area under the curve (AUC) from time of the last measurable concentration to infinity as a percentage of the area under the curve extrapolated to infinity (terminal period only)	%	DP	2
T1/2	Terminal elimination half-life (terminal period only)	h	DP	2

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Parameter	Definition	Unit	DP or SF	No. of DP/SF
lambda-z	First order rate constant associated with the terminal (log-linear) portion of the curve (terminal period only)	1/h	DP	4
CL/F24	Total body clearance calculated using AUC(0-24) after repeated extravascular administration, where F (fraction of dose bioavailable) is unknown	mL/min	SF	3
Vz/F24	Apparent volume of distribution based on the terminal phase calculated using AUC(0-24) after extravascular administration where F (fraction of dose bioavailable) is unknown	L	SF	3
Frel Cmax	Relative bioavailability based on Cmax	%	DP	2
Frel AUC(0-24)	Relative bioavailability based on AUC(0-24)	%	DP	2
lambda-z lower*	Lower limit on time for values to be included in the calculation of lambda-z	h	DP	2
lambda-z upper*	Upper limit on time for values to be included in the calculation of lambda-z	h	DP	2

DP=decimal places; NA=not applicable; SF=significant figures

\*=these values should be listed but omitted from the descriptive statistics

Observed PK parameters (i.e. based on the observed last quantifiable concentration (Clast)) will be reported.

Dose will be used in the calculation of relevant PK parameters as per [Table 4](#).

**Table 4 Dose Specifications**

Dose (nominal/actual)	Nominal
Precision	0 decimal places

Non-dose corrected relative bioavailability (Frel) will be calculated as follows:

$$Frel = \left\{ \frac{AUC \text{ or } C_{max} (\text{test})}{AUC \text{ or } C_{max} (\text{reference})} \right\} \times 100$$

Frel will be calculated using Cmax and AUC(0-24). If for any reason the AUC(0-24) is not calculable then an alternative or additional AUC over a partial area may be used to calculate Frel for all participants.

The following comparisons will be made using the Day 24, 30 and 36 profiles:

- LY3502970 Prototype Tablet X vs LY3502970 Reference Capsule
- Fed (test) vs fasted (reference) (Part B Only)
- With Proton Pump Inhibitor (test) vs without Proton Pump Inhibitor (reference) (Part B Only)

### 9.1.2 Rules for Pharmacokinetic Parameter Estimation using WinNonlin

The imputation of non-numerical (e.g. below the limit of quantification [BLQ]) or negative values (e.g. pre-dose sampling times) reported in the input data set will be performed as follows for calculation of PK parameters:

- Pre-dose sample times will be entered as zero. If a pre-dose concentration is missing on a multiple-dosing day, the pre-dose concentration value will be set to the minimum observed quantifiable concentration (C<sub>min</sub>) for the dosing interval.
- Values that are BLQ obtained prior to C<sub>max</sub> on Day 1 will be entered as zero; values that are BLQ obtained prior to C<sub>max</sub> on multiple dosing days will be entered as missing.
- Values that are BLQ after C<sub>max</sub> will be treated as missing but where BLQ concentrations are defined as parameters these will be reported as BLQ.
- Values that are BLQ after C<sub>max</sub> may be imputed as zero for the calculation of partial AUCs, in cases where lambda-z cannot be determined.
- Values that are measurable after at least 2 consecutive BLQ values after C<sub>max</sub> will be treated as missing for the calculation of PK parameters.
- Values that are reported as "No Result" or "Not Reportable" (NR), "Not Calculated" (NC) or "No Sample" (NS) etc. will be generally be considered missing.
- C<sub>max</sub> and T<sub>max</sub> will be reported from observed values. If C<sub>max</sub> occurs at more than one time point, T<sub>max</sub> will be assigned to the first occurrence of C<sub>max</sub>.

Missing or unusual concentration values in the input data may be queried to ascertain any underlying cause. Exclusion of missing or unusual concentration values, or repeat bioanalysis of samples, will only be performed if a definitive root cause can be established and approval from Eli Lilly and Company has been obtained. Any exclusions of concentration values or repeat analysis of samples will be documented appropriately.

Plasma PK parameters will be estimated using standard Phoenix WinNonlin methods, details of which may be found in the documentation accompanying the WinNonlin software package. The rules specified in Table 5 will be applied:

**Table 5 PK Parameter Estimation Details**

Sampling times	Actual sampling times
Calculation method	Linear Log Trapezoidal
Number of points used for lambda-z	At least 3, not including C <sub>max</sub>
Minimum requirements for AUC	At least 3 consecutive measurable concentrations

Where possible, the terminal elimination rate constant (lambda-z) will be calculated for all participant profiles. The value of lambda-z will be determined by the slope of the regression line of the natural log transformed concentrations vs time.

The WinNonlin determined choice of data points for determination of lambda-z will be reviewed by the Quotient pharmacokineticist who may adjust the selection in order to provide a more appropriate fit. The choice of data points for determination of lambda-z for each profile will be confirmed following a documented peer review.

### 9.1.3 Bioanalytical and PK Parameter Reporting Specifications

Where a PK sample is collected  $\geq \pm 10\%$  from the nominal sampling time outlined in the protocol, the resulting concentration will be excluded from the concentration summary tables and figures. Excluded values will be flagged in the listings.

Summary statistics (i.e., both summary tables and figures) will be calculated for a given sampling timepoint only if  $\geq 2/3$  of the individual concentrations at the timepoint have quantifiable concentrations (i.e., are not  $< \text{LLOQ}$ ), that are within the sampling time window (i.e. within  $\pm 10\%$  from the nominal sampling time). Summary statistics estimated with  $< 2/3$  of concentrations which are quantifiable, but with  $> 3$  data points, may be calculated if determined to be appropriate, and will be documented in the PK Populations documentation.

Non-measurable values reported in the plasma concentration data (i.e. values that are BLQ), will be entered as missing for the determination of summary statistics (including summary figures). This is with the exception of the Day 1, pre-dose timepoint, where BLQ values will be entered as zero for both calculation of arithmetic summary statistics and individual plots on the linear scale (for geometric means, geometric SD and geometric CV% and individual plots on the log scale they will continue to be treated as missing). Data recorded as NR, NS or NC will be handled as missing (i.e. no assumption will be made about the actual concentration).

The following parameters will be reported for each Study Part and Study Day as applicable, according to the rounding specifications provided in [Table 3](#) and [Table 4](#):

**Part A, Day 1 (Titration Period)**

Tmax, Cmax, AUC(0-last), AUC(0-24)

**Part A, Day 19 and Day 24 (Reference Period)**

Tmax, Cmax, AUC(0-24), AUC(0-last), CL/F24, Vz/F24

**Part A, Day 25, Day 30 and Day 31 (Test Periods 1 and 2)**

Tmax, Cmax, AUC(0-24), AUC(0-last), CL/F24, Vz/F24

Additionally Frel Cmax and Frel AUC(0-24) for Day 30 only

**Part A, Day 36 (Terminal PK Period)**

Tmax, Cmax, AUC(0-24), AUC(0-last), AUC(0-inf), AUCextrap, T1/2, lambda-z, CL/F24, Vz/F24, Frel Cmax, Frel AUC(0-24), lambda-z lower, lambda-z upper

**Part B, Day 1 (Titration Period)**

Tmax, Cmax, AUC(0-last), AUC(0-24)

**Part B, Day 19 and Day 24 (Reference Period)**

Tmax, Cmax, AUC(0-24), AUC(0-last), CL/F24, Vz/F24

**Part B, Day 25, Day 30 and Day 31 (Test Periods 1 and 2)**

Tmax, Cmax, AUC(0-24), AUC(0-last), CL/F24, Vz/F24

Additionally, Frel Cmax and Frel AUC(0-24) for Day 30 only

**Part B, Day 36 (Terminal PK Period)**

Tmax, Cmax, AUC(0-24), AUC(0-last), AUC(0-inf), AUCextrap, T1/2, lambda-z, CL/F24, Vz/F24, Frel Cmax, Frel AUC(0-24), lambda-z lower, lambda-z upper

The flags/footnotes given in [Table 6](#) will be applied to the PK parameters where relevant and will be shown in the PK parameter listings. Additional flags may be applied based on emerging data.

**Table 6 PK Parameter Flags and Footnotes**

Flag	Footnote
a	Adjusted rsq of regression (the goodness of fit statistic for the elimination phase) was <0.9
b	Period used for regression analysis was less than 2-fold the calculated half-life
c	Extrapolated portion of AUC(0-inf) >20%
d	Insufficient post-Cmax data points for estimation of lambda-z
e	Entire profile BLQ, no PK parameters could be calculated
f	Fewer than 3 consecutive measurable concentrations, AUCs not calculated

In the event that the adjusted rsq of regression is <0.9 ("a" flag) then lambda-z and parameter estimates derived using lambda-z and AUC(0-inf) will be deemed unreliable and will be flagged and listed but excluded from the summary statistics and formal statistical analysis.

In the event that the time period used for regression analysis is less than 2-fold the calculated half-life ("b" flag) will be flagged, listed, and included in summary statistics and formal statistical analysis.

In the event that the extrapolated portion of AUC(0-inf) >20% ("c" flag), then AUC(0-inf) and parameter estimates derived using AUC(0-inf) will be deemed unreliable and will be flagged and listed but excluded from the summary statistics and formal statistical analysis.

In the event that there are insufficient post-Cmax data points for estimation of lambda-z ("d" flag) then lambda-z and parameter estimates derived using lambda-z and AUC(0-inf) will be reported as NC.

In the event that there are fewer than 3 consecutive measurable concentrations ("f" flag) then all AUC parameter estimates will be reported as NC.

#### 9.1.4 Bioanalytical and Pharmacokinetic Summary Tables

Summary statistics (i.e. n, mean, SD, coefficient of variation [CV%], median, minimum, maximum, geometric mean, geometric SD and geometric CV%) of concentration data will be calculated for each time point, dosing day and treatment for LY3502970 in plasma. The number of BLQ values (n#) per time point will also be presented. Geometric statistics will not be calculated for Day 1, pre-dose concentrations.

Summary statistics (i.e. n, mean, SD, CV%, median, minimum and maximum) of plasma PK parameters will be calculated for LY3502970 for each treatment and dosing day as applicable. The metrics presented for each parameter are presented in [Table 7](#).

**Table 7 Summary Statistics - Metric Presentation**

Parameter	Summary Statistics									
	Metric Required									
	n	Mean	SD	CV%	gMean	gSD	gCV%	Median	Min	Max
Tmax	✓	X	X	X	X	X	X	✓	✓	✓
Cmax	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
AUC(0-24)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
AUC(0-last)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
AUC(0-inf)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
AUCextrap	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
T1/2	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
lambda-z	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CL/F24	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Vz/F24	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Frel Cmax	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Frel AUC(0-24)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
lambda-z lower*	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
lambda-z upper*	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

✓ = presented; X = excluded

**9.1.5 Bioanalytical and Pharmacokinetic Figures**

Mean, spaghetti and individual plasma concentration vs time plots will be produced on both the linear/linear scale and on log10/linear scale.

Where curves from multiple treatment regimens or participants are overlaid on the same plot, symbols will be used to identify different participants/ treatment regimens and a legend will be included on the plots to define the symbols used.

Mean plasma concentration vs time plots (using nominal times) will be produced for:

**Part A**

- Each treatment in the reference and test periods displaying the final dosing day of each period (i.e., Study Day 24, 30 and 36) on the same plot (1 plot in total) with Day 36 capped at 24 hours.
- All treatments on the same plot

**Part B**

- Each treatment in the reference and test periods the final dosing day of each period (i.e., Study Day 24, 30 and 36) on the same plot (1 plot in total) with Day 36 capped at 24 hours.
- All treatments on the same plot

These will be produced as follows:

- Linear/linear scale using arithmetic mean concentrations (error bars  $\pm$  arithmetic SD)
- Log10/linear scale using arithmetic mean concentrations

Separate plasma concentration vs time spaghetti plots (using actual sampling time after dosing) will be produced for each treatment and Study Day with each plot displaying 1 line per participant.

Individual plasma concentration vs time plots (using actual sampling times after dosing) will be produced separately for each individual participant with all treatment regimens on the same plot.

### 9.1.6 Bioanalytical and Pharmacokinetic Listings

The sample collection data (e.g. collection times) for PK samples will be listed. In addition, all concentration data and PK parameters will be listed on a per participant basis. Any flags used will be included as a footnote with the appropriate definition. Values which are BLQ will have the same notation in the data listing as received in the raw data (i.e. if BLQ values are received as <LLOQ then <LLOQ will be presented in the listings).

### 9.1.7 Statistical Analysis of Pharmacokinetic Parameters

For each parametric analysis, distributional assumptions underlying the statistical analyses will be assessed by visual inspection of residual plots. Normality will be examined by normal probability plots, while homogeneity of variance will be assessed by plotting the residuals against the predicted values for the model. If the distributional assumptions for the parametric approach are not satisfied, then additional sensitivity analyses may be performed including the removal of potential outliers or the use of non-parametric methods to assess the robustness of the original analysis. This will be documented in the CSR together with the reasoning supporting the most appropriate action taken, if applicable. In general terms the results of the original analysis will always be presented in the CSR.

Where assumptions on homogeneity of variance do not appear, satisfied consideration will be given to fitting alternate covariance structures to the data (e.g. heterogeneous compound symmetry or unstructured). The decision to report these structures will be made based on common measures of model fit in the PROC MIXED output and reason/justification will be provided in the CSR.

### Assessment of Relative Bioavailability: Part A and Part B (Options 3, 4 & 5) (Randomized)

Formal statistical analysis will be performed on the PK parameters C<sub>max</sub> and AUC(0-24) at steady state (i.e., dosing Day 6) to assess relative bioavailability. Data from the titration period will not be included in the model. The PK parameters will undergo a natural logarithmic transformation and will be analysed using mixed effect modelling techniques. The model will include terms for treatment fitted as a fixed effect and participant as a random effect. The null hypothesis is that there is no difference between test and reference.

The following pairwise treatment comparisons (*test versus reference*) are of interest:

#### Part A

- CCI Prototype Formulation 1 vs CCI Reference Capsule
- CCI Prototype Formulation 2 vs CCI Reference Capsule

## Part B

- CCI Prototype Formulation X vs CCI Reference Capsule
- CCI Prototype Formulation X vs CCI Reference Capsule

Only participants who complete both the test and reference study periods within the relevant periods will be included in the statistical analysis.

The least squares (LS) means including differences from the pairwise comparisons and their associated 90% confidence intervals (CIs) obtained from the model will be back transformed on the log scale to obtain geometric LS mean ratios (GLSMRs) and 90% CIs of the ratios. In addition, p-values associated with the pairwise treatment comparisons will also be presented.

The intra-participant variability values will be calculated for all treatments combined and are obtained from the residual term from the SAS Software output. These values are calculated as follows:

$$CVw = 100 \times (\exp(\text{Mean Square Error}) - 1)^{1/2}$$

The statistical analysis will be performed using actual treatment received and planned sequence as detailed on the randomisation schedule. The model will be fitted using the SAS Software procedure PROC MIXED, the method will specified as Restricted Maximum Likelihood and the denominator degrees of freedom for the fixed effects will be calculated using Kenward and Roger's method [1]. The following is an example of the SAS Software code that will be used:

```
PROC MIXED DATA=<input dataset name> METHOD=REML ORDER=INTERNAL;
  CLASS SUBJIDN TRTAN;
  MODEL LVAR = TRTAN / OUTP=PRED DDFM=KR;
  RANDOM SUBJIDN;
  ESTIMATE <relevant pairwise treatment comparisons> / CL ALPHA=0.10;
  LSMEANS TRTAN / ALPHA=0.10;
  ODS OUTPUT LSMEANS=MEANS ESTIMATES=EST COVPARMS=CVW;
RUN;
```

where

- LVAR is the natural log transformed PK parameter of interest
- SUBJIDN is the numeric participant identifier variable
- TRTAN is the numeric treatment variable for the actual treatment received
- 

#### Assessment of Relative Bioavailability: Part B (Options 1 & 2) (Non-randomized)

Formal statistical analysis will be performed on the PK parameters C<sub>max</sub> and AUC(0-24), at steady state (i.e., dosing Day 5), to assess relative bioavailability. Data from the titration period will not be included in the model. The PK parameters will undergo a natural logarithmic transformation and will be analysed using mixed effect modelling techniques. The model will include terms for treatment fitted as fixed effects and participant as a random effect. The null hypothesis is that there is no difference between test and reference.

The following pairwise treatment comparisons (*test versus reference*) are of interest:

- Prototype Formulation X, Fed (Test) vs Prototype Formulation X (Reference)

- Prototype Formulation X + PPI, Fasted (Test) vs Prototype Formulation X (Reference)

The LS means including differences from the pairwise comparisons and their associated 90% CIs obtained from the model will be back transformed on the log scale to obtain GLSMRs and 90% CIs of the ratios. In addition, p-values associated with the pairwise treatment comparisons will also be presented.

The intra-participant variability values will be calculated for all treatments combined and are obtained from the residual term from the SAS Software output. These values are calculated as follows:

$$CVw = 100 \times (\exp(\text{Mean Square Error}) - 1)^{1/2}$$

The statistical analysis will be performed using actual treatment received and planned sequence as detailed on the randomisation schedule. The model will be fitted using the SAS Software procedure PROC MIXED, the method will be specified as Restricted Maximum Likelihood and the denominator degrees of freedom for the fixed effects will be calculated using Kenward and Roger's method [4]. The following is an example of the SAS Software code that will be used:

```
PROC MIXED DATA=<input dataset name> METHOD=REML ORDER=INTERNAL;
  CLASS SUBJIDN TRTAN;
  MODEL LVAR = TRTAN / OUTP=PRED DDFM=KR;
  RANDOM SUBJIDN
  ESTIMATE <relevant pairwise treatment comparisons> / CL ALPHA=0.10;
  LSMEANS TRTAN / ALPHA=0.10;
  ODS OUTPUT LSMEANS=MEANS ESTIMATES=EST COVPARMS=CVW;
RUN;
```

where

- LVAR is the natural log transformed PK parameter of interest
- SUBJIDN is the numeric participant identifier variable
- TRTAN is the numeric treatment variable for the actual treatment received

#### Non-Parametric Analysis: Part A and Part B

The untransformed PK parameter Tmax at steady state (i.e., dosing Day 5) for Reference and Test products will be analysed using the non-parametric Friedman Chi-squared test at the 10% level of significance. The data will be ranked and subsequent calculations will be performed on the ranked data, using the PROC FREQ procedure. The analysis will be stratified by participant in order to reduce the background variation due to participant differences. PROC FREQ handles ties by assigning mid-ranks to tied response values. The Cochran-Mantel-Haenszel test statistic and corresponding p-value for comparing the means will be presented. The following is an example of the SAS Software code that will be used:

```
PROC FREQ DATA=<input dataset name>;
  TABLES SUBJIDN*TRTAN*TMAX / CMH2 SCORES=RANK NOPRINT;
  OUTPUT OUT=<output dataset name> (KEEP=_CMHRMS_ P_CMHRMS
  RENAME=( _CMHRMS_=TSTAT P_CMHRMS=PVALUE)) CMH2;
RUN;
```

where

- SUBJIDN is the numeric participant identifier variable
- TRTAN is the numeric treatment variable for the actual treatment received

## 9.2 Interim Pharmacokinetic Analysis

The details of the planned interim PK analysis are described in this section. However, as the analysis will be performed in real time it may be necessary to change the planned analysis in response to the emerging data.

Summary tables and figures for the interim PK analysis will be presented in an Interim PK Summary Report after being exported from WinNonlin. The formatting of this output will differ slightly from the final PK output which will be produced using SAS to include in the CSR.

The interim PK analysis will be performed on QC checked concentration data for LY3502970 in plasma following Part A using nominal sampling times and doses.

The following PK parameters will be calculated for the interim analysis of Part A data:

### Day 19 and 24 (Reference Period)

Tmax, Cmax, AUC(0-24), AUC(0-last)

### Day 25, Day 30 and Day 31 (Test Periods 1 and 2)

Tmax, Cmax, AUC(0-24), AUC(0-last), CL/F24, Vz/F24

Additionally, Frel Cmax and Frel AUC(0-24) for Day 30 only

### Day 36 (Terminal PK Period)

Tmax, Cmax, AUC(0-24), AUC(0-last), AUC(0-inf), AUCextrap, T1/2, lambda-z, Frel Cmax, Frel AUC(0-24)

## 10 Safety Assessments

Safety data summaries will be presented by actual treatment and the safety analysis set will be used throughout.

Separate summary tables, figures and listings will be provided for each study part.

### 10.1 Extent of Exposure

The number and percentage of participants dosed with each IMP will be summarised by actual treatment received, duration in each period, and overall. Percentages will be based on the number of subjects dosed.

In addition, the total number of days of exposure will be summarised (i.e., n, mean, SD, median, minimum and maximum) by treatment and overall. A subject's duration of exposure will be calculated as follows for each treatment and overall in the study:

$$\text{Total number of days of exposure to IMP} = (\text{Date of last dose} - \text{Date of first dose}) + 1$$

Duration of exposure to PPI will also be calculated if applicable.

Dosing details (including the date and time of all IMP administrations and any comments) will be listed for all enrolled participants. Any recorded deviations from the planned dosing regimen will be listed as protocol deviations.

## 10.2 Meal Details

In Part B Fed regimens only, meal details as recorded on the eCRF study build specification will be listed for all enrolled participants. Any recorded deviations from the planned meal times will be listed as protocol deviations.

## 10.3 Adverse Events

Throughout the study, all adverse events (AE) will be evaluated by the principal investigator (PI) and noted in the AE section of the eCRF study build specification. An AE is any untoward medical occurrence in a participant that occurs either before dosing (referred to as a pre-dose AE) or once a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

AEs will be coded using MedDRA v24.0 (or more recent version), and reported by SOC and PT.

AEs will be classified into the following categories:

- Pre-dose AEs: AEs recorded at screening or with a start date and time prior to the first dose of IMP
- Treatment-emergent adverse events (TEAEs): AEs that commence during/after the first dose of IMP or commence before first dose of IMP (i.e., a pre-dose AE or existing medical condition) but worsen in intensity during exposure to IMP

TEAEs will be assigned to the treatment of the period in which the AE first occurred. Where the severity of an AE intensifies or symptoms change in a subsequent period, this will be defined as a new AE and included under the treatment associated with the subsequent period. Adverse events that occur during the washout period will be assigned to the treatment the participant received during the period immediately before the washout period.

Adverse events will be classified as "not related", "unlikely related", "possibly related", "probably related", and "definitely related" when considering their relationship to IMP. TEAEs classified as "possibly related", "probably related" and "definitely related" will be defined as IMP-related events. Pre-dose AEs will always have the classification of "not related".

Adverse events will be classified as "mild," "moderate" or "severe" when considering their severity.

If the severity or relationship to IMP of a treatment-emergent adverse event (TEAE) is missing, the severity/relationship will be tabulated as "missing" in the summary tables.

Adverse events that meet criteria of being an Adverse events of special interest (AESIs) will be categorised as such in the subjects eCRF.

Where the start date of an AE is missing and the stop date is on or after the day of first dose of IMP or both the start and stop dates are missing then a "worst-case" scenario will be assumed i.e., the AE is assumed to have occurred post-dose and is therefore considered

treatment-emergent. If a partial start date/time is available then the event will be considered as treatment-emergent unless the partial information suggests otherwise.

### 10.3.1 Summary Tables for Adverse Events

All pre-dose AEs (as defined in [Section 10.3](#)) will be excluded from the summary tables but will be listed for all enrolled participants.

Descriptive statistical methods will be used to summarise the TEAE data.

The number and percentage of participants reporting each TEAE will be summarised for both SOC and PT. For summaries by SOC and PT, with the exception of TEAEs by severity and relationship to IMP, the number of participants and the number of events will be summarised. For summaries by severity and relationship only the number of participants will be summarised.

For counts of participants experiencing events the following will apply:

- A participant experiencing TEAEs in more than one body system, within a study part/period, will be counted once in the total number of participants with TEAEs in that study part/period;
- A participant with more than 1 TEAE in the same SOC, within a study part/period, counts only once at the SOC level;
- A participant with more than 1 TEAE in the same PT, within a study part/period, counts only once at the PT level.

For event counts, all events are included.

When it is necessary to calculate percentages, the denominator will be the total number of participants in the safety analysis set for that treatment or study period/part and the numerator will be the total number of participants reporting a TEAE within the relevant category.

Summaries presented for SOC and PT will be presented in descending order of frequency overall i.e., most frequently reported SOC in the study part and then by most frequently reported PT in the study part within each SOC.

#### 10.3.1.1 Overall Summary of Adverse Events

The following will be summarised by treatment for the safety analysis set:

- Number and percentage of participants reporting at least 1 TEAE
- Number and percentage of participants reporting severe TEAEs
- Number and percentage of participants reporting IMP-related TEAEs
- Number and percentage of participants reporting serious TEAEs
- Number and percentage of participants reporting TEAEs leading to participant withdrawal
- Number and percentage of participants reporting TEAEs leading to death
- Number and percentage of participants reporting AESI
- Total number of TEAEs
- Total number of severe TEAEs
- Total number of IMP-related TEAEs

- Total number of serious TEAEs
- Total number of TEAEs leading to participant withdrawal
- Total number of TEAEs leading to death
- Total number of TEAEs leading to AESI

#### 10.3.1.2 Summary of Treatment-Emergent Adverse Events

All participants reporting TEAEs will be summarised by treatment. Counts will be given for number of participants and number of events. Participants experiencing more than 1 TEAE treatment will be counted only once for number of participants but will be counted more than once for number of events.

Additionally, participants reporting TEAEs will be summarised for SOC and PT by treatment. Counts will be given for number of participants and number of events. For programming purposes counts of number of participants will be by maximum severity ie, participants experiencing more than 1 episode of a TEAE within a treatment will be counted only once within each SOC and PT using the most severe episode.

#### 10.3.1.3 Summary of Treatment-Emergent Adverse Events by Severity

All participants reporting TEAEs will be summarised by severity (i.e., mild, moderate or severe) and treatment. Counts will be given for number of participants, not number of events. Counts will be given by maximum severity (i.e., participants experiencing more than 1 TEAE within a treatment will be counted only once using the most severe episode).

Additionally, participants reporting TEAEs will be summarised for SOC and PT by maximum severity (i.e., mild, moderate or severe) and treatment. Counts will be given for total number of participants, not for events. Counts by maximum severity will be given (i.e., participants experiencing more than 1 TEAE within a treatment will be counted only once within each SOC and PT using the most severe episode).

#### 10.3.1.4 Summary of Treatment-Emergent Adverse Events by Relationship to IMP

All participants reporting TEAEs will be summarised by relationship to IMP (i.e., "not related", "unlikely related", "possibly related", "probably related", and "definitely related") and treatment. Counts will be given for number of participants, not number of events. Counts will be given by the closest relationship to IMP (i.e., participants experiencing more than 1 TEAE within a treatment will be counted only once using the most closely related event).

Additionally, participants reporting TEAEs will be summarised for SOC and PT by closest relationship to IMP (i.e. "not related", "unlikely related", "possibly related", "probably related", and "definitely related") and treatment. Counts will be given for total number of participants, not for events. Counts by closest relationship will be given (i.e., participants experiencing more than 1 TEAE within a treatment will be counted only once within each SOC and PT using the most closely related event).

#### 10.3.1.5 Summary of IMP-related Adverse Events by System Organ Class and Preferred Term

All participants reporting TEAEs will be summarised by treatment. Counts will be given for number of participants and number of events. Participants experiencing more than 1 TEAE within a treatment will be counted only once for the number of participants, but will be counted more than once for number of events.

Additionally, participants reporting IMP related events will be summarised for SOC and PT by treatment. Counts will be given for number of participants and number of events. For programming purposes counts of number of participants will be by maximum severity i.e., participants experiencing more than 1 episode of a TEAE within a treatment will be counted only once within each SOC and PT using the most severe episode.

#### 10.3.1.6 Summary of Serious Adverse Events

All participants reporting treatment-emergent SAEs will be summarised by treatment. Counts will be given for number of participants and number of events. Participants experiencing more than 1 serious adverse event (SAE) within a treatment will be counted only once for number of participants but will be counted more than once for number of events.

Additionally, participants reporting treatment-emergent SAEs will be summarised for SOC and PT by treatment. Counts will be given for number of participants and number of events. For programming purposes counts of number of participants will be by maximum severity i.e., participants experiencing more than 1 episode of a SAE within a treatment will be counted only once within each SOC and PT using the most severe episode.

#### 10.3.2 Listings for Adverse Events

All pre-dose AEs (as defined in [Section 10.3](#)) will be listed including SOC and PT.

A separate data listing of all TEAEs will be provided including the SOC and PT. In addition separate listings of all SAEs and AESIs will be provided.

### 10.4 Laboratory Evaluations

The details of sample collection for laboratory safety analysis are described in the study protocol.

Where a value is provided by the safety laboratory as either above or below the limit of detection (LOD) this will be set to the respective LOD itself for descriptive summaries. No imputations will be made in the individual listings.

#### 10.4.1 Summary Tables for Laboratory Evaluations

Haematology, clinical chemistry and point of care (POC) glucose data will be summarised (n, mean, SD, median, minimum and maximum) for each laboratory parameter at each time point, including changes from baseline (Day 1, pre-dose) at each scheduled post-baseline time point by treatment.

Shift tables from baseline to each scheduled post-baseline time point (with respect to the number and percentage of participants with values below, within or above the reference range) will be presented by treatment. Percentages will be based on the number of participants with measurements at baseline and the relevant post-baseline time point.

Reference ranges for each laboratory parameter will be presented for the relevant parameter in each summary table.

#### 10.4.2 Listings for Laboratory Evaluations

The sample collection data (e.g., collection times) for laboratory analysis and urinalysis data will be listed.

All individual participant data, for planned haematology, clinical chemistry, POC glucose and urinalysis data including derivations, such as change from baseline, will be listed. If applicable, data from unscheduled laboratory tests will also be listed and flagged with a “#” to indicate it will not be used in the summary statistics. In these listings, individual data will be flagged with an “H” or an “L” for values that are higher or lower than their reference ranges, respectively.

Separate listings of all haematology, clinical chemistry, POC glucose and urinalysis values outside their reference ranges, by participant will also be provided. Reference ranges will be supplied by the safety laboratory for haematology and clinical chemistry. The same range as provided by the safety laboratory will be used for POC glucose. The reference range for urinalysis is provided below:

- pH: 5.0 to 9.0
- Specific gravity: 1.000 to 1.030

## 10.5 Vital Signs

The details of measurement of supine vital signs (i.e., body temperature, blood pressure, pulse rate). Vital signs parameters will be reported in the order given above, i.e. both summary tables and data listings with the exception of body temperature which will only be listed.

If orthostatic measurements are required these will be listed separately.

### 10.5.1 Summary Tables for Vital Signs

Vital signs data, including change from baseline (Day 1, pre-dose), will be summarised (i.e., n, mean, SD, median, minimum and maximum) at each post-baseline time point by treatment.

In addition, the number of participants with ‘substantial’ increases or decreases or no substantial change from baseline in systolic blood pressure (BP) (>20 mmHg), diastolic BP (>10 mmHg) and heart rate (>15 bpm) will be summarised.

### 10.5.2 Listings for Vital Signs

All individual vital signs data including derivations, such as change from baseline, will be listed. Individual data will be flagged with an “H” or an “L” for values that are higher or lower than their reference ranges, respectively, and participants with ‘substantial’ increases or decreases from baseline (as defined in [Section 10.5.1](#)) in systolic BP, diastolic BP and heart rate will be flagged with an ‘I’ (increase) or ‘D’ (decrease), respectively. If applicable, data from unscheduled vital signs assessments will also be listed and flagged with a “#” to indicate it will not be used in the summary statistics.

In addition, a separate listing of all vital signs data outside their reference ranges by participant will also be provided.

The reference ranges (from Quotient SOP “The Interpretation of the Electrocardiogram, Vital Signs and Clinical Laboratory Data During Phase I / II Clinical Trials”) defined in [Table 8](#) will be used.

**Table 8 Vital Signs Reference Ranges**

Parameter	Split	Lower limit	Upper limit
Systolic BP	18-45 years	90 mmHg	140 mmHg
Systolic BP	>45 years	90 mmHg	160 mmHg
Diastolic BP	NA	50 mmHg	90 mmHg
Heart rate	NA	40 bpm	100 bpm
Oral Body Temperature	NA	35.5°C	37.5°C

NA=Not applicable

**10.6 ECGs**

The details of measurement of supine electrocardiogram (ECG) parameters (i.e. QT interval, QTcF interval, PR Interval, QRS duration, QRS axis, interpretation and clinical significance and findings) are described in the study protocol. ECG parameters will be reported in the order given above, i.e. both summary tables and data listings.

**10.6.1 Summary Tables for ECGs**

ECG data, including change from baseline (Baseline [Day 1]), will be summarised (i.e., n, mean, SD, median, minimum and maximum) at each post-baseline dosing day by treatment.

The number and percentage of participants with normal and prolonged QT intervals corrected for heart rate using Fridericia's correction (i.e., QTcF), and increases in QTcF from baseline within the categories defined in [Table 9](#) (based on the International Council on Harmonisation [ICH] E14 guideline [\[2\]](#)) will be summarised. Percentages will be based on the number of participants with measurements at the relevant time point.

**Table 9 ICH E14 Ranges for QTcF Intervals**

Parameter	ICH E14 Range
QTcF	≤450 msec (normal)
	451-480 msec
	481-500 msec
	>500 msec
Increase in QTcF from baseline	<30 msec
	30-60 msec
	>60 msec

**10.6.2 Listings for ECGs**

All ECG measurements (i.e., single readings) including derivations, such as change from baseline, will be listed.

All ECG measurements will be flagged with an "H" or an "L" for values that are higher or lower than their reference ranges, respectively. If applicable, data from unscheduled ECG assessments will also be listed and flagged with a "#" to indicate it will not be used in the summary statistics.

In addition, measurements with increase in QTcF interval from baseline (30-60 msec) and with 'substantial increases' (>60 msec) will be flagged with 'I' and 'SI', respectively.

A separate listing of all ECG parameters outside their reference range by participant will also be provided.

The reference ranges (from Quotient SOP "The Interpretation of the Electrocardiogram, Vital Signs and Clinical Laboratory Data During Phase I / II Clinical Trials", except of QT interval which is defined by the PI) and defined in Table 10 will be used.

**Table 10 ECG Reference Ranges**

Parameter	Split	Lower limit	Upper limit
Ventricular Rate (HR)	NA	40 bpm	100 bpm
QT Interval	NA	NA	500 msec
QTcF Interval	Males	NA	450 msec
	Females	NA	470 msec
PR Interval	NA	120 msec	220 msec
QRS Duration	NA	NA	120 msec
QRS Axis	NA	-30°	100°

HR=heart rate

NA=Not applicable

## 10.7 Body Weight

### 10.7.1 Summary Tables for Body Weight

Body weight, including change from baseline (Day 1, Pre-dose) at each post-baseline time point will be summarised (n, mean, SD, median, minimum and maximum) by treatment.

### 10.7.2 Listings for Body Weight

All body weight data including derivations such as change from baseline will be listed.

## 10.8 Physical Examination

All physical examination details and comments on any physical examination findings will be listed by participant for all participants.

## 11 Interim Statistical Analyses

No interim statistical analysis is planned for this study.

## 12 Changes in the Conduct of the Study or Planned Analysis

### 12.1 Changes in the Conduct of the Study

No changes in the conduct of the study had been reported at the time this document was written.

### 12.2 Changes to the Planned Analyses

The protocol states that the non-parametric Kruskal – Wallis test is to be used for the analysis of Tmax, however as the data is paired (i.e. participants will be to receive both treatments), it would be more appropriate to use the Friedman test which ranks the scores for each participant. The ranks then replace the observations, and the total of the ranks for each participant is the same, thus removing differences between participants.

### 12.3 Any Other Relevant Changes

Not applicable.

## 13 Overall Considerations

### 13.1 Statistical Programming and Analysis

The Data Sciences Department at Quotient will perform the statistical programming and analysis to produce all analysis datasets, summary tables, figures and data listings using the statistical SAS Software v9.4.

In general terms, categorical data will be presented using counts and percentages, while continuous variables will be presented using the number of participants with an observation (n), mean, median, standard deviation (SD), minimum and maximum. For PK data additional statistics including coefficient of variation (CV%), geometric mean, geometric SD, geometric CV% and geometric n will be presented, as appropriate. The geometric n is the number of participants included in the calculation of the geometric mean, geometric SD and geometric CV%.

The geometric mean is obtained by applying a natural log transformation to the raw data, calculating the arithmetic mean of the transformed values and then back transforming the arithmetic mean.

The following formula will be used to calculate the geometric SD:

$$\text{geometric SD} = \exp\{\text{SD}[\log(\text{raw data})]\}$$

i.e., a natural log transformation is applied to the raw data, the arithmetic SD of the transformed values is calculated, and then the arithmetic SD of the transformed values is back transformed.

The following formula will be used to calculate the geometric CV%:

$$\text{geometric CV\%} = 100 \times (\exp\{\text{SD}[(\log(\text{raw data}))^2 - 1]\}^{1/2})$$

ie, a natural log transformation is applied to the raw data, the arithmetic SD of the transformed values is calculated. This value is then squared. The square value is back transformed and a value of 1 is subtracted from the back transformed value. A square root is then applied and the resulting value is multiplied by 100.

In general summary statistics and statistical analysis results will be presented as detailed in [Table 11](#), unless otherwise stated:

**Table 11 Reporting Conventions for Summary Statistics and Statistical Analysis**

Data Type	Statistic	Number of decimal places for reporting (i)
Frequency	Counts (n)	None
	Percentages (%)	1 decimal place
Summary statistic	n	None
	Mean	i + 1 decimal places
	Median	i + 1 decimal places
	SD	i + 1 decimal places
	Min	i decimal places
	Max	i decimal places
	CV%	1 decimal place
	Geometric Mean	i + 1 decimal place
	Geometric SD	i + 1 decimal places
	Geometric CV%	1 decimal place
Statistical analysis	Ratios (%)	2 decimal places
	Confidence intervals (%)	2 decimal places
	p-values	if <0.001: presented as <0.001
		if ≥0.001 and <0.099: presented to 3 decimal places
		all other p-values will be presented to 2 decimal places
	Cochran-Mantel-Haenszel test statistic	2 decimal places

i refers to the number of decimal places reported in the eCRF study build specification or other appropriate source data for the original data. Where bioanalytical or PK data are received rounded in significant figures rather than decimal places, summary statistics will be supplied to the same precision.

\* Where ratios are not presented as (%)

Details of how the individual PK parameters will be presented are detailed in [Section 9.1.1](#). Where data requires rounding, values ending with 1 to 4 will be rounded down and values ending with 5 to 9 will be rounded up.

All data listings will be based on all enrolled participants i.e., participants who signed informed consent and have met the inclusion/exclusion criteria and are not considered screen failures. Details of age and sex will be included on all data listings.

All statistical tests relating to PK parameters will be 2-sided and will be performed using a 10% significance level, leading to 90% (2-sided) CIs.

If any baseline measurements are found to be missing then consideration will be given to imputation using the preceding time point (e.g., Screening, Admission, if applicable). Unscheduled assessment may be used if appropriate. Details of any such imputations will be documented as part of the safety analysis set.

There will be no other imputations for the safety data with regard to missing values or study discontinuation (i.e., participants who do not complete the study). Imputation for PK parameter estimation using WinNonlin is described in [Section 9.1.2](#), and imputations for reporting PK data are described in [Section 9.1.3](#).

If partial dates are available for smoking history, prior medications or medical history, there will be no date imputations. The data listings will only show the date information for the date part that is available, e.g., if only the year part of the date is available then YYYY will be presented in the listing. If the full date information is missing, then this will be presented as missing on the data listing.

If all or part of this study is conducted during the COVID-19 pandemic and there is evidence that data relating to primary and/or key secondary endpoints may have been affected in a way that may bias results, then sensitivity analyses may be conducted. Requirements for any sensitivity analyses will be documented at the same time as the related population (i.e., safety/PK population) and details of any sensitivity analyses which were carried out would be fully documented in the CSR.

### 13.2 Quality Control of Summary Tables, Figures and Listings and Statistical Analysis

Isolated data errors detected as a result of the QC checks that are deemed significant (ie, errors that would impact the interpretation of the results in relation to the study objectives) will be corrected as per the data management plan. Systematic data errors will be investigated further. The data will be corrected if necessary, and the appropriate table, figure, and/or listing re-generated and then re-checked.

In addition to QC checks, a documented peer review will be performed of all SAS Software-generated report standard summary tables, figures and data listings, including a review of SAS Software code and program log files.

All QC documentation will be archived in the ISF which will be transferred to Lilly at the end of the study.

#### 13.2.1 Quality Control - Summary Tables

Manual QC methods (i.e., comparison of results in the table to results calculated by a calculator or spreadsheet) will be used for all analyses and summary tables. All summary tables will be QC'd as follows:

- Where tables are presented by treatment (i.e., no time points), QC will alternate between treatment to avoid the same treatment being QC'd every time. For tables presented by treatment only (i.e., no time points), all summary statistics for 1 treatment will be QC'd.
- Where tables are presented by treatment and time point, QC will alternate between treatment to avoid the same treatment being QC'd every time.
- For tables presented by treatment and time point, a single treatment at 1 time point in each table will be QC'd.
- Where tables are produced using a macro for multiple parameters, a minimum of 3 tables, using different treatments or combinations of treatment and time point as appropriate, will be QC'd.
- For AEs, the treatment details will be 100% QC'd against the randomisation schedule (Part A and Part B [Options 3, 4 & 5]), and the treatment allocation list (Part B [Options 1 & 2]) for all participants.
- AE summary tables will be 100% checked using the relevant data listing.

#### 13.2.2 Quality Control - Figures

All figures will be QC'd manually using the corresponding/appropriate summary table or data listing, as follows:

- Across all figures, QC will alternate between treatment to avoid the same treatment being QC'd every time

- Where a figure presents data from more than 1 treatment, only 1 treatment will be QC'd. However, all data points for that treatment will be checked
- Where figures are produced using a macro for individual participants and/or multiple parameters, a minimum of 3 figures will be QC'd
- Mean figures will be QC'd using the corresponding summary table
- Figures showing individual data will be QC'd using the corresponding data listing

### 13.2.3 Quality Control - Data Listings

All data listings will be subjected to a 100% manual QC check against the eCRF study build specification or other appropriate source data for a minimum of 3 participants. If appropriate, the participants checked will include at least 1 participant who withdrew early from the study.

The study treatment allocation details on the dosing data listing will be 100% QC checked against the study randomisation schedule.

### 13.2.4 Quality Control - Statistical Analysis

QC of statistical analyses will be performed by peer review of program code, log and output. This will be performed by a statistician at Quotient who is not responsible for performing the statistical analysis.

## 14 SAS Data Transfer

Prior to final issue of all study data there will be one draft (RAW, SDTM and ADaM) transfer and one final (SDTM and ADaM) transfer. The datasets will be structured according to Quotient CDISC standards. All SAS Software study data used for analysis and reporting, including safety data will be transferred to Lilly on issue of the final CSR. These will be performed in compliance with CDISC ADaM. This will include define.xml output as well as a Data Reviewers Guide in pdf which will be linked to the relevant SDTM or ADaM define.xml. Quotient will provide metadata files and data will be transferred as SAS Software transport files.

## 15 Programming Conventions

Quotient standards for layout of tables, figures and data listings and programming conventions will be used as follows:

- courier new, font size 8
- landscape
- A4 paper

Tables and listings will be produced as MS Word 2013 (or more recent version) documents and figures will be produced as PDF files. Listings will be sorted by participant ID number and visit.

The mock tables ([Section 20](#)) presented are a representation of Quotient reporting standards. However, these are provided for illustrative purposes only. The numbering, titles and formatting of all tables, figures and listings may be modified. Additional labelling/footnotes may be required during analysis and reporting, for clarification purposes. Any such changes will not be regarded as changes to planned analyses.

## 16 Reference List

- [1] Brown, Prescott, "Repeated Measures Data". In Brown H and Prescott R, 3<sup>rd</sup> edition. Applied Mixed Models in Medicine. Chichester, UK: John Wiley & Sons Ltd, 2015: 242-243,
- [2] International Council for Harmonisation (ICH) Topic E 14, The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs Guidelines approved by the Committee for Medicinal Products for Human Use (CHMP) in May 2005 which came into force November 2005.

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16.2.4.1.4	Prior and Concomitant Medication Individual Values: All Enrolled Participants Part A
16.2.4.1.5	Serum Pregnancy Test Individual Values: All Enrolled Female Participants Part A
16.2.4.1.6	Urine Pregnancy Test Individual Values: All Enrolled Female Participants Part A
16.2.4.1.7	Follicle Stimulating Hormone Individual Values: All Enrolled Female Participants Part A
16.2.4.1.8	Serum Calcitonin Individual Values: All Enrolled Participants Part A
16.2.4.1.9	Serology Individual Values: All Enrolled Participants Part A
16.2.4.1.10	SARS-CoV-2 Antibody Test Individual Values: All Enrolled Participants Part A
16.2.4.1.11	SARS-CoV-2 Antigen Test Individual Values: All Enrolled Participants Part A
16.2.4.1.12	Urine Drug Screen Individual Values: All Enrolled Participants Part A
16.2.4.1.13	Ethanol Breath Test Individual Values: All Enrolled Participants Part A

Listing Number	Listing Title
16.2.4.2.1	Demographics and Baseline Characteristics Individual Values: All Enrolled Participants Part B
16.2.4.2.2	Lifestyle Details: Smoking History and Alcohol Consumption Individual Values: All Enrolled Participants Part B
16.2.4.2.3	Medical History Individual Values: All Enrolled Participants Part B
16.2.4.2.4	Prior and Concomitant Medication Individual Values: All Enrolled Participants Part B
16.2.4.2.5	Serum Pregnancy Test Individual Values: All Enrolled Female Participants Part B
16.2.4.2.6	Urine Pregnancy Test Individual Values: All Enrolled Female Participants Part B
16.2.4.2.7	Follicle Stimulating Hormone Individual Values: All Enrolled Female Participants Part B
16.2.4.2.8	Serum Calcitonin Individual Values: All Enrolled Participants Part B
16.2.4.2.9	Serology Individual Values: All Enrolled Participants Part B
16.2.4.2.10	SARS-CoV-2 Antibody Test Individual Values: All Enrolled Participants Part B
16.2.4.2.11	SARS-CoV-2 Antigen Test Individual Values: All Enrolled Participants Part B
16.2.4.2.12	Urine Drug Screen Individual Values: All Enrolled Participants Part B
16.2.4.2.13	Ethanol Breath Test Individual Values: All Enrolled Participants Part B
	<b>Dosing Details and Meal Details</b>

Listing Number	Listing Title
16.2.5.1.1.1	Dosing Details Individual Values: All Enrolled Participants Part A
16.2.5.1.2.1	Dosing Details Individual Values: All Enrolled Participants Part B
16.2.5.1.2.2	Meal Details Individual Values: All Enrolled Participants Part B
	<b>Plasma Pharmacokinetic Concentration Data</b>
16.2.5.3.1.1	Blood Sample Collection Details for Analysis and Plasma Pharmacokinetic Concentrations: LY3502970 (<units>) Individual Values: All Enrolled Participants Part A
16.2.5.3.2.1	Blood Sample Collection Details for Analysis and Plasma Pharmacokinetic Concentrations: LY3502970 (<units>) Individual Values: All Enrolled Participants Part B
	<b>Plasma Pharmacokinetic Parameter Data</b>
16.2.6.1.1	Plasma Pharmacokinetic Parameters: LY3502970 Individual Values: All Enrolled Participants Part A
16.2.6.1.2	Pharmacokinetic Parameter Flags Part A <i>(Programming note: Details of the PK parameter flags will be added to listing 16.2.6.x as footnotes if length of these details allows – in which case do not produce this listing. Otherwise display PK parameter flags in this listing).</i>
16.2.6.2.1	Plasma Pharmacokinetic Parameters: LY3502970 Individual Values: All Enrolled Participants Part B
16.2.6.2.2	Pharmacokinetic Parameter Flags Part B <i>(Programming note: Details of the PK parameter flags will be added to listing 16.2.6.x as footnotes if length of these details allows – in which case do not produce this listing. Otherwise display PK parameter flags in this listing).</i>

Listing Number	Listing Title
	<b>Adverse Events</b>
16.2.7.1.1	Pre-dose Adverse Events Individual Values: All Enrolled Participants Part A
16.2.7.1.2	All Treatment-Emergent Adverse Events Individual Values: All Enrolled Participants Part A
16.2.7.1.3	Serious Adverse Events Individual Values: All Enrolled Participants Part A
16.2.7.1.4	Adverse Events of Special Interest Individual Values: All Enrolled Participants Part A
16.2.7.2.1	Pre-dose Adverse Events Individual Values: All Enrolled Participants Part B
16.2.7.2.2	All Treatment-Emergent Adverse Events Individual Values: All Enrolled Participants Part B
16.2.7.2.3	Serious Adverse Events Individual Values: All Enrolled Participants Part B
16.2.7.2.4	Adverse Events of Special Interest Individual Values: All Enrolled Participants Part B
	<b>Laboratory Data</b>
16.2.8.1.1	Blood Sample Collection Details for Laboratory Analysis Individual Values: All Enrolled Participants Part A
16.2.8.1.2	Haematology Individual Values: All Enrolled Participants Part A
16.2.8.1.3	Haematology Individual Values Outside the Reference Range: All Enrolled Participants Part A
16.2.8.1.4	Clinical Chemistry Individual Values: All Enrolled Participants Part A

Listing Number	Listing Title
16.2.8.1.5	Clinical Chemistry Individual Values Outside the Reference Range: All Enrolled Participants Part A
16.2.8.1.6	Urinalysis Sample Collection Individual Values: All Enrolled Participants Part A
16.2.8.1.7	Urinalysis Individual Values: All Enrolled Participants Part A
16.2.8.1.8	Urinalysis Individual Values Outside the Reference Range: All Enrolled Participants Part A
16.2.8.2.1	Blood Sample Collection Details for Laboratory Analysis Individual Values: All Enrolled Participants Part B
16.2.8.2.2	Haematology Individual Values: All Enrolled Participants Part B
16.2.8.2.3	Haematology Individual Values Outside the Reference Range: All Enrolled Participants Part B
16.2.8.2.4	Clinical Chemistry Individual Values: All Enrolled Participants Part B
16.2.8.2.5	Clinical Chemistry Individual Values Outside the Reference Range: All Enrolled Participants Part B
16.2.8.2.6	Urinalysis Sample Collection Individual Values: All Enrolled Participants Part B
16.2.8.2.7	Urinalysis Individual Values: All Enrolled Participants Part B
16.2.8.2.8	Urinalysis Individual Values Outside the Reference Range: All Enrolled Participants Part B

Listing Number	Listing Title
	<b>Vital Signs and ECGs</b>
16.2.9.1.1.1	Vital Signs Individual Values: All Enrolled Participants Part A
16.2.9.1.1.2	Vital Signs Individual Values Outside the Reference Range: All Enrolled Participants Part A
16.2.9.1.2.1	ECGs Individual Values: All Enrolled Participants (Programming note: The order of ECG parameters is to be as per Section X.XX) Part A
16.2.9.1.2.2	ECGs Individual Values Outside the Reference Range: All Enrolled Participants Part A
16.2.9.2.1.1	Vital Signs Individual Values: All Enrolled Participants Part B
16.2.9.2.1.2	Vital Signs Individual Values Outside the Reference Range: All Enrolled Participants Part B
16.2.9.2.2.1	ECGs Individual Values: All Enrolled Participants (Programming note: The order of ECG parameters is to be as per Section X.XX) Part B
16.2.9.2.2.2	ECGs Individual Values Outside the Reference Range: All Enrolled Participants Part B
	<b>Other Data</b>
16.2.9.1.4	Physical Examination Data Individual Values: All Enrolled Participants Part A
16.2.9.1.5	Body Weight Data Individual Values: All Enrolled Participants Part A

Listing Number	Listing Title
16.2.9.2.4	Physical Examination Data Individual Values: All Enrolled Participants Part B
16.2.9.2.5	Body Weight Data Individual Values: All Enrolled Participants Part B

Final

## 20 Mock Tables

Final

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TABLE 14.1.1.1  
Subject Disposition by Reason  
Summary Statistics: All Enrolled Subjects  
Part A

	P2/P1 (N=XX) n (%)	P1/P2 (N=XX) n (%)	OVERALL (N=XX) n (%)
Subjects enrolled (1)			xx (xx.x)
Subjects dosed			xx (xx.x)
Subjects randomised (2)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects completed	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects discontinued	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason for discontinuation			
REASON 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
REASON 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
REASON 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
...			
<All categories on source>	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, cc capsule in the reference period, and separate cc Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

(1) An enrolled participant signed the informed consent, qualified per the inclusion/exclusion criteria and were assigned to a treatment sequence

(2) A randomized participant is defined as a participant who signed the informed consent, qualified per the inclusion/exclusion criteria and were randomized and assigned to a treatment sequence in tests Period 1 and Period 2.

A participant may be discontinued for 1 reason only

P1 = Prototype formulation 1, P2 = Prototype Formulation 2

Percentages are based on the number of participants enrolled with the exception of percentage of subjects completing the study within a sequence which will be based on the number of subjects randomised to the sequence.

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Programming note: This table will be continued for all reasons for discontinuation as recorded on the source

If none of the participants discontinued from the study early, then reasons for discontinuation will not be populated in the summary table

Percentages are based on the number of participants enrolled

A similar table will be produced for Part B, i.e. Table [14.1.2.1] Where Part B is not randomised only the overall column will be presented

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TABLE 14.1.1.2.1  
Analysis Populations  
Summary Statistics: All Enrolled Subjects  
Part A

	OVERALL (N=XX) n (%)
Subjects in Safety Population	xx (xx.x)
Reasons for exclusion from Safety Population	
<All categories from source>	xx (xx.x)
	...
Subjects in PK Population	xx (xx.x)
Reasons for exclusion from PK Population	
<All categories from source>	xx (xx.x)
	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, [redacted] capsule in the reference period, and separate [redacted] Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

A participant may be excluded for more than 1 reason

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Programming note: Percentages are based on the number of participants enrolled

A similar table will be produced for Part B, i.e. Table [14.1.2.2.1]

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TABLE 14.1.1.2.2  
Safety Analysis Set  
Summary Statistics: Safety Population  
Part A

	CCI CAP (N=XX) n (%)	CCI CAP (N=XX) n (%)	CCI CAP (N=XX) n (%)	CCI CAP (N=XX) n (%)	...
Subjects in safety analysis set	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
Reasons for exclusion from safety analysis set					
<All categories from source>	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
...	...	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

A participant may be excluded for more than 1 reason

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Programming note: This table will be continued for all treatments and overall

A similar table will be produced for the PK Analysis Set (and Subset[s], if required), i.e. Table [14.1.1.2.3]

Similar tables will also be produced for Part B, i.e. Tables [14.1.2.2.2] and [14.1.2.2.3]

Each analysis set/subset will be a subset of their respective population and percentages

will be based on number of participants in each population

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TABLE 14.1.1.3  
Demographic and Baseline Characteristics  
Summary Statistics: Safety Analysis Set  
Part A

		OVERALL (N=XX) n (%)
Age (years)	n	xx
	Mean	xx.xx
	SD	xx.xx
	Median	xx.xx
	Min	xx.x
	Max	xx.x
Ethnicity n(%)	<All categories on source>	xx (xx.x)
Race n(%)	<All categories on source>	xx (xx.x)
Sex n(%)	Male	xx (xx.x)
	Female	xx (xx.x)
Height (cm)	...	...
Weight (kg)	...	...
BMI (kg/m <sup>2</sup> )	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

DDMMYYYY HH:MM

Programming note: This table will continue for all categories of ethnicity and race  
Height, Weight and BMI will be summarised using the same descriptive statistics as Age  
If any values are missing, then a "missing" row will be included in the table, as applicable  
A similar table will be produced using the PK analysis set if required with table numbering updated appropriately  
A similar table will be produced for Part B, i.e. Table [14.1.2.3]

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TABLE 14.1.1.4  
Demographic and Baseline Characteristics  
Summary Statistics: PK Analysis Set  
Part A

		P2/P1 (N=XX) n (%)	P1/P2 (N=XX) n (%)	OVERALL (N=XX) n (%)
Age (years)	n	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Min	xx.x	xx.x	xx.x
	Max	xx.x	xx.x	xx.x
Ethnicity n(%)	<All categories on source>	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race n(%)	<All categories on source>	xx (xx.x)	xx (xx.x)	xx (xx.x)
Sex n(%)	Male	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Female	xx (xx.x)	xx (xx.x)	xx (xx.x)
Height (cm)	...	...	...	...
Weight (kg)	...	...	...	...
BMI (kg/m <sup>2</sup> )	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, **cc** capsule in the reference period, and separate **cc** Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

P1 = Prototype formulation 1, P2 = Prototype Formulation 2

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Programming note: This table will continue for all categories of ethnicity and race

Height, Weight and BMI will be summarised using the same descriptive statistics as Age

If any values are missing, then a "missing" row will be included in the table, as applicable

A similar table will be produced for Part B, i.e. Table [14.1.2.4]

Sequence will only be displayed if applicable in Part B

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TABLE 14.1.1.5  
Lifestyle Details: Smoking History and Alcohol Consumption  
Summary Statistics: Safety Analysis Set  
Part A

		OVERALL (N=XX) n (%)
Does the participant smoke (1)	NO	xx (xx.x)
	PREVIOUSLY	xx (xx.x)
Alcohol Consumption (2)	NONE	xx (xx.x)
	YES: NOT EXCESSIVE	xx (xx.x)

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, [REDACTED] capsule in the reference period, and separate [REDACTED] Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

(1) Anyone who smokes >10 cigarettes per day, or the equivalent, is excluded from the study

(2) Anyone who excessively consumes alcohol (>21 units/week in males up to 65 and >14 units/week in females up to 65) is excluded from the study. 1 unit = 12oz or 360ml of beer, 1.5oz or 45ml of distilled spirit, 5oz or 150ml of wine

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

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Programming note: A similar table will be produced using the PK analysis set if required with table numbering updated appropriately  
A similar table will be produced for Part B, i.e. Table [14.1.2.5]

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TABLE 14.1.1.6  
Lifestyle Details: Smoking History and Alcohol Consumption  
Summary Statistics: PK Analysis Set  
Part A

		P2/P1 (N=XX) n (%)	P1/P2 (N=XX) n (%)	OVERALL (N=XX) n (%)
Does the participant smoke (1)	NO	xx (xx.x)	xx (xx.x)	xx (xx.x)
	PREVIOUSLY	xx (xx.x)	xx (xx.x)	xx (xx.x)
Alcohol Consumption (2)	NONE	xx (xx.x)	xx (xx.x)	xx (xx.x)
	YES: NOT EXCESSIVE	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, **cc** capsule in the reference period, and separate **cc** Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

(1) Anyone who smokes >10 cigarettes per day, or the equivalent, is excluded from the study

(2) Anyone who excessively consumes alcohol (>21 units/week in males up to 65 and >14 units/week in females up to 65) is excluded from the study. 1 unit = 12oz or 360ml of beer, 1.5oz or 45ml of distilled spirit, 5oz or 150ml of wine

P1 = Prototype formulation 1, P2 = Prototype Formulation 2

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

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Programming note: A similar table will be produced using the PK analysis set if required with table numbering updated appropriately

A similar table will be produced for Part B, i.e. Table [14.1.2.6]

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TABLE 14.1.1.5.1  
Extent of Exposure  
Summary Statistics: Safety Analysis Set  
Part A

Regimen	Subjects Dosed (N=XX) n (%)
CCI CAP	xx (xx.x)
CCI CAP	xx (xx.x)
CCI CAP	xx (xx.x)
CCI CAP	xx (xx.x)
CCI P TAB 1	xx (xx.x)
CCI P TAB 2	xx (xx.x)

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

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Programming note: A similar table will be produced using the PK analysis set if required with table numbering updated appropriately  
A similar table will also be produced for Part B, i.e. Table [14.1.2.5.1]

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TABLE 14.1.1.5.2  
Extent of Exposure: Subjects Dosed by Period  
Summary Statistics: Safety Analysis Set  
Part A

	CCI CAP (N=XX)	CCI CAP (N=XX)	CCI CAP (N=XX)	CCI CAP (N=XX)	CCI P TAB X (N=XX)	...
n	XX	XX	XX	XX	XX	...
mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	...
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	...
Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	...
Min	XX.X	XX.X	XX.X	XX.X	XX.X	...
Max	XX.X	XX.X	XX.X	XX.X	XX.X	...

Note: The data in this table are presented in listing x.x  
All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

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Programming note: This table will be continued for all treatments and overall  
If required, a similar table will also be produced for duration of exposure to PPI, with table numbering updated appropriately  
A similar table will also be produced for Part B, i.e. Table [14.1.2.5.2]

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TABLE 14.2.1.1  
Plasma Pharmacokinetic Concentrations: LY3502970 <(units)>  
Summary Statistics: PK Analysis Set  
Part A

Treatment	Visit	Time Point	Arithmetic (1)								Geometric (2)			
			n	n#	Mean	SD	CV%	Median	Min	Max	n	Mean	SD	CV%
CCI CAP (N=XX)	DAY 1	PRE-DOSE	XX	XX	XX.XX	XX.XX	XX.X	XX.XX	XX.X	XX.X	XX	NC	NC	NC
		TIMEPOINT 1	XX	XX	XX.XX	XX.XX	XX.X	XX.XX	XX.X	XX.X	XX	XX.XX	XX.XX	XX.X
		TIMEPOINT 2	XX	XX	XX.XX	XX.XX	XX.X	XX.XX	XX.X	XX.X	XX	XX.XX	XX.XX	XX.X
		...	...	...	...	...	...	...	...	...	...	...	...	...
CCI CAP (N=XX)	DAY 7	PRE-DOSE	XX	XX	XX.XX	XX.XX	XX.X	XX.XX	XX.X	XX.X	XX	XX.XX	XX.XX	XX.X
		TIMEPOINT 1	XX	XX	XX.XX	XX.XX	XX.X	XX.XX	XX.X	XX.X	XX	XX.XX	XX.XX	XX.X
		TIMEPOINT 2	XX	XX	XX.XX	XX.XX	XX.X	XX.XX	XX.X	XX.X	XX	XX.XX	XX.XX	XX.X
		...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

(1) For arithmetic summary statistics, concentration values reported as BLQ have been set to zero

(2) For calculation of geometric summary statistics, values reported as BLQ have been set to  $\frac{1}{2} \times \text{LLOQ}$ , except for pre-dose values which will not be summarised. The LLOQ value was <value, units>

n# indicates the number of participants with a BLQ value recorded at the time point

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Programming note: This table will be continued for all treatments and time points  
A similar table will be produced for Part B, i.e. Table [14.2.2.1]

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TABLE 14.2.1.2.1  
Plasma Pharmacokinetic Parameters: LY3502970  
Summary Statistics: PK Analysis Set  
Part A

Treatment	Visit	Statistic	Parameter 1 (units)	Parameter 2 (units)	Parameter 3 (units)	All Other PK Parameters (units)
CC1 CAP (N=XX)	DAY 1	n	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX
		SD	XX.XX	XX.XX	XX.XX	XX.XX
		CV%	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX
		Min	XX.X	XX.X	XX.X	XX.X
		Max	XX.X	XX.X	XX.X	XX.X
		Geometric n	XX	XX	XX	XX
		Geometric Mean	XX.XX	XX.XX	XX.XX	XX.XX
		Geometric SD	XX.XX	XX.XX	XX.XX	XX.XX
		Geometric CV%	XX.X	XX.X	XX.X	XX.X
CC1 CAP (N=XX)	DAY 19	...	...	...	...	...
		...	...	...	...	...
		...	...	...	...	...
...	...	...	...	...	...	...
...	...	...	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

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Programming note: This table will be continued for all treatments and PK parameters  
A similar table will be produced for Part B, i.e. Table [14.2.2.2.1]

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TABLE 14.2.1.2.2

Plasma Pharmacokinetic Parameters: LY3502970

Statistical Analysis Results - Assessment of Relative Bioavailability: &lt;PK Analysis Set/Subset&gt;

Part A

Comparison (Test/Reference)	Parameter	TEST		REFERENCE		Ratio (%) (2)	90% CI (3)	p-value (4)	CVw (%) (5)
		n	Adj LS Mean (1)	n	Adj LS Mean (1)				
CCI P TAB 1 vs CAP	Cmax	xx	xx.xx	xx	xx.xx	xx.xx	(xx.xx, xx.xx)	0.xxx	xx.xx
	AUC(0-24)	xx	xx.xx	xx	xx.xx	xx.xx	(xx.xx, xx.xx)	0.xxx	xx.xx
CCI P TAB 2 vs CAP	Cmax	xx	xx.xx	xx	xx.xx	xx.xx	(xx.xx, xx.xx)	0.xxx	xx.xx
	AUC(0-24)	xx	xx.xx	xx	xx.xx	xx.xx	(xx.xx, xx.xx)	0.xxx	xx.xx

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule. Results obtained from mixed effects model of natural log transformed steady state PK parameters including terms for treatment as a fixed effect and participant as a random effect.

(1) Adj LS mean = Least Squares mean from model, (2) Ratio of adj geo means with comparison presented as Test/Reference

(3) CI = confidence interval for ratio of adj geo means

(4) p-value (from 2-sided test) representing the null hypothesis of no treatment difference

(5) CVw = Intra-participant variability

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

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Programming note: A similar table will be produced for Part B, i.e. Table [14.2.2.2.2]

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TABLE 14.2.1.2.4  
Statistical Analysis Results - Friedman Test for Tmax: <PK Analysis Set/Subset>  
Part A

CCI CAP Median	CCI P TAB 1 Median	CCI P TAB 2 Median	Test Statistic (1)	P-value (2)
xx.xx	xx.xx	xx.xx	xx.xx	0.xxx

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

Results from non-parametric Friedman's test of steady state PK parameter Tmax

(1) Cochran-Mantel-Haenszel test statistic

(2) P-value for the Cochran-Mantel-Haenszel test statistic

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Programming note: A similar table will be produced for Part B, i.e. Table [14.2.2.2.3]

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TABLE 14.3.1.1  
Overall Summary of Treatment-Emergent Adverse Events  
Summary Statistics: Safety Analysis Set  
Part A

Event	[REDACTED] CAP (N=XX)		[REDACTED] CAP (N=XX)		.....
	n (%)	Total Number of Events	n (%)	Total Number of Events	
TEAEs	xx (xx.x)	xx	xx (xx.x)	xx	...
Severe TEAEs	xx (xx.x)	xx	xx (xx.x)	xx	...
IMP-related TEAEs	xx (xx.x)	xx	xx (xx.x)	xx	...
Serious TEAEs	xx (xx.x)	xx	xx (xx.x)	xx	...
TEAEs Leading to Participant Withdrawal	xx (xx.x)	xx	xx (xx.x)	xx	...
TEAEs leading to death	xx (xx.x)	xx	xx (xx.x)	xx	...
AESIs	xx (xx.x)	xx	xx (xx.x)	xx	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, [REDACTED] capsule in the reference period, and separate [REDACTED] Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

TEAEs are coded using MedDRA vXX.X

TEAEs are AEs that commence during/after the first dose of IMP or commence before first dose of IMP but worsen in intensity during exposure to IMP. n is the number of participants reporting at least 1 event

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

DDMMYYYY HH:MM

Programming note: Continue table for all treatments

A similar table will be produced for Part B i.e. Table [14.3.2.1]

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TABLE 14.3.1.2  
Treatment-Emergent Adverse Events  
By MedDRA System Organ Class and Preferred Term  
Summary Statistics: Safety Analysis Set  
Part A

System Organ Class Preferred Term	CC1 CAP (N=XX)		CC1 CAP (N=XX)		.....
	n (%)	Total Number of Events	n (%)	Total Number of Events	
TEAEs	xx (xx.x)	xx	xx (xx.x)	xx	...
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 1	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 2	xx (xx.x)	xx	xx (xx.x)	xx	...
etc	xx (xx.x)	xx	xx (xx.x)	xx	...
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 1	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 2	xx (xx.x)	xx	xx (xx.x)	xx	...
etc	xx (xx.x)	xx	xx (xx.x)	xx	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule  
TEAEs are coded using MedDRA vXX.X and are presented in descending order of frequency  
Subjects experiencing more than 1 episode of a TEAE are counted only once within each SOC and PT

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

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Programming note: Counts of number of participants are by maximum severity, i.e. participants experiencing more than 1 episode of a TEAE are counted only once within each SOC and PT using the most severe episode  
This table will be continued for all SOC, PT, and treatment  
A similar table will be produced for Part B, i.e. Table [14.3.2.2]

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TABLE 14.3.1.3  
Treatment-Emergent Adverse Events  
By MedDRA System Organ Class, Preferred Term and Severity  
Summary Statistics: Safety Analysis Set  
Part A

System Organ Class Preferred Term	CC1 CAP (N=XX)			.....	CC1 CAP (N=XX)		
	Mild n (%)	Moderate n (%)	Severe n (%)		Mild n (%)	Moderate n (%)	Severe n (%)
TEAEs	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	xx (xx.x)	xx (xx.x)	xx (xx.x)	...	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule  
TEAEs are coded using MedDRA vXX.X and are presented in descending order of frequency  
Counts are given for total number of participants, not for events

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

DDMMYYYY HH:MM

Programming note: Counts of number of participants are by maximum severity, i.e. participants experiencing more than 1 episode of a TEAE are counted only once within each SOC and PT using the most severe episode  
This table will be continued for all treatments  
A similar table will be produced for Part B, i.e. Table [14.3.2.3]

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TABLE 14.3.1.4  
Treatment-Emergent Adverse Events  
By MedDRA System Organ Class, Preferred Term and Relationship to IMP  
Summary Statistics: Safety Analysis Set  
Part A

System Organ Class Preferred Term	[REDACTED] CAP (N=X)					[REDACTED] CAP (N=X)	
	Not related n(%)	Unlikely related n(%)	Possibly related n(%)	Probably related n(%)	Definitely related n(%)	Not related .....	
TEAEs	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
etc	...	...	...	...	...	...	...
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	...
etc	...	...	...	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, [REDACTED] capsule in the reference period, and separate [REDACTED] Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule  
TEAEs are coded using MedDRA vXX.X and are presented in descending order of frequency  
Counts are given for total number of participants, not for events

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

DDMMYYYY HH:MM

Programming note: Counts are given by closest relationship, i.e. participants experiencing more than 1 TEAE are counted only once within each SOC and PT using the most closely related event  
This table will be continued for all SOC, PT and treatments  
A similar table will be produced for Part B, i.e. Table [14.3.2.4]

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TABLE 14.3.1.5  
IMP-Related Events  
By MedDRA System Organ Class and Preferred Term  
Summary Statistics: Safety Analysis Set  
Part A

System Organ Class Preferred Term	CC1 CAP (N=XX)		CC1 CAP (N=XX)		.....
	n (%)	Total Number of Events	n (%)	Total Number of Events	
IMP-related (1)	xx (xx.x)	xx	xx (xx.x)	xx	...
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 1	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 2	xx (xx.x)	xx	xx (xx.x)	xx	...
etc	xx (xx.x)	xx	xx (xx.x)	xx	...
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 1	xx (xx.x)	xx	xx (xx.x)	xx	...
PREFERRED TERM 2	xx (xx.x)	xx	xx (xx.x)	xx	...
etc	xx (xx.x)	xx	xx (xx.x)	xx	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

(1) An IMP-related TEAE is any AE where a causal relationship with the IMP is at least a reasonable possibility  
i.e. "related" TEAEs are coded using MedDRA vXX.X and are presented in descending order of frequency

Subjects experiencing more than 1 episode of an IMP-related TEAE are counted only once within each SOC and PT

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Programming note: Counts of number of participants are by maximum severity, i.e. using the most severe episode  
This table will be continued for all SOC, PT and treatments  
A similar table will be produced for Serious Adverse Events i.e. Table [14.3.1.6]  
Similar tables will also be produced for Part B, i.e. Tables [14.3.2.5] and [14.3.2.6]

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TABLE 14.4.1.1  
Haematology  
Summary Statistics: Safety Analysis Set  
Part A

<Parameter> (<units>) [ref range xxx-xxx (male), xxx-xxx (female)]

Treatment	Visit	Result						Change from Baseline					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
CC1 CAP (N=XX)	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
	DAY 25	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
CC1 P TAB X (N=XX)	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
	DAY 31/37	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
...	...	...	...	...	...	...	...	...	...	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

BASELINE is defined as Day 1, pre-dose

DAY 31/37 is equivalent to Day 6 in each test period.

PROGRAM PATH: X:\~\QSC202755\~\TFLS\PRODUCTION\TAB-XX

DDMMYYYY HH:MM

Programming note: This table will be continued for all haematology parameters and treatments

A similar table will be produced for Clinical Chemistry and POC Glucose, i.e. Tables [14.4.1.3], and [14.4.1.5]

Similar tables will also be produced for Part B, i.e. Tables [14.4.2.1], [14.4.2.3] and [14.4.2.5]

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TABLE 14.4.1.2  
Haematology  
Shift Analysis: Safety Analysis Set  
Part A

<Parameter> (<units>) [ref range xxx-xxx (male), xxx-xxx (female)]

Treatment	Visit	Baseline		
		Below n (%)	Within n (%)	Above n (%)
CCI CAP (N=XX)	BASELINE	xx (xx.x)	xx (xx.x)	xx (xx.x)
	DAY 25	xx (xx.x)	xx (xx.x)	xx (xx.x)
CCI P TAB X (N=XX)	BASELINE	xx (xx.x)	xx (xx.x)	xx (xx.x)
	DAY 31/37	xx (xx.x)	xx (xx.x)	xx (xx.x)
...	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CCI capsule in the reference period, and separate CCI Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule  
BASELINE is defined as Day 1, pre-dose

N# indicates the number of participants with a baseline and a post baseline assessment at the time point indicated. Below/within/above indicate the n (%) of participants with assessments below/within/above the normal reference range

DAY 31/37 is equivalent to Day 6 in each test period.

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DDMMYYYY HH:MM

Programming note: This table will be continued for all haematology parameters and treatments

A similar table will be produced for Clinical Chemistry and POC Glucose, i.e. Tables [14.4.1.4] and [14.4.1.6]

Similar tables will also be produced for Part B, i.e. Tables [14.4.2.2], [14.4.2.4] and [14.4.2.6]

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TABLE 14.5.1.1  
Vital Signs  
Summary Statistics: Safety Analysis Set  
Part A

<Parameter> (<units>) [ref range xxx - xxx (age xx - xx), xxx - xxx (age > xx)]

Treatment	Visit	Result						Change from Baseline						Substantial Change (1)		
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max	DEC	NONE	INC
CC1 CAP (N=XX)	BASELINE	XX	XX.XX	XX.XX	XX.XX	XX.X	XX.X									
	DAY 7	XX	XX.XX	XX.XX	XX.XX	XX.X	XX.X	XX	XX.XX	XX.XX	XX.XX	XX.X	XX.X	XX	XX	XX
CC1 CAP (N=XX)	BASELINE	XX	XX.XX	XX.XX	XX.XX	XX.X	XX.X									
	DAY 13	XX	XX.XX	XX.XX	XX.XX	XX.X	XX.X	XX	XX.XX	XX.XX	XX.XX	XX.X	XX.X	XX	XX	XX
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

BASELINE is defined as Day 1, Pre-dose

Substantial change is defined as:  $> \pm 20$  mmHg Systolic BP,  $> \pm 10$  mmHg Diastolic BP and  $> \pm 15$  bpm HR

DEC: number of participants with substantial decrease from baseline NONE: number of participants with no substantial change from baseline, INC: number of participants with substantial increase from baseline

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Programming note: This table will be continued for all vital signs parameters (except oral temperature) and treatments  
Substantial change column only required for systolic BP, diastolic BP and HR  
A similar table will be produced for Part B, i.e. Table [14.5.2.1]

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TABLE 14.5.1.2.1  
ECGs  
Summary Statistics: Safety Analysis Set  
Part A

<Parameter> (<units>) [<ref range xxx - xxx (age xx - xx), xxx - xxx (age > xx)> / <ref range xxx - xxx (male), xxx-xxx (female)>]

Treatment	Visit	Result						Change from Baseline					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
CC1 CAP (N=XX)	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
	DAY 13	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.
CC1 CAP (N=XX)	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
	DAY 19	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
---	---	---	---	---	---	---	---	---	---	---	---	---	---

Note: The data in this table are presented in listing x.x  
All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule  
BASELINE is defined as Day 1, Pre-dose

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Programming note: This table will be continued for all ECG parameters and treatments  
The order of ECG parameters is to be as per Section 10.6  
A similar table will be produced for Part B, i.e. Table [14.5.2.2.1]

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TABLE 14.5.1.2.2  
ECGs  
QTcF Categorical Data  
Summary Statistics: Safety Analysis Set  
Part A

Treatment	Visit	N#	QTcF Interval (msec)				QTcF Interval Increase (msec)		
			<=450 n (%)	451-480 n (%)	481-500 n (%)	>500 n (%)	<30 n (%)	30-60 n (%)	>60 n (%)
CC1 CAP (N=XX)	BASELINE	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)			
	DAY 13	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CC1 CAP (N=XX)	BASELINE	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)			
	DAY 19	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
---	---	---	---	---	---	---	---	---	---

Note: The data in this table are presented in listing x.x

All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule

BASELINE is defined as pre-dose for each dosing period

Categories for QTcF interval and QTcF interval increases are based on ICH E14 guidelines

N# is the number of participants with a value at baseline and the relevant post-dose time point and is used in the denominator for calculating the percentages of participants, n indicates the number of participants with observations at the given time point

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DDMMYYYY HH:MM

Programming note: This table will be continued for all treatments

A similar table will be produced for Part B, i.e. table [14.5.2.2.2]

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TABLE 14.5.1.3.1  
Body Weight  
Summary Statistics: Safety Analysis Set  
Part A

Treatment	Visit	Result						Change from Baseline					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
CC1 CAP (N=XX)	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
	DAY 7	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
CC1 CAP (N=XX)	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
	DAY 13	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
...	...	...	...	...	...	...	...	...	...	...	...	...	...

Note: The data in this table are presented in listing x.x  
All participants were planned to receive ascending doses of LY3502970 capsule in the titration period, CC1 capsule in the reference period, and separate CC1 Prototype 1 & 2 formulations of LY3502970 according to the randomisation schedule  
BASELINE is defined as Day 1, pre-dose

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DDMMYYYY HH:MM

Programming note: This table will be continued for all treatments  
A similar table will be produced for Part B, i.e. table [14.5.2.3.1]

## Appendix 1: Study Schedule for Part A

### Screening, Baseline, Early Termination and Follow-up Procedures

Procedure	Screening Visit	Preadmission	Baseline	Safety Follow-up Visit <sup>a</sup>	Comments
Day	-28 to -2	-2	-1	43 to 53	The Screening Visit and Safety Follow-up Visit may occur anytime during the specified window.
Informed consent	X				
Outpatient visit	X			X	
CRU admission			X		
Medical history and physical exam	X				Full physical at screening to include vein assessment. Symptom-directed exams at all other timepoints.
Height/weight	X		X	X	Height at screening only. Weight will be measured in a consistent see Section 8.2.3 of the study protocol.
Body temperature	X				
Vital signs (supine)	X			X	Blood pressure and pulse rate measurements will be taken after approximately 5 minutes in the supine position.
Safety laboratory tests	X			X	Participants will be required to fast for at least 8 hours before each blood sample is drawn. See Section 10.2 of the study protocol for details.

Point of care safety glucose samples	X			X	Samples will be taken with a capillary blood glucose monitor.
Pregnancy test	X		X	X	Females only. Serum pregnancy test at screening. Urine pregnancy test at all other times.
Genetic sample			X		See Section 10.5 of the study protocol for details.
Follicle-stimulating hormone	X				For females with a history of spontaneous amenorrhea for 6 to 12 months.
Serum calcitonin	X				
Serology tests	X				See Section 10.2 of the study protocol for details.

Procedure	Screening Visit	Preadmission	Baseline	Safety Follow-up Visit <sup>a</sup>	Comments
Day	-28 to -2	-2	-1	43 to 53	The Screening Visit and Safety Follow-up Visit may occur anytime during the specified window.
SARS-CoV-2 Antibody <sup>b</sup>	X				
SARS-CoV-2 Antigen <sup>b</sup>	X	X			
Urine drug screen and ethanol breath test	X		X		See Section 10.2 of the study protocol for details.
Medical Assessment				X	A symptom-directed physical examination
AE/medication review	X		X	X	
Single 12-lead ECG	X		X	X	ECGs must be recorded before collecting any vital signs or blood samples. Participants must be supine for approximately 5 minutes before ECG collection and remain supine but awake during ECG collection.

Abbreviations: AE = adverse event; COVID-19 = Coronavirus Disease 2019; CRU = clinical research unit; ECG = electrocardiogram; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: If multiple procedures take place at the same time point, the following order of the procedure should be used: ECG, vital signs, and blood draws.

a Participants who discontinue early will undergo safety follow-up procedures approximately 120 hours post final dose.

b Testing for SARS-CoV-2 may be performed based on current infection rates and availability of tests. If required, testing will comprise an antibody blood test performed at screening and an antigen PCR test performed at screening, the day before admission, and discharge or the day before discharge. The decision on COVID-19 testing and the definition of the testing time points will be agreed by the study team and documented in the investigator site files via the clinical kick-off meeting minutes.

## Treatment Period Procedures

Procedure	Titration Period <sup>a</sup>			Reference Period <sup>a</sup>	Test Period 1 <sup>a</sup>	Test Period 2 <sup>a</sup>	Terminal PK Period (Day 37 to 41) & Discharge (Day 41 <sup>b</sup> )
	1 to 6	7 to 12	13 to 18				
CRU discharge							Day 41
Weight (predose)	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
Vital signs (≤2 hours predose; supine) <sup>c</sup>	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
Safety laboratory tests (predose) <sup>d</sup>	Day 1			Day 19	Day 25	Day 31	Day 37 Day 41
Point of care safety glucose samples (predose) <sup>e</sup>	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
SARS-CoV-2 Antigen							x <sup>f</sup>
Medical Assessment (symptom driven)	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
AE/medication review	→						
Single 12-lead ECG (≤2 hours predose; supine)	Day 1		Day 13	Day 19	Day 25	Day 31	Day 41
Administer study intervention (QD)	→						

Randomization (predose)					Day 25		
LY3502970 PK samples (hour) <sup>c,g</sup>	Day 1: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 7: Predose	Day 13: Predose	Day 19: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 25: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 31: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 37 <sup>g</sup> : 24, 36  Day 38 <sup>g</sup> : 48  Day 40 <sup>g</sup> : 96  Day 41 <sup>g</sup> : 120
	Day 2: Predose			Day 20: Predose	Day 26 Predose	Day 32: Predose	
				Day 24: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 30: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 36: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	

Abbreviations: AE = adverse event; COVID-19 = Coronavirus Disease 2019; CRU = clinical research unit; ECG = electrocardiogram; PCR = polymerase chain reaction; PK = pharmacokinetics; QD = once daily; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: If multiple procedures take place at the same time point, the following order of the procedure should be used: ECG, vital signs, and blood draws.

<sup>a</sup> Participants who discontinue early will undergo safety follow-up procedures approximately 120 hours post final dose.

<sup>b</sup> Day 41 procedures begin approximately 120 hours post final dose.

<sup>c</sup> Blood pressure and pulse rate measurements will be taken after approximately 5 minutes in the supine position.

<sup>d</sup> Sampling times are relative to the time of study intervention administration each day (0 hour). Sampling times may be adjusted after review of preliminary data.

<sup>e</sup> Samples will be taken with a capillary blood glucose monitor.

<sup>f</sup> Testing for SARS-CoV-2 may be performed based on current infection rates and availability of tests. If required, testing will comprise an antibody blood test performed at screening and an antigen PCR test performed at screening, the day before admission, and discharge or the day before discharge. The decision on COVID-19 testing and the definition of the testing time points will be agreed by the study team and documented in the investigator site files via the clinical kick-off meeting minutes.

<sup>g</sup> Sampling times in the terminal PK period are relative to the time of the final dose of study intervention received (0 hour) and may be adjusted after review of preliminary data.

## Appendix 2: Study Schedule for Part B

### Screening, Baseline, Early Termination and Follow-up Procedures

Procedure	Screening Visit	Preadmission	Baseline	Safety Follow-up Visit <sup>a</sup>	Comments
Day	-28 to -2	-2	-1	43 to 53	The Screening Visit and Safety Follow-up Visit may occur anytime during the specified window.
Informed consent	X				
Outpatient visit	X			X	
CRU admission			X		
Medical history and physical exam	X				Full physical at screening to include vein assessment. Symptom-directed exams at all other timepoints.
Height/weight	X		X	X	Height at screening only. Weight will be measured in a consistent way (see Section 8.2.3 of the study protocol).
Body temperature	X				
Vital signs (supine)	X			X	Blood pressure and pulse rate measurements will be taken after approximately 5 minutes in the supine position.

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Safety laboratory tests	X			X	Participants will be required to fast for at least 8 hours before each blood sample is drawn. See Section 10.2 of the study protocol for details.
Point of care safety glucose samples	X			X	Samples will be taken with a capillary blood glucose monitor.
Pregnancy test	X		X	X	Females only. Serum pregnancy test at screening. Urine pregnancy test at all other times.
Genetic sample			X		See Section 10.5 of the study protocol for details
Follicle-stimulating hormone	X				For females with spontaneous amenorrhea for 6 to 12 months.
Serum calcitonin	X				
Serology tests	X				See Section 10.2 of the study protocol for details.

Procedure	Screening Visit	Preadmission	Baseline	Safety Follow-up Visit <sup>a</sup>	Comments
Day	-28 to -2	-2	-1	43 to 53	The Screening Visit and Safety Follow-up Visit may occur anytime during the specified window.
SARS-CoV-2 Antibody <sup>b</sup>	X				
SARS-CoV-2 Antigen <sup>b</sup>	X	X			
Urine drug screen and ethanol breath test	X		X		See Section 10.2 of the study protocol for details.
Medical Assessment				X	A symptom-directed physical examination.
AE/medication review	X		X	X	
Single 12-lead ECG	X		X	X	ECGs must be recorded before collecting any vital signs or blood samples. Participants must be supine for approximately 5 minutes before ECG collection and remain supine but awake during ECG collection.

Abbreviations: AE = adverse event; COVID-19 = Coronavirus Disease 2019; CRU = clinical research unit; ECG = electrocardiogram; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: If multiple procedures take place at the same time point, the following order of the procedure should be used: ECG, vital signs, and blood draws.

<sup>a</sup> Participants who discontinue early will undergo safety follow-up procedures.


<sup>b</sup> Testing for SARS-CoV-2 may be performed based on current infection rates and availability of tests. If required, testing will comprise an antibody blood test performed at screening, and an antigen PCR test performed at screening, the day before admission, and discharge or the day before discharge. The decision on COVID-19 testing and the definition of the testing time points will be agreed by the study team and documented in the investigator site files via the clinical kick-off meeting minutes.

## Treatment Period Procedures

Procedure	Titration Period <sup>a</sup>			Reference Period <sup>a</sup>	Test Period 1 <sup>a</sup>	Test Period 2 <sup>a</sup>	Terminal PK Period (Day 37 to 41) & Discharge (Day 41 <sup>b</sup> )
Day	1 to 6	7 to 12	13 to 18	19 to 24	25 to 30	31 to 36	37 to 41
CRU discharge							Day 41
Weight (predose)	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
Vital signs (≤2 hours predose; supine) <sup>c</sup>	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
Safety laboratory tests (predose) <sup>d</sup>	Day 1			Day 19	Day 25	Day 31	Day 37 Day 41
Point of care safety glucose samples (predose) <sup>e</sup>	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
SARS-CoV-2 Antigen							x <sup>f</sup>
Medical Assessment	Day 1	Day 7	Day 13	Day 19	Day 25	Day 31	Day 41
AE/medication review							

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Single 12-lead ECG ( $\leq 2$ hours predose)	Day 1		Day 13	Day 19	Day 25	Day 31	Day 41
Administer study intervention (QD)							
Administer PPI (PPI options only) <sup>9</sup>						X	
LY3502970 PK samples trough (predose; PPI options only)						Day 33 Day 34 Day 35	
High-fat meal (food effect options only) <sup>9</sup>					X		

Procedure	Titration Period <sup>a</sup>			Reference Period <sup>a</sup>	Test Period 1 <sup>a</sup>	Test Period 2 <sup>a</sup>	Terminal PK Period (Day 37 to 41) & Discharge (Day 41 <sup>b</sup> )
Day	1 to 6	7 to 12	13 to 18	19 to 24	25 to 30	31 to 36	37 to 41
Randomization (predose) <sup>h</sup>					Day 25		
LY3502970 PK samples (hour) <sup>d,i</sup>	Day 1: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16  Day 2: Predose	Day 7: Predose	Day 13: Predose	Day 19: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16  Day 20: Predose  Day 24: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 25: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16  Day 26 Predose  Day 30: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 31: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16  Day 32: Predose  Day 36: Predose, 0.5, 1, 2, 4, 6, 8, 12, 16	Day 37 <sup>i</sup> : 24, 36  Day 38 <sup>i</sup> : 48  Day 39 <sup>i</sup> : 72  Day 40 <sup>i</sup> : 96  Day 41 <sup>i</sup> : 120

Abbreviations: AE = adverse event; CRU = clinical research unit; ECG = electrocardiogram; PK = pharmacokinetics; PPI = proton pump inhibitor; QD = once daily.

Note: If multiple procedures take place at the same time point, the following order of the procedure should be used: ECG, vital signs, and blood draws.

<sup>a</sup> Participants who discontinue early will undergo safety follow-up procedures.

<sup>b</sup> Day 41 procedures begin approximately 120 hours post final dose.

<sup>c</sup> Blood pressure and pulse rate measurements will be taken after approximately 5 minutes in the supine position.

<sup>d</sup> Sampling times are relative to the time of study intervention administration each day (0 hour). Sampling times may be adjusted after review of preliminary data.

<sup>e</sup> Samples taken with a capillary blood glucose monitor.

<sup>f</sup> Testing for SARS-CoV-2 may be performed based on current infection rates and availability of tests. If required, testing will comprise an antibody blood test performed at screening and an antigen PCR test performed at screening, the day before admission, and discharge or the day before discharge. The decision on COVID-19 testing and the definition of the testing time points will be agreed by the study team and documented in the investigator site files via the clinical kick-off meeting minutes.

<sup>g</sup> Administration of PPI and a high-fat meal will take place only if treatment option 1 or 2 is chosen by the sponsor.

<sup>h</sup> Randomization at Day 25 will take place only if treatment option 3, 4, or 5 is chosen by the sponsor.

<sup>i</sup> Sampling times in the terminal PK period are relative to the time of the final dose of study intervention received (0 hour) and may be adjusted after review of preliminary data.

## Signature Page for VV-TMF-4142728 v1.0

Reason for signing: Approved	Name: PPD Role: Stats - Statistician Date of signature: 06-Oct-2021 20:22:32 GMT+0000
Reason for signing: Approved	Name: PPD Role: PK/PD Date of signature: 06-Oct-2021 20:32:00 GMT+0000
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